

Oxygen during neonatal
resuscitation :
To give or not to give ?

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Introduction



- ~140 million births/year worldwide
- 5-10% of newborns require some assistance to begin breathing (7-14 mio)
- ~1% require extensive intervention (1.4 mio)
(ILCOR 2005)

Newborn resuscitation : one of the most frequent procedures carried out in medicine!

Introduction

Perinatal asphyxia

~20% of the >5 million neonatal deaths/year worldwide
(WHO 1997)

Neonatal encephalopathy

- 1-6/1000 live births
- 15-20% die during neonatal period
- 25% of survivors have permanent neurological deficits

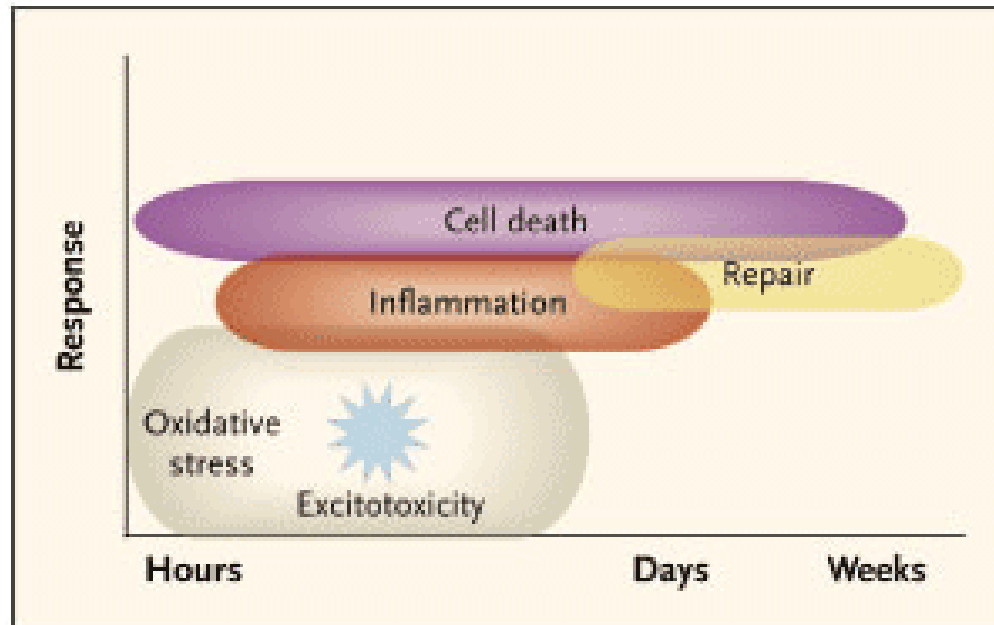
Introduction

« Newborns should be resuscitated with 100% oxygen »

International Liaison Committee on Resuscitation
(ILCOR), 1999

Supported by little scientific evidence!

