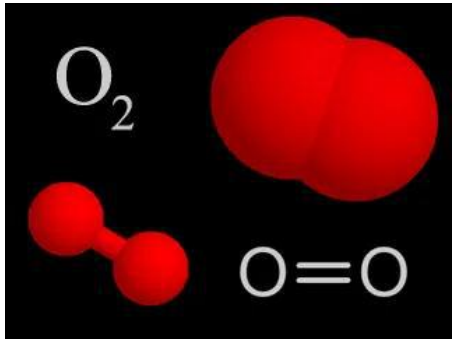
Malaysian Society of Paediatric Anaesthesiologists (MSPA)

Asian Society of Paediatric Anaesthesiologists




# Oxygen: Too little or Too much

Dr Agnes Ng

KK Women's and Children's Hospital

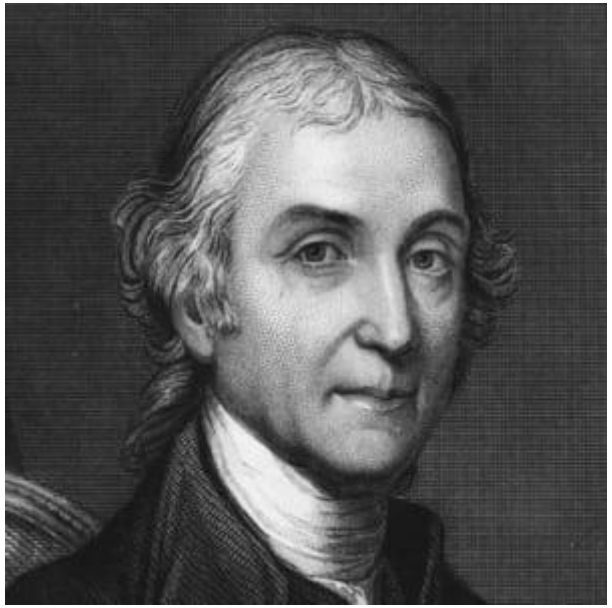
Singapore

No disclosure

# 1700s: Discovery of Oxygen

The credit for discovering oxygen is shared a Swede, an Englishman and a Frenchman”

Carl Wilhelm Scheele
- Swede

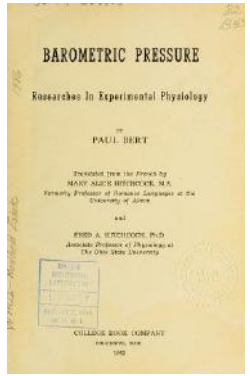


Joseph Priestly- English

Warned toxic effects
“Might be useful as a medicine, might not be so proper in the usual healthy state”

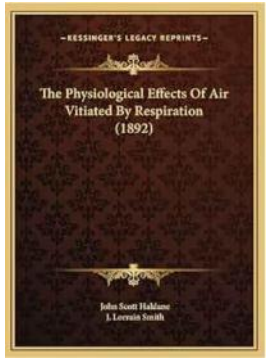
Antoine-Laurent Lavoisier- French

# Historical overview of O2 toxicity




1878 Paul Bert, French physiologist
– Larks exposed to 15-20 atm air convulsed and died (CNS effect)

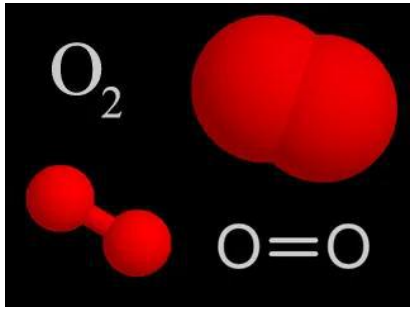
1899 James Lorrain Smith, Scottish pathologist
– Animals breathing O2 moderately high tensions over prolonged period suffered severe and finally fatal lung damage (Pulmonary effect)




Humans

1950s O2 therapy and retrolental fibroplasia (stage 5 retinopathy of prematurity)

1970s 50%-100% O2 potential lungs effects

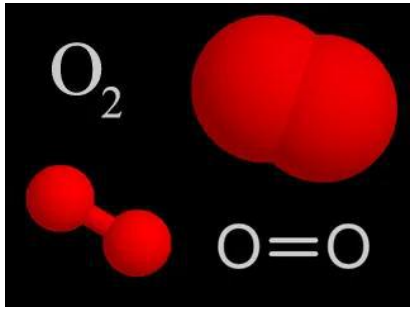



# Oxygen: Too little or Too much

Objectives

- Understand the pathophysiology of O2 toxicity
- Discuss patient groups at risk and
- O2 strategies of patients at risks

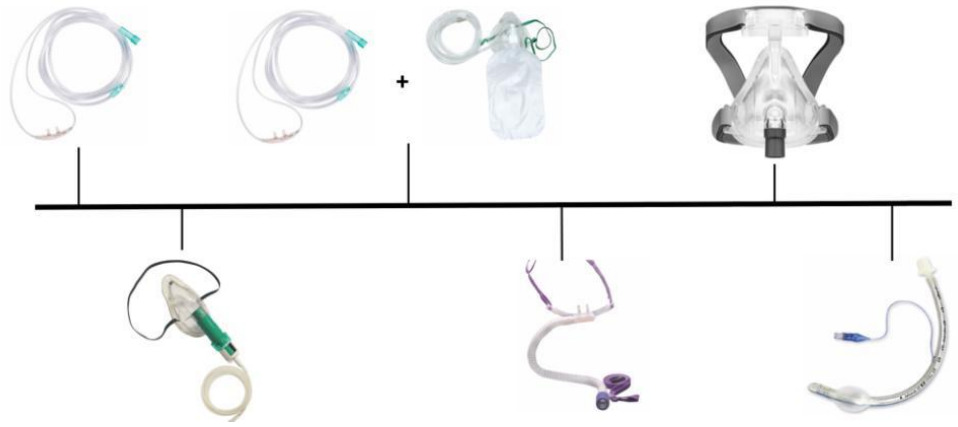
# Oxygen: Too Little




**HYPOXIA**

A state in which oxygen is not available in sufficient amounts at the tissue level to maintain adequate homeostasis.

