Infants with chronic neonatal lung disease: recommendations for the use of home oxygen therapy

A position statement from the Thoracic Society of Australia and New Zealand

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This is a position statement developed by the working party (the authors, chaired by Dominic Fitzgerald) of the Australasian Paediatric Respiratory Group (APRG) within the Thoracic Society of Australia and New Zealand (TSANZ). We performed a MEDLINE search with the keywords bronchopulmonary dysplasia, chronic neonatal lung disease and home oxygen among articles dated from 1966 to July 2007. Sixty-two articles were identified, of which 23 publications of relevance were considered. Levels of evidence were derived and designated E1–E4 (according to the ratings of the National Health and Medical Research Council [NHMRC]). The position statement was presented in a workshop at the annual meeting of the APRG. All co-authors provided additional comments from their respective centres. A revised manuscript was circulated to the entire group for final comment before further peer review and endorsement by the Clinical Care and Resources Subcommittee of the TSANZ. A summary of our recommendations is provided in the Box at the end of this article. This document is due for review in 2012.

The development of home oxygen programs for infants born prematurely who have chronic neonatal lung disease (CNLD) followed the successful introduction of such schemes for adults with chronic obstructive pulmonary disease. In adults, long-term home oxygen therapy is prescribed for the relief of breathlessness in the presence of hypoxia, defined by an arterial oxygen tension (PaO₂) of less than 55 mmHg (7.3 kPa; an oxygen saturation [SpO₂] level of ≈ 88%). In contrast, the assessment of home oxygen requirements for infants involves a combination of clinical assessment, oximetry and intermittent blood gas analyses. Levels of evidence, E3, E4).

The first significant report on the utility of home oxygen therapy for children was published in 1976, and it reported on the use of home oxygen therapy in children with CNLD allowing earlier discharge from hospital (E3). Over the past 30 years, small-scale home oxygen programs were developed to shorten hospitalisation and reduce health care costs for young infants with CNLD (E3). However, there remains little objective evidence to guide the use of home oxygen therapy in infants with CNLD.

Features of chronic neonatal lung disease

Predominantly a consequence of preterm birth

Most infants with CNLD are born prematurely (<28 weeks' gestation) at extremely low birthweight (<1000 g). CNLD results from a combination of arrested pulmonary development occurring as a consequence of antenatal factors, preterm delivery coupled with ventilator-induced barotrauma, volutrauma, oxygen toxicity and complications of persistent patent ductus arteriosus, lower respiratory tract infections and, possibly, undetermined genetic susceptibilities to chronic lung disease. In adults, long-term home oxygen therapy is prescribed for the relief of breathlessness in the presence of hypoxia, defined by an arterial oxygen tension (PaO₂) of less than 55 mmHg (7.3 kPa; an oxygen saturation [SpO₂] level of ≈ 88%). In contrast, the assessment of home oxygen requirements for infants involves a combination of clinical assessment, oximetry and intermittent blood gas analyses (levels of evidence, E3, E4).

ABSTRACT

- Chronic neonatal lung disease (CNLD) is defined as a supplemental oxygen requirement beyond 36 weeks' postmenstrual age, with more severely affected infants requiring oxygen beyond a full-term-equivalent age.
- Low-flow supplemental oxygen facilitates discharge from hospital of infants with CNLD who develop hypoxia in air.
- There is a lack of data on the most appropriate minimum mean target oxygen saturation (SpO₂) level. Reflecting a variety of clinical practices and infant comorbidities (frequency of oxygen desaturation, presence of pulmonary hypertension, retinopathy of prematurity, and adequacy of growth), the minimum mean target range for SpO₂ during overnight oximetry should be 93%–95%.
- The effect of supplemental oxygen on carbon dioxide retention should be considered before deciding on an oxygen flow.
- Most infants with CNLD are not ready for discharge until their supplemental oxygen requirement is ≤ 0.5 litres per minute delivered through a nasal cannula.
- The safety of short-term disconnection from supplemental oxygen should be assessed before discharge.
- Assessment of oxygenation during sleep with continuous overnight oximetry or polysomnography is recommended when weaning infants from supplemental oxygen.
- Discontinuation of oxygen therapy is based on clinical assessments and documentation of adequate oxygenation in room air.
- There is limited objective evidence on which to base recommendations.

Can CNLD occur in a full-term infant?