Oxidative Stress in Newborns



Ferriero D, N Engl J Med. 2004

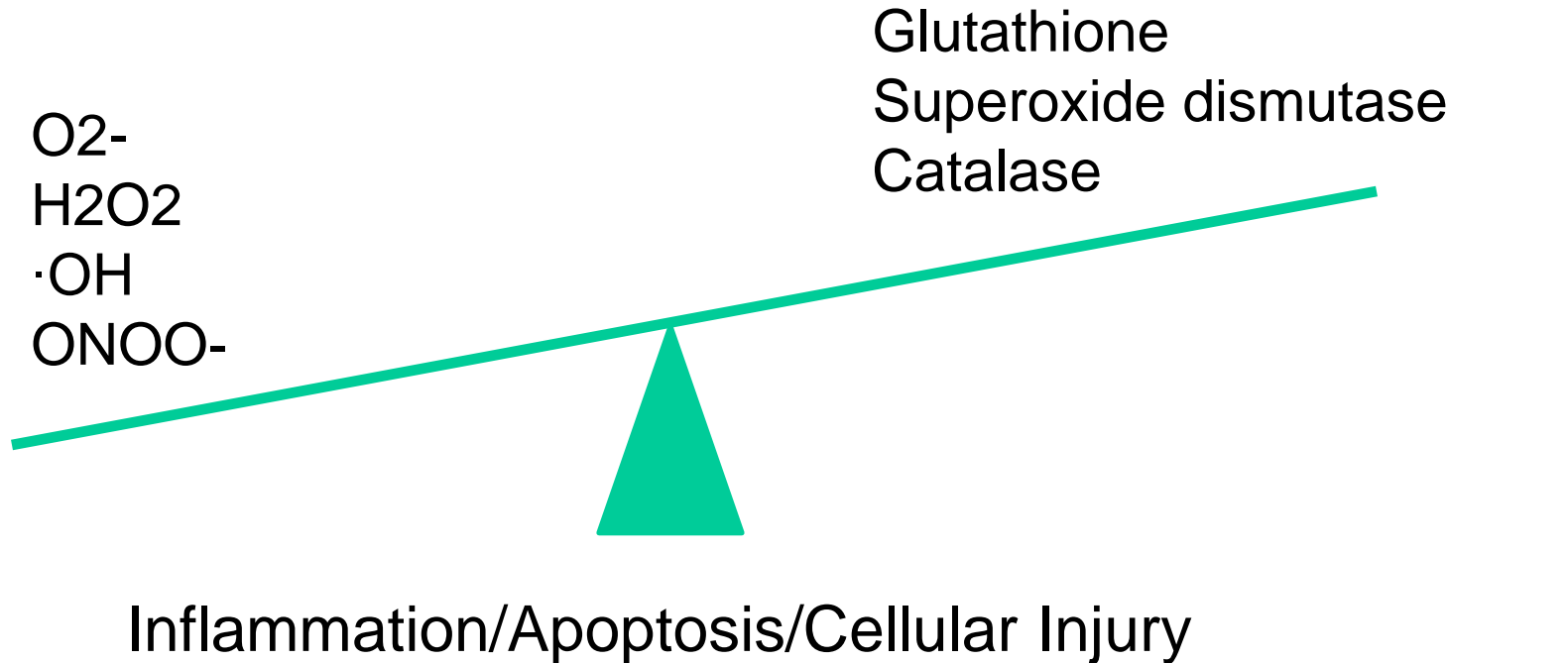
Central nervous system

Retinopathy of prematurity
Periventricular Leucomalacia
Hypoxic-Ischemic encephalopathy

Lungs

Lung injury
Bronchopulmonary Dysplasia

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Room air vs 100% oxygen: animal studies

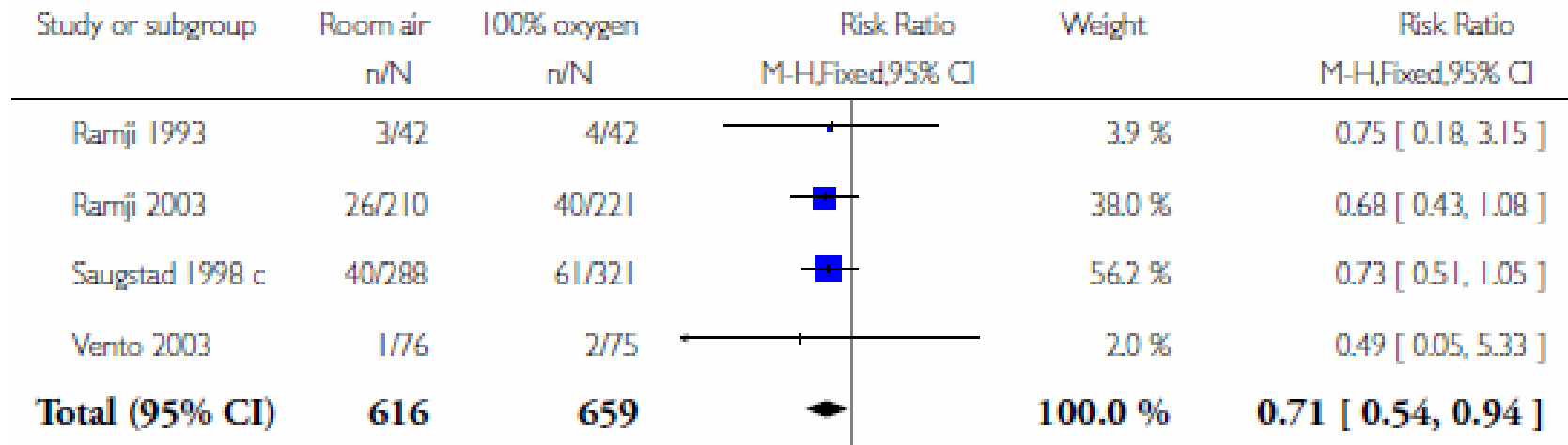
- Room air is as effective as 100% O₂ for resuscitation of newborn rabbits.
- Exposure to 100% O₂ during resuscitation from hypoxia is associated with oxidative stress.
- In newborn rats, hyperoxia causes:
 - lung injury
 - brain damage