Unresolved, results in permanent organ damage and potential fatality

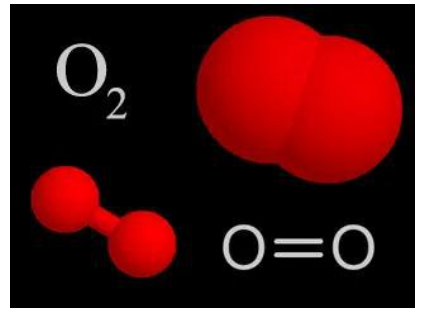



# Goal of O2 therapy

Achieve adequate oxygenation

To ensure normal function of cells/tissue

# Oxygen: Too Much



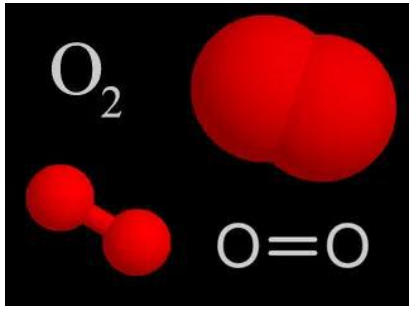

Supplemental O2 i.e. inspiratory O2 concentration oxygen FiO2 >0.21 may cause cause hyperoxaemia

Hyperoxaemia refers to **excess of oxygen in the blood** and subsequently, Hyperoxia, **excess of O2 in tissue**

*Hyperoxemia is reflected by the arterial oxygen tension (arterial $PaO_2$ > 100 mmHg,) most often due to high $FiO_2$.*

*vs Hypoxemia PaO2 < 60 mmHg*

# Radicals (chemistry)




Radicals are atoms/molecules which contain at least one unpaired electron in the shells of the atomic nucleus, capable of independent existence

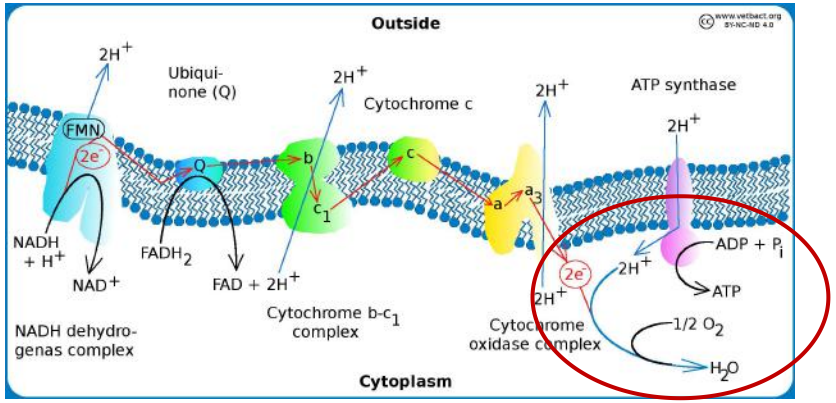
Oxygen generally exists as di-atomic molecule ($O_2$); its two atoms bond to each other through single bonds leaving **two unpaired electrons**.

Unpaired of electrons are continually searching for a partner, to pair up to form a more stable configuration

$O_2$ performs its actions through these unpaired electrons which act as radicals.

# Oxygen

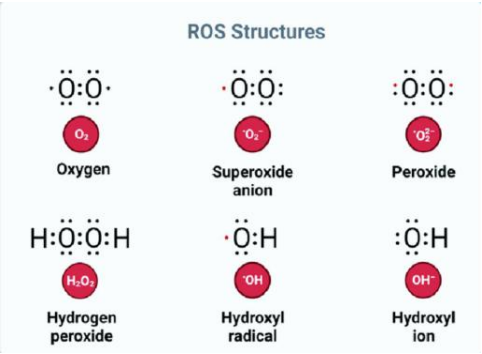
ETC/Electron transport chain




O2 is utilised by mitochondria to facilitate oxidative phosphorylation
Derived from food, high energy electrons transfers along ETC, develop proton gradient that ultimately generates energy rich ATP

O2 (its two unpaired electrons) is the final electron acceptor in this respiratory cascade, clearing the mitochondrial chain of low-energy, spent electrons,
With the gain of electrons, O2 is fully reduced,  combining with 2H+ to form H2O

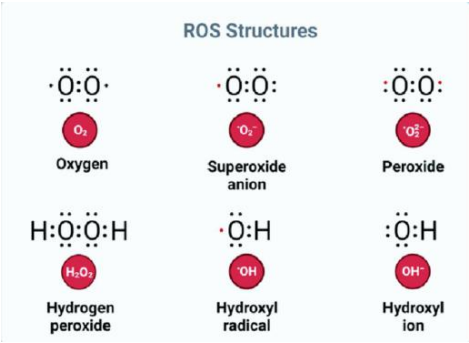
Incomplete reduction of O2 leads to O2 containing free radicals; superoxides, hydroxyl radicals, hydrogen peroxide;
**highly unstable and reactive**, generating further O2 containing radicals collectively called **reactive oxygen species/ROS,**



