

# Guideline on the Use of Oxygen in the Newborn

## Background

Retinopathy of prematurity (ROP), formerly known as retrolental fibroplasia (RLF) was first described in 1942.<sup>1</sup> In the 1950's reports started to appear suggesting that oxygen toxicity was a possible cause<sup>2</sup> and by 1956 four randomised clinical trials on oxygen restriction had been published establishing the association between the unrestricted use of oxygen and ROP.<sup>3-6</sup> A systematic review of these trials showed that restricted oxygen use led to a marked reduction in the prevalence of ROP without any increase in neonatal morbidity and mortality.<sup>7</sup> During the 1960's the measurement of arterial oxygen tension was introduced and it was found that oxygen levels could be controlled. With the advent of neonatal intensive care in the seventies and the increasing survival of smaller babies, the incidence of ROP began to increase again.

In a population-based study encompassing 3 British National Health Service authorities, Ng *et al* found an incidence of any grade of ROP of 49.1% in babies less than 1700g.<sup>8</sup> Reported incidences of any Grade 3 or 4 ROP ranged from 4.2 to 9% of very low birth-weight babies.<sup>8-10</sup> Immaturity is the most important risk factor but oxygen also plays a role. Apart from these, many other factors may be important in the pathogenesis of ROP. The American Academy of Pediatrics and American College of Obstetricians and Gynecologists (*Guidelines For Perinatal Care*) states that "Vitamin E deficiency; ambient light; clinical conditions including acidosis, shock, sepsis, apnea, anemia, and patent ductus arteriosus; and prolonged ventilatory support (especially when accompanied by episodes of hypoxia and hyperoxia) have been associated with ROP. ROP has occurred in premature infants who have never received supplemental oxygen and in infants with cyanotic congenital heart disease."<sup>11</sup> A recent systematic review has shown that ambient light does not influence the development of ROP.<sup>12</sup>

Intermittent arterial blood gas sampling is widely practiced but has never been proven as a means of reducing ROP. The safe limits of PaO<sub>2</sub> are 50-80 mmHg.<sup>11</sup> The risk of ROP has been shown to be related to the length of time that the PaO<sub>2</sub> is more than 80 mmHg.<sup>13</sup> Infants with increased variability of the TcPO<sub>2</sub> in the first 2 weeks of life are at increased risk of ROP.<sup>14</sup> Arterialised capillary gases in a well perfused infant are useful in excluding hypoxia but will not reliably rule out hyperoxia.<sup>15</sup> It is not reliable in the first 24 hours of life, in seriously ill infants, or those with shock, hypotension or peripheral vasoconstriction.<sup>16</sup>

Transcutaneous oxygen monitoring and/or pulse oximetry allows for continuous monitoring of oxygen therapy. The Guidelines for Perinatal Care state that "because neither technique measures PaO<sub>2</sub> directly, they should be used as adjuncts to, rather than substitutes for, arterial blood gas sampling, especially in infants with moderate to severe respiratory distress. In infants whose condition is unstable, noninvasive measurements should be correlated with PaO<sub>2</sub> at least every 8-12 hours. More frequent analyses of arterial blood gas may be indicated for the assessment of pH and PaCO<sub>2</sub>. In infants whose condition is stable, correlation with arterial blood gas samples may be performed less frequently. The use of either transcutaneous oxygen measurement or pulse oximetry may shorten the time required to determine optimum inspired oxygen concentration and ventilator settings in the acute care setting." The Australian National Health and Medical Research Council have stated that pulse oximeters are probably safe if levels of 89 - 94% are maintained.<sup>17</sup>

There should be an institutional policy for the documentation of oxygen therapy and monitoring.

Current evidence suggests that ROP is linked to the duration of oxygen rather than the concentration, thus the use of 100% oxygen to resuscitate the newborn does not pose a problem. The American Academy of Pediatrics and American Heart Association recommend that "...since the

risk of hyperoxia over a short period is negligible compared with the risks of hypoxia, infants requiring resuscitation at birth should be given 100% oxygen,"<sup>18</sup> and the Guidelines to Perinatal Care states that "The use of supplemental oxygen other than for resuscitation should be monitored by regular assessments of PaO<sub>2</sub>."<sup>11</sup>

There is now clear evidence in the form of a systematic review that ablative therapy to the retina can reduce the risk of progression of threshold disease.<sup>19</sup> It is therefore important that ROP be detected early and the affected neonates followed up until they are no longer at risk. Eye examination should begin with indirect ophthalmoscopy at 4 - 6 weeks of age for all infants < 1250g and less than 32 weeks gestation. This should be repeated at 2-4 weekly intervals until vascularisation reaches Zone 3 using the International Classification for Retinopathy of Prematurity or the risk of threshold disease passes. If disease develops then these examinations should be repeated every 1-2 weeks until the need for treatment is established. The need for surveillance in babies of higher gestations is not clear. Infants of 32 – 36 weeks who had a complicated clinical course felt at high risk for ROP should probably be followed up to term.<sup>20</sup>

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## Recommendations

1. An understanding is required that Retinopathy of Prematurity (ROP) is currently not preventable in some neonates, even with optimal monitoring of oxygen therapy. Many factors other than hyperoxia may contribute to the pathogenesis in this condition.
2. Nevertheless, supplemental oxygen should only be used when there are specific indications such as respiratory distress, cyanosis or documented hypoxia.
3. In an emergency when oxygen is needed, it should be used without restriction, and concern for ROP should not override the need to save a life. Transient elevations of do not cause ROP.
4. The use of supplemental oxygen beyond the emergency period should be monitored by means of regular arterial PaO<sub>2</sub> measurements. Arterialised capillary sampling is an acceptable alternative if arterial sampling is not possible.
5. Term infants requiring oxygen therapy for periods longer than a few hours and all preterm infants requiring oxygen should be managed in a facility where monitoring of oxygen therapy is available. When this is not possible, the concentration of oxygen administered should be just enough to abolish cyanosis. It should be safe in the term neonate to administer oxygen for a few hours without monitoring arterial oxygen.
6. Transcutaneous oxygen measurement and/or pulse oximetry allow for continuous monitoring of oxygen therapy. The recommended levels of SaO<sub>2</sub> are 89 to 95%. This should be supported by intermittent arterial blood gas analysis. A recommended range for most preterm neonates would be a PaO<sub>2</sub> of 50-80 mmHg (6.7 –10.7 kPa).
7. In some neonates, efforts to keep the PaO<sub>2</sub> within this range may result in unacceptable episodes of hypoxia. In such a situation, it might be necessary to accept PaO<sub>2</sub> levels above this range. Such decisions should be documented clearly.
8. Institutions should have a written protocol for the documentation and monitoring of oxygen therapy.

Recognising the benefits of early detection and treatment of ROP, eye examination at 4-6 weeks of age is recommended for:

- a. all babies less than 32 weeks gestation at birth or weight less than 1250gm.
  - b. other babies above 32 weeks and 1250 gm depending on individual risk as assessed by the clinician.
9. Eye examination should be repeated at 2-4 weekly intervals until vascularisation reaches Zone 3 or there is no longer a risk of threshold disease. If threshold disease develops then ablative therapy should be considered for at least one eye within 72 hours of detection. (Every effort should be made to provide such a service for all these neonates, although it is recognised that access to ophthalmological examination might be difficult some parts of Malaysia.)
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