Campbell AG et al, J Pediatr. 1966
Appelby CJ, Pediatr Res. 2001
Hoehn T, Pediatr Res. 2003

Resuscitation with room air vs 100% oxygen

Outcome: death at latest followup

5 studies : 1302 patients

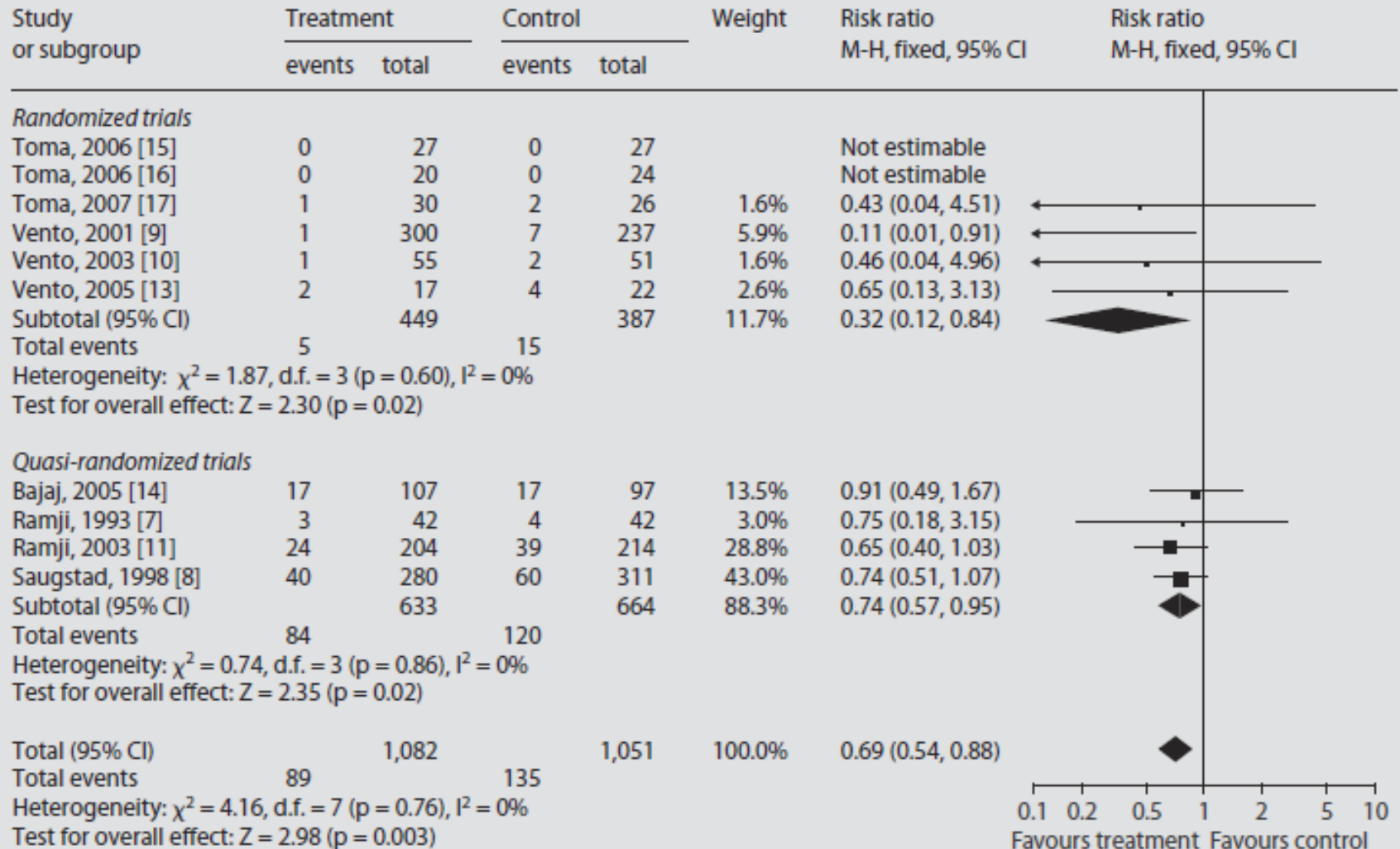


NNT 20

Tan A et al, Air versus oxygen for resuscitation of infants at birth.
Cochrane Database Syst Rev. 2005 Apr 18;(2)

Resuscitation with room air vs 100% oxygen

Outcome: death at latest followup

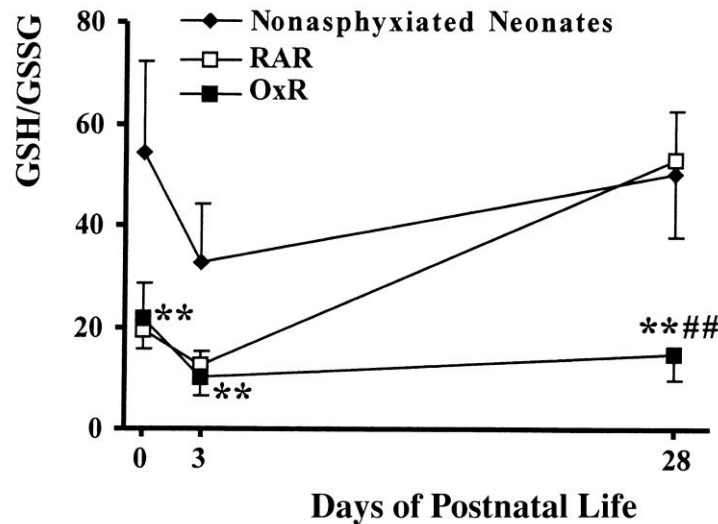


Resuscitation with room air vs 100% oxygen: Clinical studies

- Shorter time to onset of first breath with RAR
 1.2 ± 0.6 min vs 1.7 ± 0.5 min
- Shorter time to establish regular respirations with RAR
 4.6 ± 0.7 min vs 7.5 ± 1.8 min
- Decreased cerebral perfusion with 100%O₂
- No difference in short term neurological outcome
- No difference in neurodevelopmental outcome at 12-24 months

Resuscitation with room air vs 100% oxygen: Clinical studies

Markers of oxidative stress



100% O₂

- ↑ activity of SOD
- ↑ activity of catalase
- ↓ GSH/GSSG ratio

100% O₂: ↑ plasma cTnT, ↑ urinary NAG

Vento M et al, Pediatrics. 2001

Vento M et al, Am J Respir Crit Care Med. 2005

Oxygen at birth and risk of cancer

- A case control study found an association between the duration of exposure to 100% O₂ at birth and the risk of developing **childhood lymphatic leukemia**. OR was 3.54 for an exposure time ≥ 3 min (95 CI 1.16-10.80).
- The Collaborative Perinatal Project found increased risk of cancer if exposure to O₂ at birth was ≥ 3 min, OR 2.87 (95 CI 1.46-5.66).

Naumburg E et al, Acta Paediatr. 2002
Spector LG et al, J Paediatr. 2005

Resuscitation with room air vs 100% oxygen

- No evidence of harm with room air resuscitation.
- Room air is effective to resuscitate most babies.
- Even a brief exposure to 100%O₂ may have toxic effects.