# ROS Reactive Oxygen Species

In health, 1-3% of mitochondrial O2 consumption produces ROS

- Essential in regulation of physiological cell function
- Contribute to both innate and adaptive immunity
- Differentiate and self renewal of stem cells and apoptosis (programed cell death)
- Participate in muscle contractions and regulation of vascular tone

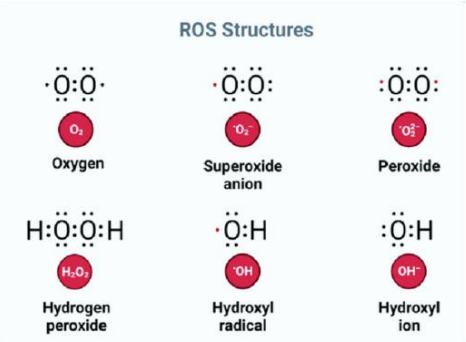


# ROS Reactive Oxygen Species

Mitochondrial increases ROS production during either **O2 Deficit or Excess**, particularly during excess O2 (hyperoxia).

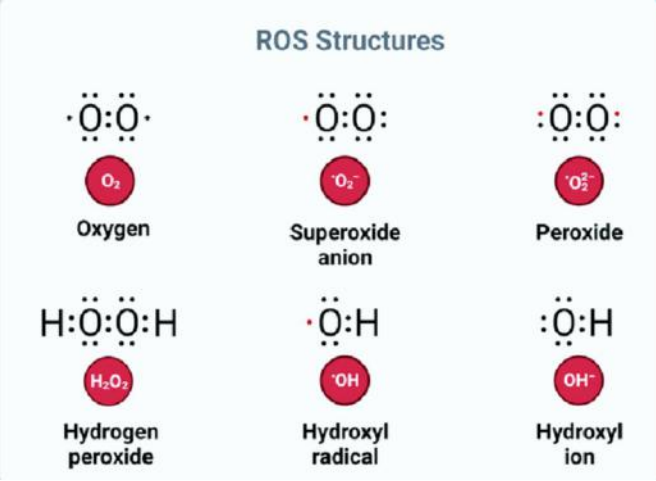
Pathologic conditions include;
ischemia/reperfusion, hypoxia/reoxygenation, sepsis & inflammation

Body has buffer system of **antioxidant** molecules that neutralise unwanted effects of ROS, but can be overwhelmed when ROS concentration rises



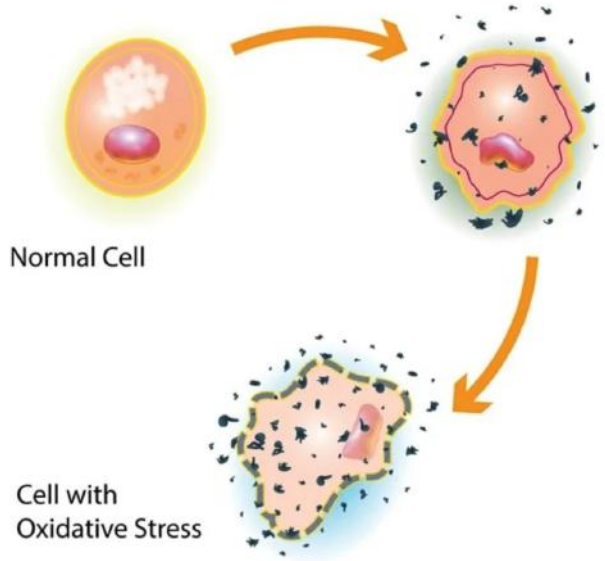
# Oxidative Stress OS

**Oxidative stress** occurs when there is imbalance between mitochondrial ROS production and removal, either an overproduction of ROS and/or decreased antioxidants defence activity

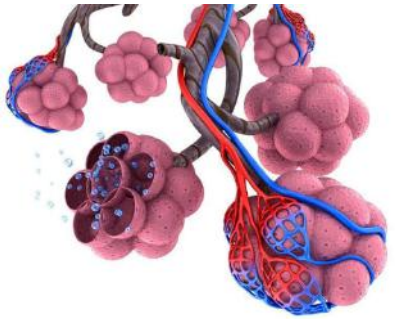



Oxidative stress

- Increases the vulnerability of tissues to oxidative injury during periods of both hypoxaemia and hyperoxaemia
- Damages cellular components such as DNA, proteins, lipids and subsequently cell death
- Causes functional impairment to vital tissues such as the circulatory, respiratory and nervous systems



# Pulmonary effect



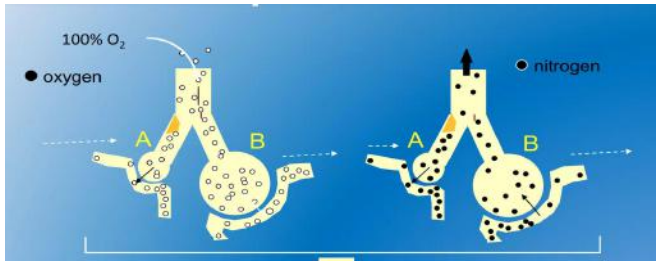
The lungs, as organ of gaseous exchange are the first at risk

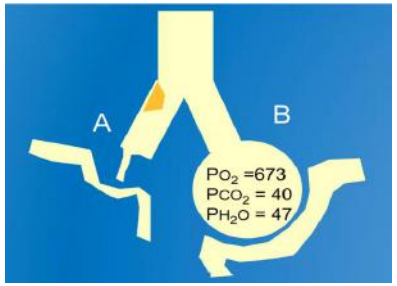
There is **direct damage** to tracheobronchial mucosa, capillary endothelium and alveoli, from the exposure to oxygen of inspired gas on lung tissue (hyperoxia), as well as the amount of oxygen in the blood (hyperoxemia).