CNLD is a descriptive term rather than a histopathological diagnosis. Positive-pressure ventilation delivered at high pressure and a high concentration of inspired oxygen used in full-term infants may also result in CNLD. Conditions that may require home oxygen therapy in full-term infants include structural lung disease, meconium aspiration syndrome with pulmonary hypertension, or severe cyanotic congenital heart disease.

Phenotype and pathophysiology of CNLD

The predominant clinical findings in infants with CNLD are tachypnoea, wheeze, cough, chest wall retractions, and paradoxical respirations that occur as a consequence of small airways disease (airflow obstruction, hyperplasia of bronchial epithelium, increased mucus production from glandular hyper-
plasia, decreased mucociliary clearance and bronchial hyper-reactivity). Additional complications may include parenchymal and interstitial lung damage, dynamic obstruction from degrees of bronchomaliaclia, and fixed obstruction from subglottic narrowing related to damage from endotracheal tube positioning and frequent suctioning. Other abnormalities include increased dead space ventilation, decreased lung compliance, maldistribution of ventilation and increased work of breathing, and ventilation-perfusion mismatching.

Definition of CNLD

There is agreement within the neonatal literature, for the purposes of statistical reporting and research, that an infant (born at less than 32 weeks’ gestation) who has a supplemental oxygen requirement at the arbitrary age of 36 weeks’ postmenstrual age has CNLD. However, most clinicians recognise a clinical spectrum of CNLD whereby infants born preterm who are weaned from ventilation and supplemental oxygen by 36 weeks may have mild CNLD, those weaned by term have moderate CNLD, and those requiring home oxygen therapy beyond a full-term-equivalent age have severe CNLD.

A definition of CNLD based on whether supplemental oxygen is required fails to consider the underlying pathophysiology. Similarly, an infant can have an abnormal chest radiograph and be classified as not having CNLD if supplemental oxygen is not necessary. In clinical practice, there is no way to estimate reduced lung function in infants to predict the need for supplemental oxygen.

Demographic characteristics of CNLD

CNLD is the commonest form of chronic lung disease in infancy, occurring in up to 20% of infants with respiratory distress syndrome and about 40%–50% of infants born at less than 28 weeks’ gestation. The risk of CNLD increases with decreasing gestational age and decreasing birthweight. CNLD has been reported in up to 85% of infants with birthweights of 501–750 g, up to 45% of infants with birthweights of 751–1000 g, but decreasing to 5% of infants with birthweights over 1500 g.

Estimated extent of CNLD in Australasia

Supplemental oxygen is used in neonatal intensive care units for over 95% of infants born before 28 weeks’ gestation in Australia and New Zealand. Supplemental oxygen is required by about 75% at 28 days of life and 50% at 36 weeks’ postmenstrual age. The median (interquartile range) duration of supplemental oxygen therapy in infants born before 28 weeks’ gestation is 53 days (12–95 days). The survival rate to discharge from hospital for infants born at 27 weeks’ gestation or later is at least 90%. In Australasia, 214 babies were discharged on home oxygen therapy in 2004, which represented 6.1% of survivors born at less than 32 weeks’ gestation (Robert Halliday, Neonatologist, The Children’s Hospital at Westmead, Sydney, personal communication). The proportion of preterm infants being discharged on home oxygen therapy varies widely between neonatal units, and is largely dependent on target oxygenation strategies.

Determining adequate oxygenation

Intermittent oximetry is unreliable and should not be used as the basis for determining adequate oxygenation. Continuous oximetry provides better screening information. More information can be determined from polysomnography, which may provide an objective physiological measure of the impact of different oxygen levels on the carbon dioxide profile and sleep quality.

Just as the oxygenation threshold for providing home oxygen therapy varies, so do the indications for home oxygen therapy. However, these commonly include lung disease, pulmonary hypertension and retinopathy of prematurity (ROP). It is unclear whether recommendations based on evidence acquired from the Benefits of Oxygen Saturation Targeting (BOOST) trial in preterm infants should be extrapolated to a full-term-equivalent age and beyond. In particular, the available data are limited to assessment of growth and development at 12-months corrected age rather than to cognitive outcome at school age.

Thus, despite the existence of home oxygen programs in Australia, New Zealand and overseas, there has been limited consensus on:

- indications for supplemental oxygen therapy;
- target SpO2 levels;
- duration of supplemental oxygen therapy;
- logistics and ongoing care;
- indications for weaning infants from supplemental oxygen; and
- long-term outcomes of oxygen supplementation strategies applied in infancy.