Resuscitation with room air vs 100% oxygen: Methodological limitations

- Most studies included patients with moderate asphyxia
- Most patients were recruited in developing countries
- Only 2 studies (191 patients) were double blinded with adequate randomisation
- Little information on long term follow up
- ¼ of patients were crossed over
- Most patients were term newborns

International Recommendations

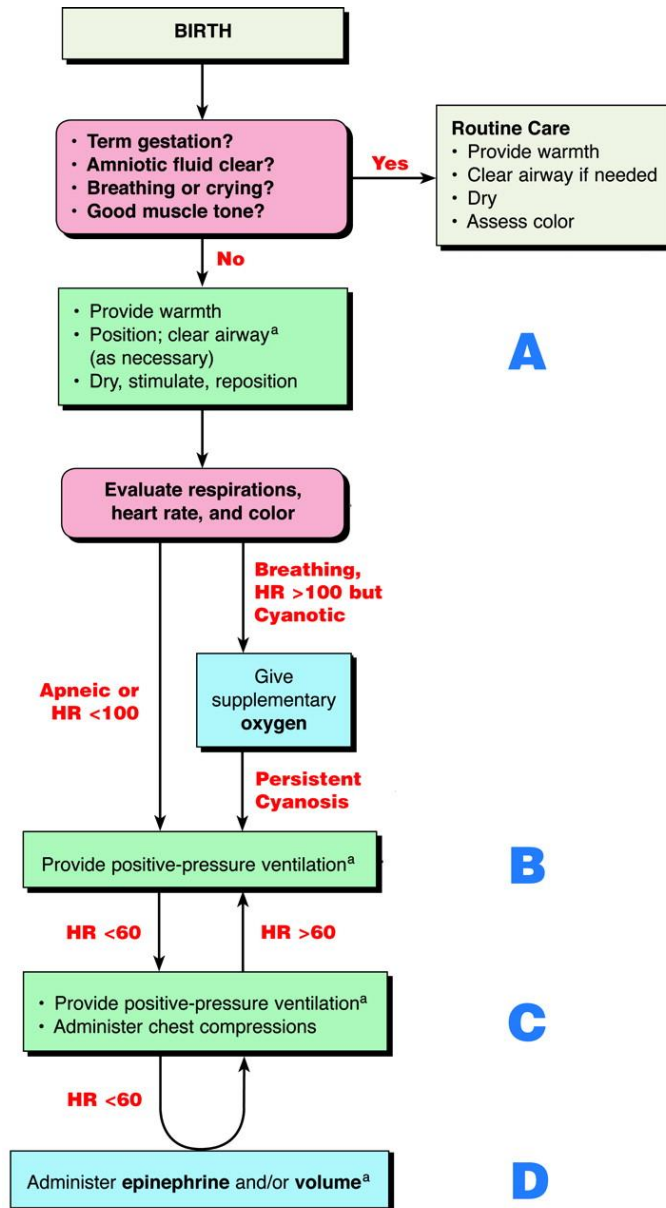
American Academy of Pediatrics, 2006 (NRP)

«If the baby is breathing but appears blue, administration of supplemental O₂ is indicated.»

«100% O₂ should be used when positive pressure ventilation is required during resuscitation of term babies.»

International Liaison Committee on Resuscitation, 2005

«There is currently insufficient evidence to specify the concentration of O₂ to be used at the initiation of resuscitation.»



A

^a Endotracheal intubation may be considered at several steps.

B

C

D

The International Liaison Committee on Resuscitation, Pediatrics 2006;117:e978-e988

International Recommendations

Canadian Paediatric Society, 2006

«Positive pressure ventilation should be initiated with 21% O₂.» www.cps.ca

Australian Resuscitation Council, 2006

«The best available evidence suggests that air should be used initially with supplemental O₂ reserved for infants whose condition does not improve during the first minutes of life.» www.resus.org.au.

Should we use pulse oximetry at birth?