By contrast, for the rest of the body, cellular exposure to oxygen is only determined by the hyperoxemia; (hence hyperoxia is the same as hyperoxemia).

**Additional risk**

FiO2>05, Nitrogen wash out occurs, resulting in significant risk of absorption of atelectasis



# Children at risk

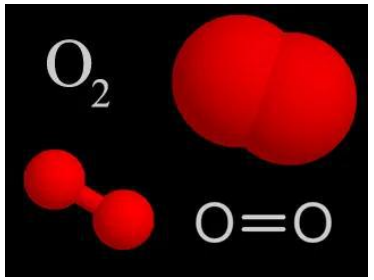
# Newborns susceptibility to Oxidative stress

- The fetus intrauterine, lives in relatively hypoxic 20-25mmHg PO2

- Upon birth exit to extrauterine normoxic environment, the baby faces > tripling of PaO2 in air

- When supplementary O2 resuscitation is administered, an abrupt increase in O2 availability results in a physiologic production of ROS

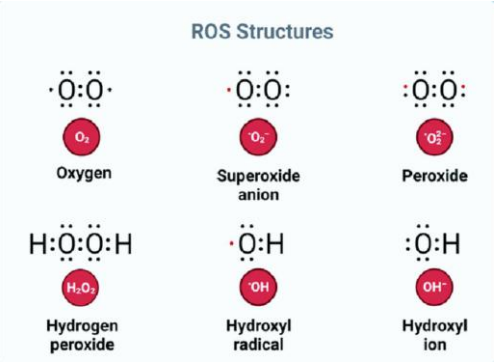
- The newborn is susceptible to oxidative stress, having lower total amount of antioxidants and the corresponding enzymes; these enzymes also being less effective




# Term newborns/NB

Term infants who require resuscitation at birth usually suffer from intrauterine and birth asphyxia

Resuscitation with supplemental O2 in a hypoxia/re-oxygenation exposes NB to increased oxidative stress

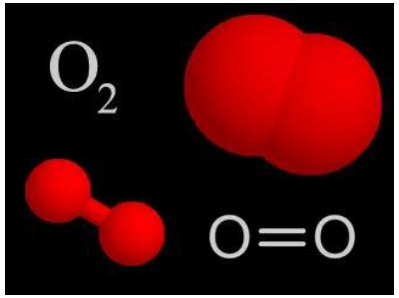


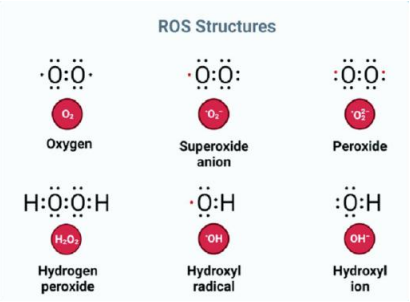
# Premature newborns

Frequently require support to establish respiration at birth due to various factors including surfactant deficiency and weak respiratory muscles and immaturity of the elastic thoracic cage.

Positive pressure support and supplemental oxygen are required to facilitate this transition. This abrupt increase in O2 availability causes an increase in ROS production

The immature antioxidant defence system of extremely preterm infants is particularly ill equipped to handle this surge and **even more vulnerable** to oxidative stress



# O2 therapy during Paediatric Resuscitation

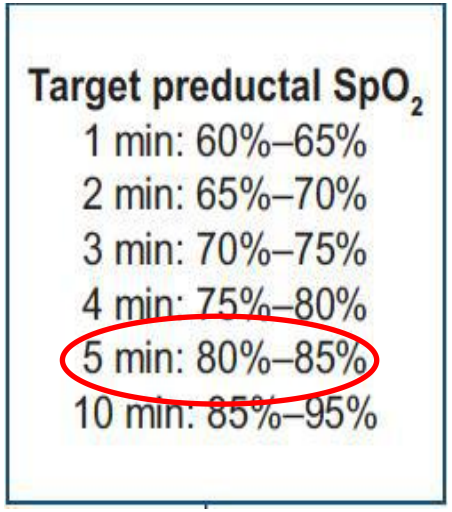
# Newborn resuscitation and support of transition of infants at birth

Initial delivered oxygen concentration depends upon gestation:

≥ 32 weeks gestation - 21% oxygen

28-32 weeks - 21-30% oxygen

< 28 weeks - 30% oxygen.




In babies < 32 weeks, delivered oxygen concentration should be titrated to achieve saturations of > 80% at 5 minutes.

- Use pulse oximetry to titrate oxygen to preductal saturation targets

- If the ***HR is < 60 after at least 30 seconds of effective PPV***,

Initiate chest compressions coordinated with PPV using 100% oxygen

Resuscitation Council UK

# O2 therapy in premies after birth

# O2 toxicity in Premature newborns

## Free radical diseases in the NB

retinopathy of prematurity (ROP), periventricular leukomalacia (PVL), bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC)

Hyperoxia is associated with **increase in mortality and morbidity** in critically ill children beyond the direct neonatal period.

This increase may be equally important with respect **to long-term disease trajectories**, as many organs and tissues, including the lungs, continue to develop and mature for several years after birth.

Oxidative stress has been associated with epigenetic changes in gene expression that can **increase lifelong risks for disease** e.g. childhood cancer

# Goal Directed O2 therapy in Premies

In premature infants, a well-defined range of SpO2 targets is recommended to reduce the detrimental effects of oxygen.

Hyperoxia (>95% SpO2) contributes to retinopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD), while

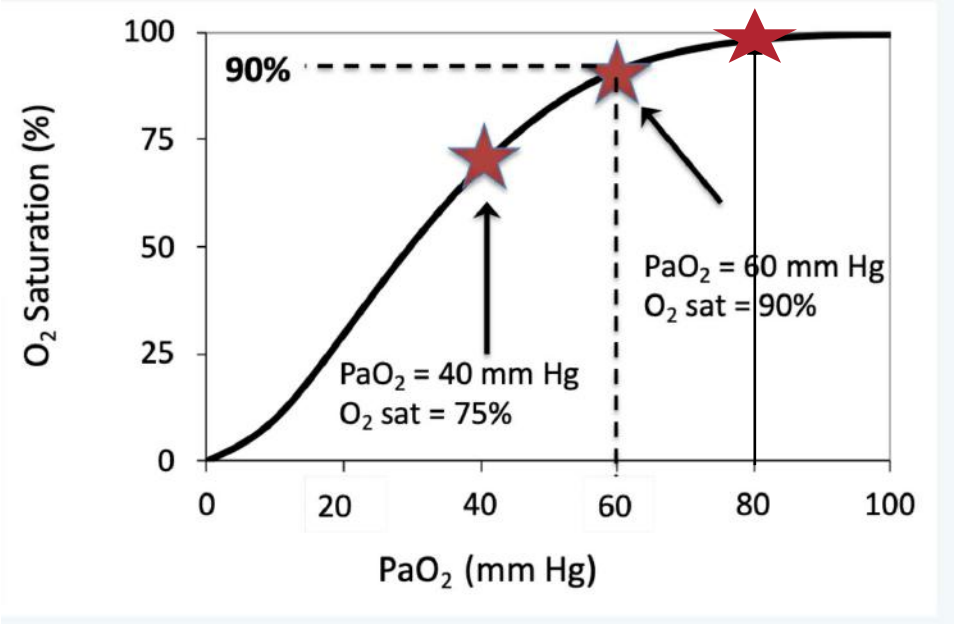
Hypoxia (<90% SpO2) is associated with increase mortality and necrotising entercolitis (NEC)

NeOProM: Neonatal Oxygenation Prospective Meta-analysis Collaboration study protocol. BMC pediatrics, 11, 6. 1471- 2431

# SpO2 target for premies in NICU

"In preterm babies receiving oxygen,
the saturation target should be between 90 and 94%."
ERC 2019

"Alarm limits should be set to 89 and 95%."
AAP 2016




| Conversion of $SpO_2$ to $P_aO_2$ | |
|---|---|
| $SpO_2$ (%) | $P_aO_2$ (mmHg) |
| 85 | 50 |
| 86 | 51 |
| 87 | 52 |
| 88 | 54 |
| 89 | 56 |
| 90 | 58 |
| 91 | 60 |
| 92 | 64 |
| 93 | 68 |
| 94 | 73 |
| 95 | 80 |
| 96 | 90 |
| 97 | 110 |

# Surgery in premies/ex-prem

- **PDA ligations**
- **Exploratory laparotomies**
- CSF drainage or ventriculoperitoneal shunt insertion for
- obstructive hydrocephalus after intraventricular haemorrhage
- Inguinal hernia repair
- Viterectomy or laser surgery for retinopathy of prematurity
- Vascular access under X-ray control
- CT and MRI scanning to evaluate cerebral damage

# O2 management of premies starts during Transport

Neonatal Transport ventilator

- Maintenance of PEEP

- O2 blender to allow replication of FiO2 in NICU and graded titration if required

Standby Self inflating bag (PEEP valve)

If no blender, omission of reservoir bag will give approx. 40% O2

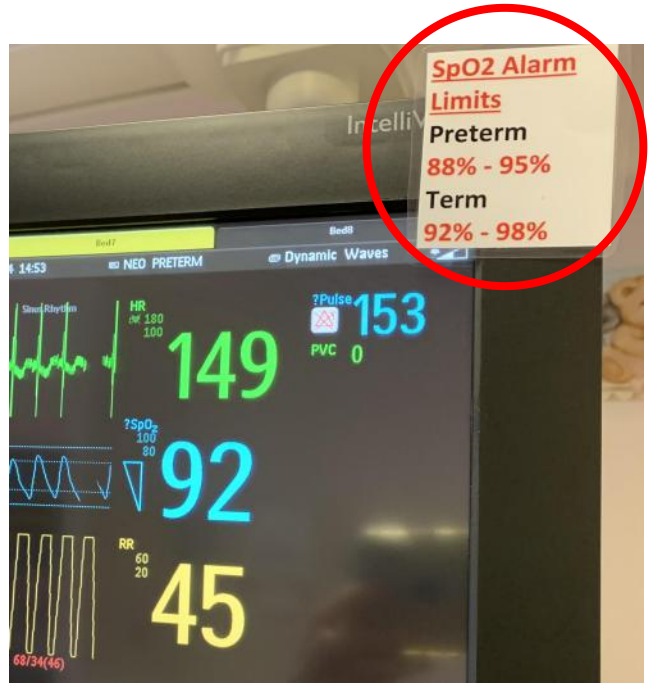
For rescue if O2 cylinder runs out or ventilator breaks down