Tight SpO₂ control in the NICU (85-93%) for VLBW:

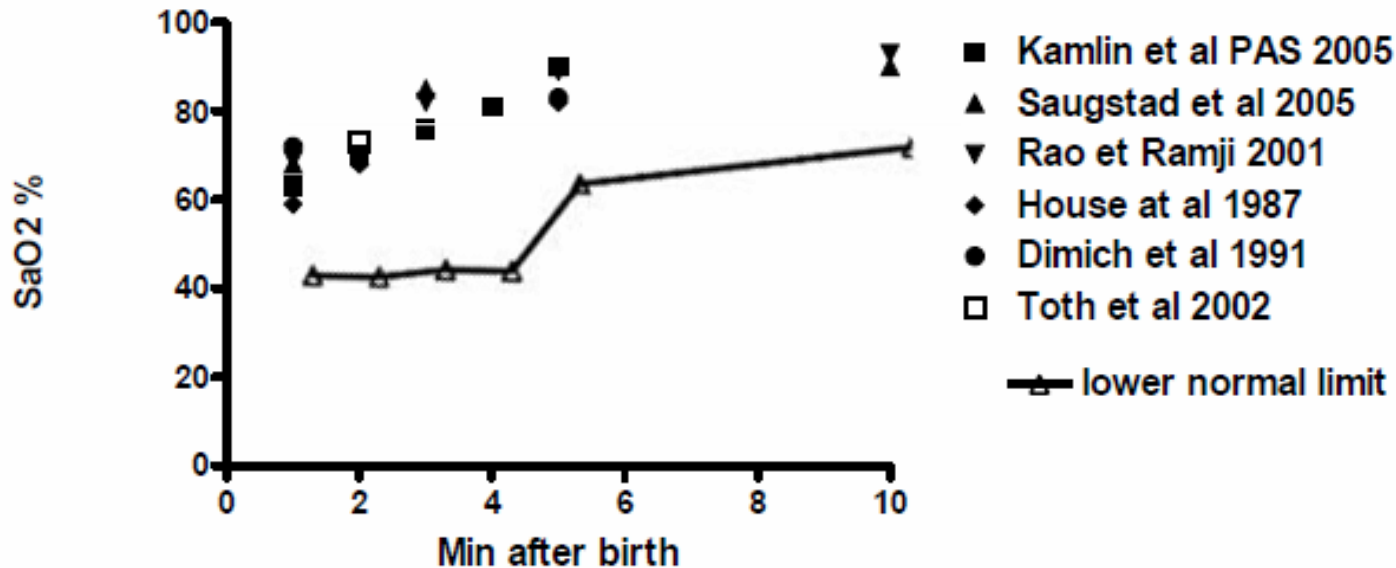
- ↓ ROP
- ↓ BPD
- ↓ nosocomial sepsis
- improved neurodevelopmental outcome

Sola A, 2007



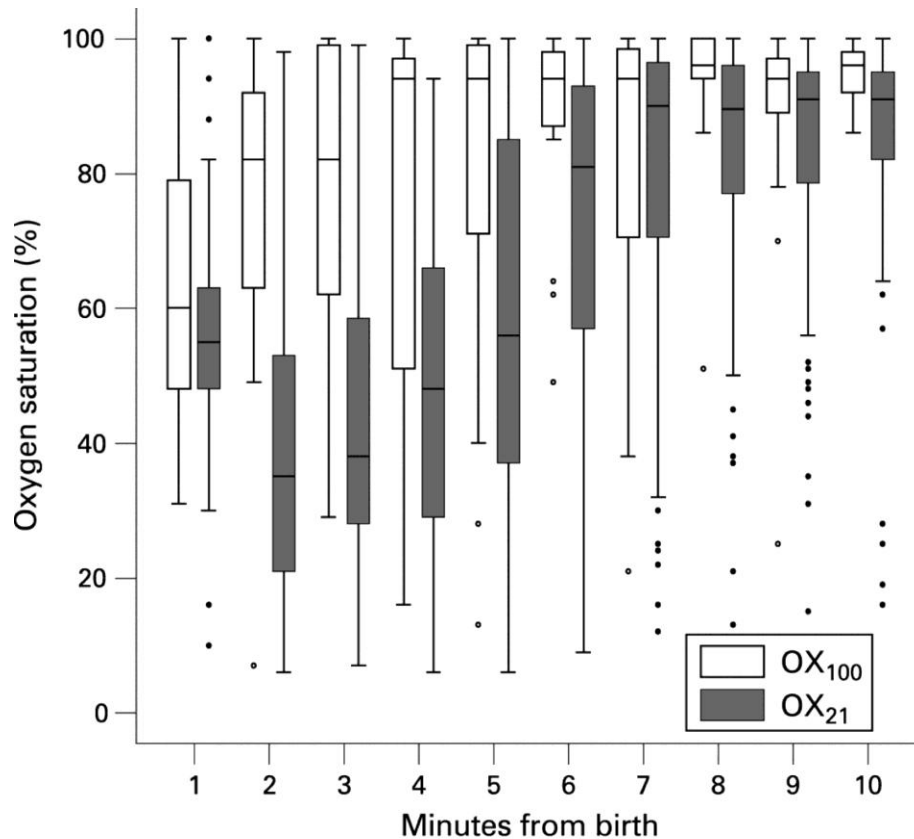
- What is the target SpO₂ in the first minutes of life?
- Can we reliably measure SpO₂ at birth?
- Should we mimick the normal rise in SpO₂ observed in healthy term newborns?