# SpO2 targets during anaesthesia – follow NICU targets 90-94%?

The ideal physiologic target range for oxygen saturation should be premie-specific and dynamic especially during surgery

Consider

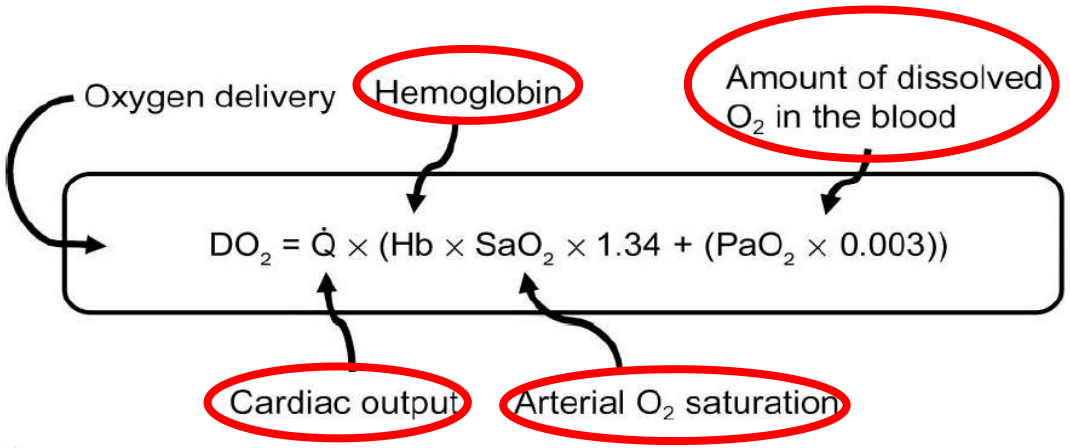
- Gestational age at birth
- Chronologic age at surgery
- Existing premie-related complications
- Underlying respiratory requirements, transfusion status
- Surgical pathology, systemic sepsis, haemodynamic status
- Anticipated surgical and bleeding complications

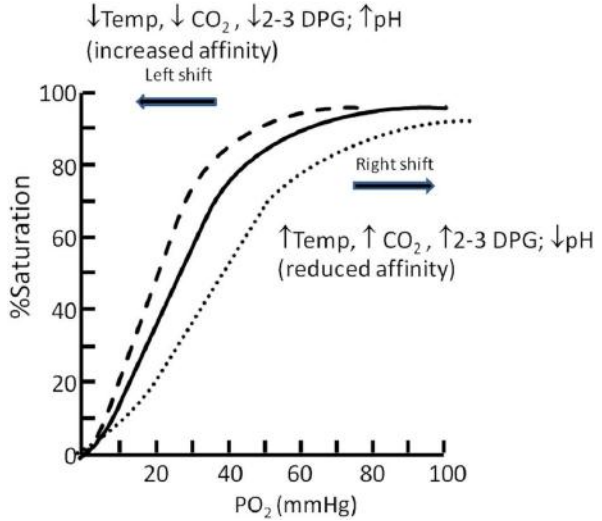


# Perioperative O2 in premie during anaesthesia

Balance between is to achieve normoxia; avoid tissue hypoxia and hyperoxemia (excess oxygen in blood)

- **Gaseous exchange** (passive diffusion of oxygen from alveolus to the pulmonary capillary)
- **Oxygen consumption** by tissues
- **Oxygen delivery** (rate of oxygen transport from the lungs to peripheral tissues)




Do2 rate of O2 delivery
Hb haemoglobin concentration
SaO2 % Saturated Hb with O2
1.34 O2 capacity of Hb
PaO2 PO2 in the arterial blood.
The 0.003 solubility coefficient of O2 in blood

# Babies with Congenital heart disease during non cardiac surgery

# O2 strategy in Congenital Heart Disease CHD

- Neonates with (CHD) are another specific group where O2 supplementation should be considered with great care and where O2 therapy is challenging.

- Critical congenital heart disease (cCHD) is a heart lesion for which neonates require early surgical intervention to survive.

- Certain c-CHD lesions require a patent ductus arteriosus for survival.

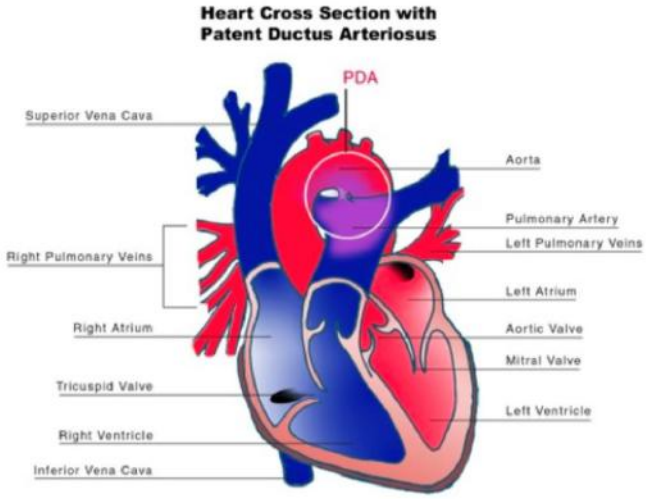



*Figure 1. Anatomy of the patent ductus arteriosus. Source: Wikimedia Commons. Link Public Domain*

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# Duct Dependent in c-CHD

- In Ductus-dependent c-CHD, O2 therapy can jeopardize patency of the ductus arteriosus despite administration of prostaglandin.
  Ductus arteriosus is very sensitive to O2 vasoconstriction

- Oxygen is a potent pulmonary vasodilator.