Oxygen saturation immediately after birth



Preductal SpO₂ is ~9% higher in the first 10 min of life
Lower SpO₂ in preterm and after C-section

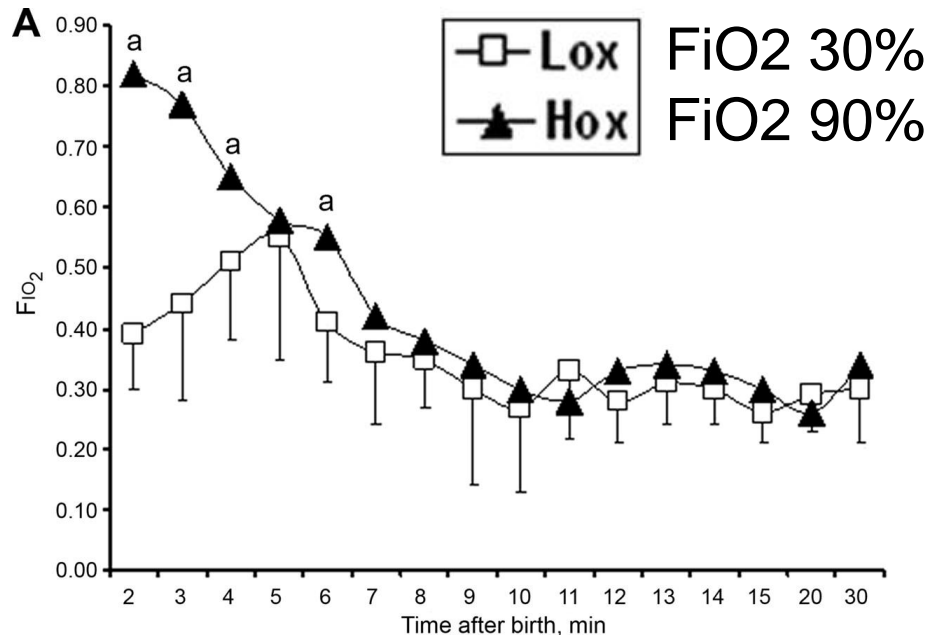
Resuscitation with room air vs 100% oxygen in preterm newborns < 30 weeks GA