Systemic O2 delivery and Perfusion are optimised by balancing the systemic and pulmonary circulation

- Hyperoxia should be avoided in neonates to avoid **pulmonary over-circulation**, **systemic hypoperfusion** and its sequelae

In cyanotic heart disease and duct dependant cardiac lesions: A target range of 75- 85% is typically recommended for neonates with mixed circulation

# Perioperative Huddle

Anaesthesiologist, Surgeon and primary Paediatrician

(intensivist, neonatologist, specialist physician)

# Pediatric Life Support

## 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Circulation

*Circulation.* 2020;142(suppl 1):S140–S184. I

**With ROSC (return of spontaneous circulation) after cardiac arrest**

- Given the availability of continuous pulse oximetry, targeting an oxygen saturation of 94% to 99% may be a reasonable alternative to measuring $PaO_2$ for titrating oxygen when feasible to achieve normoxia (based on expert opinion).

- $Pao_2$ after ROSC: target a value appropriate to the specific patient condition.

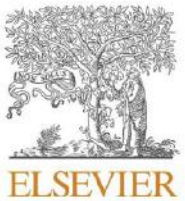
Given the **known risks of hypoxemia** and the **uncertain risks of hyperoxia**, any titration of oxygen delivery to children after ROSC must be balanced against the risk of inadvertent hypoxemia stemming from ***overzealous weaning of $Fio_2$***.

# Perioperative O2 in general paediatric population

Intraoperative hypoxaemia from **acute airway events** in children is probably the most frequent complication in anaesthesia.

Delivery of high FIO2 is the first-line strategy in the presence of hypoxia

Journal of Clinical Anesthesia 94 (2024) 111406



Contents lists available at ScienceDirect

Journal of Clinical Anesthesia

journal homepage: www.elsevier.com/locate/jclinane

Original Contribution

# Oxygenation during general anesthesia in pediatric patients: A retrospective observational study

Jan J. van Wijk, MD [a,*], Albina Musaj, MD [a], Sanne E. Hoeks, PhD [a], Irwin K.M. Reiss, MD, PhD [b], Robert Jan Stolker, MD, PhD [a], Lonneke M. Staals, MD, PhD [a]

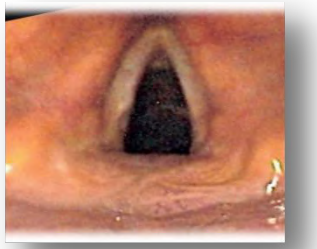
*Main results:* Data of 493 cases were obtained. Of these, 267 were excluded for various reasons. Finally, 226 cases with a total of 645 samples were analyzed. The median $FiO_2$ was 36% (IQR 31 to 43), with a range from 20% to 97%, and the median $PaO_2$ was 23.6 kPa (IQR 18.6 to 28.1); 177 mmHg (IQR 140 to 211). The median $SpO_2$ level was 99% (IQR 98 to 100%). The study showed a moderately positive association between $PaO_2$ and $FiO_2$ ($r = 0.52$, $p < 0.001$). 574 of 645 samples (89%) contained a $PaO_2$ higher than 13.3 kPa; 100 mmHg.

*Conclusions:* Oxygen administration during general pediatric anesthesia is barely regulated. Hyperoxemia is observed intraoperatively in approximately 90% of cases. Future research should focus on outcomes related to hyperoxemia.

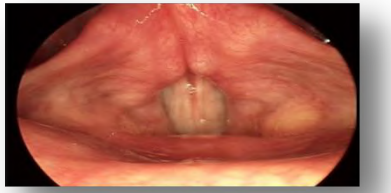
## HIGHLIGHTS

- The use of oxygen in intensive care and emergency settings is strictly regulated.
- No protocols exist to limit the use of oxygen during pediatric anesthesia.
- Intraoperative hyperoxemia was observed in 90% of patients with an arterial line in this single-center study.
- Oxygen usage during pediatric anesthesia could be more regulated.

# Paediatric perioperative O2



High levels of supplemental O2 during induction and reversal in anticipation of **hypoxia** in young children and infants



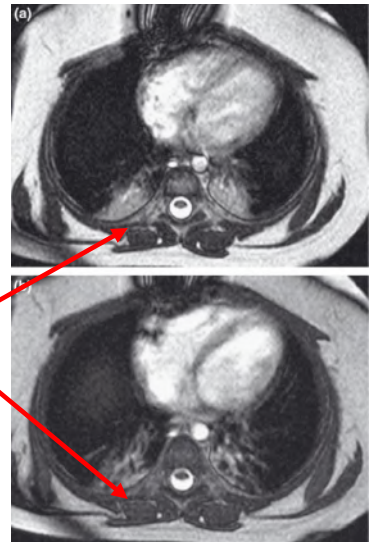
Respiratory mechanics and physiology during GA

- 3-4 x higher O2 consumption
- **Upper airway obstruction** under anaesthesia
- **VQ mismatch** as decreased FRC, increased closing volume renders child at risk airway collapse hence atelectasis
- 100% O2 during induction and high FiO2 maintenance further worsen airway closure and atelectasis (**masking the atelectasis**)