Target SpO₂ > 70% at 5 min and > 90% at 10 min

Dawson, J A et al. Arch. Dis. Child. Fetal Neonatal Ed. 2009

Room air vs 100% oxygen: ...78 other options

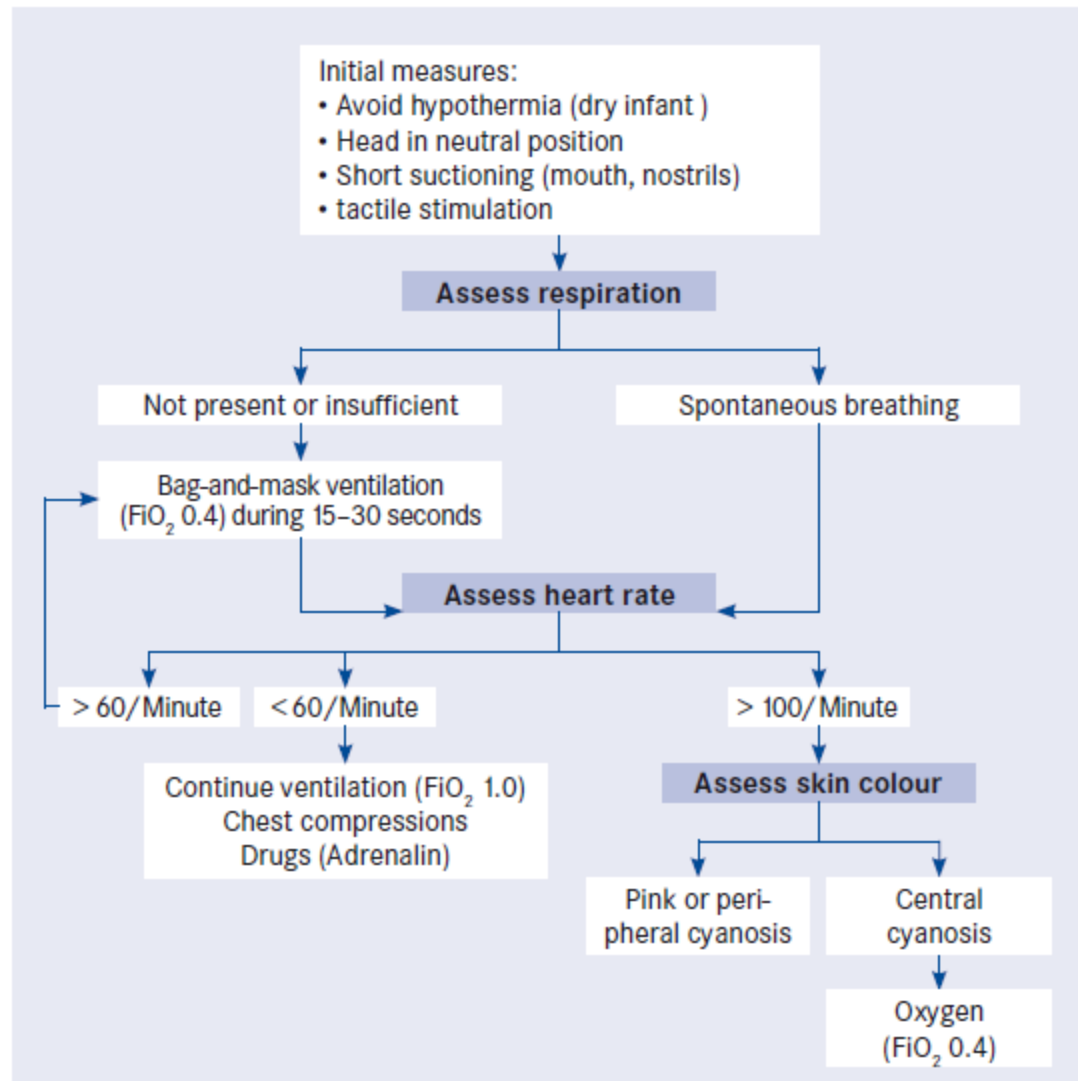


30% vs 90% O2

- ↓ oxidative stress
- ↓ TNF- α and IL-8
- ↓ BPD (15.4 vs 31.7%)

78 newborns \leq 28 weeks randomized to 30% vs 90% O2
Target SpO2 of 75% at 5 min, 85% at 10 min

Recommendations of the Swiss Society of Neonatology, 2007



Conclusions

- Most newborns do not need supplemental O₂.
- High concentrations of O₂ can be toxic to newborns.
- The optimal FiO₂ to initiate newborn resuscitation is unknown.
- If initial steps (drying, clearing airways, positioning, stimulation) are unsuccessful, the priority is to establish lung inflation.
- The Swiss Society for Neonatology recommends to use 40% O₂ initially.

Conclusions

- Adjustment of FiO₂ using **pulse oximetry** and a **blender** may help to avoid hyperoxia.
- Newborns are born **blue** and can stay blue for at least 5 min.



What are you doing!?