# Atelectasis under GA

**Atelectasis in children undergoing either propofol infusion or positive pressure ventilation anesthesia for magnetic resonance imaging**
Goetz Lutterbey Pediatric Anesthesia 2007 17: 121–125

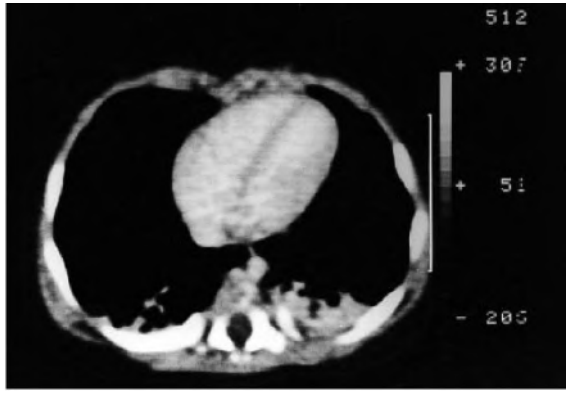
100% O2 ETT GA vs TIVA, then $FiO_2$ 0.5
PPV had higher % 80 vs 42 second scan 94% vs 82%
Younger children had higher atelectasis score
**All children had normal oxygen requirements and saturations**



Atelectasis
(a) at the beginning of the exam and (b) at the end of GA with PEEP

**Pulmonary atelectasis during paediatric anaesthesia: CT scan evaluation and effect of positive end-expiratory pressure (PEEP)**
G. SERAFINI Paediatric Anaesthesia 1999 9: 225–228

No preoxygenation and FiO2 0.4
10 children; 1-3 years old
**After ventilation with PEEP of 5 cmH2O, all the observed densities disappeared without impairment of heart rate, blood pressure, haemoglobin saturation and end tidal CO2 (PECO2).**




First CT 5 min after induction
Densities in dependent regions

# High inspired oxygen fraction impairs lung volume and ventilation heterogeneity in healthy children: a double-blind randomised controlled trial

Béatrice de la Grandville[1,2,3], Ferenc Petak[4], Gergely Albu[2,3], Sam Bayat[2,3], Isabelle Pichon[2,3] and Walid Habre[2,3,*]

*British Journal of Anaesthesia*, 122 (5): 682–691 (2019)

## Editor's key points

- Optimal inspired oxygen fraction ($FiO_2$) used perioperatively at any age remains controversial.
- This study characterises the impact of $FiO_2$ on respiratory physiological alterations over the early perioperative period in healthy children.
- In a double-blind RCT, children received either $FiO_2$>0.8 ($FiO_2$=1.0 at induction/emergence; $FiO_2$=0.8 intraoperatively) or $FiO_2$>0.35 ($FiO_2$=0.8 at induction/emergence; $FiO_2$=0.35 intraoperatively).
- $FiO_2$>0.8 decreased lung volume in the immediate postoperative period, which was accompanied by persistent ventilation inhomogeneity (assessed by serial multiple-breath nitrogen washout measurements).
- These data suggest that higher $FiO_2$ should be avoided in anaesthetised children with normal lungs.

Author concludes:
Our results show that the use of high FiO2 in children with normal lungs has deleterious effects on lung volume in the immediate postoperative period with **persistent ventilation heterogeneity at Day 1**.

Given the potential harmful effects of reactive oxygen metabolites triggered by hyperoxia, the use of a moderate FiO2 (around 35%) may be considered as optimal anaesthesia regimen in children with normal lungs

# O2 and postoperative nausea and vomiting

Anaesth Intensive Care 2005; **33:** 744-748

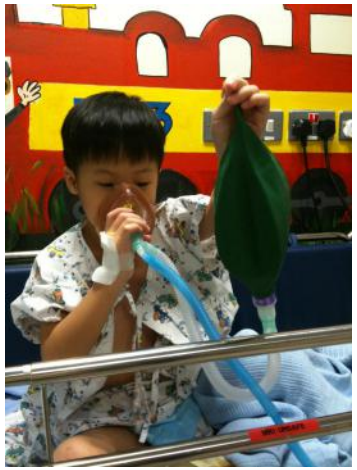
## The Effect of Supplemental Oxygen on Postoperative Nausea and Vomiting in Children Undergoing Dental Work

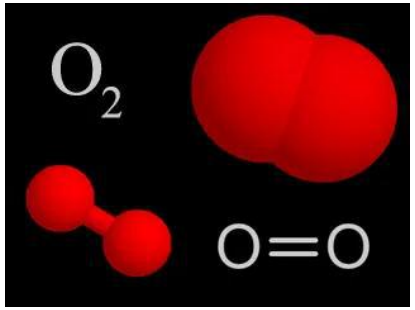
A. B. P. DONALDSON

## Effect of intra-operative high inspired fraction of oxygen on postoperative nausea and vomiting in children undergoing surgery: A prospective randomised double-blind study

Bikram Kishore Behera [1], Satyajeet Misra, Manoj Kumar Mohanty, Anand Srinivasan

Eur J Anaesthesiol. 2021 Nov 1;38(11):1124-1129.






# Conclusion

O2 though life saving, is not not benign

It has to be titrated (customised) to patient or patient groups, aiming to provide optimal oxygen i.e. the optimal arterial oxygen tension (PaO2) at the lowest inspired oxygen concentration (FiO2)

Hence maintain $PaO_2$ within the normal range, avoiding both hypoxaemia and excess hyperoxaemia.

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and

21st Meeting of the Asian Society of Paediatric Anesthesiologists

**4 to 5 April, 2025**

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