Drawing on the limited evidence available, together with the combined views of paediatric respiratory physicians experienced in the care of infants with CNLD, we suggest a practical approach to the provision of home oxygen therapy for infants with CNLD (E4).

Indications for supplemental oxygen therapy

Rationale for the prolonged use of supplemental oxygen in infants with CNLD

The goal of home oxygen therapy is to prevent the effects of chronic hypoxaemia, which include pulmonary vasoconstriction leading to pulmonary hypertension, bronchial constriction leading to airway obstruction, and changes in growth of pulmonary and ocular vasculature. Improved oxygenation may result in improved lung growth and repair. In addition, there is observational evidence to support improved nutrition and somatic growth occurring in response to improved oxygenation. However, the long-term implications for cognitive development of mild hypoxia, either persistent or intermittent, have not been adequately studied.

Assessment of gas exchange in infants usually includes a combination of oximetry, transcutaneous carbon dioxide monitoring and venous or capillary blood gas analyses (E4). Arterial blood gas analyses are rarely used after the initial weeks in neonatal intensive care units because of the risks of trauma to the smaller vessels, embolic phenomena and arterial occlusion.

As a safety measure, some physicians will conduct an air challenge for infants immediately before discharge with supplemental oxygen (E4). The purpose of this is to see the nadir of SpO2 reached in room air should oxygen become disconnected. Protocols for these air challenges vary both in the duration of the challenge and the acceptable nadir of SpO2. Most units would recommend that a minimum SpO2 of greater than 80% be maintained in air for 30 minutes before discharge as a safety check (E4). Once discharged, the tools used to assess readiness for withdrawal of supplemental oxygen include clinical assessment...
finding that a higher Sp O2 was protective was consistent with the was noted that the respiratory morbidity (rates of pneumonia or posterior pole), with a 30% lower rate of progression. However, it (tortuous and dilated vessels in at least two quadrants of the ROP trial who were in the higher Sp O2 range had a greater incidence of chest infections, 21 raising the possibility that even higher target SpO2 range at 50 weeks' postmenstrual age (approximate- mately 8 months corrected age) were more likely to remain hospitalised (12.7% v 6.8%), on supplemental oxygen (46.8% v 37.0%) and on diuretics (35.8% v 24.4%).21 Infants in the STOP-ROP trial who were in the higher SpO2 range had a greater incidence of chest infections,21 raising the possibility that even low-flow nasally delivered oxygen may be toxic to respiratory epithelium. Based on this information, our recommendation is to target a minimum mean SpO2 level of 93%–95% in infants with CNLD, as measured by continuous overnight oximetry. Despite this minimum target SpO2, some infants may have persistent tachypnoea, increased work of breathing, frequent oxygen desaturations during sleep, pulmonary hypertension and poor growth, which may require a higher target SpO2 level15–7,10,23 (E3,E4).
Summary of main recommendations

- For infants with chronic neonatal lung disease (CNLD), supplemental oxygen therapy is recommended to maintain the mean minimum oxygen saturation (SpO₂) level between 93% and 95% (E3, E4). *
- The safety of short-term disconnection from supplemental oxygen should be assessed before discharge (E4).
- Most infants with CNLD are not ready for discharge until their supplemental oxygen requirement is < 0.5 litres per minute delivered through a nasal cannula (E4).
- Assessing oxygenation during sleep by continuous overnight oximetry or polysomnography is recommended when weaning infants from supplemental oxygen (E4).
- There is limited objective evidence on which to base recommendations.

* Levels of evidence (E3, E4) we designated according to the ratings of the National Health and Medical Research Council (NHMRC).1

Fitness to fly

Air travel results in a mildly hypoxic environment where cabin pressure equivalent to 1500–2500 metres results in an equivalent fraction of inspired oxygen (Fio₂) of about 15%–17% of that at sea level.25 This can be simulated in a respiratory laboratory with the infant and parent seated in a body plethysmograph, where inspired oxygen is diluted with nitrogen to give an Fio₂ of about 15%, while oximetry is measured continuously over 20 minutes.25,26 Nasal prong oxygen can be titrated to achieve satisfactory SpO₂ levels. If such a test is not readily accessible and the infant is flying for longer than an hour, supplemental oxygen could be increased by 0.25 litres per minute or provided at 0.25 litres per minute for the flight if the infant has ceased supplemental oxygen therapy in the past 3 months (E4).

Indications for weaning infants from supplemental oxygen

Cochrane reviews in 2001 compared abrupt weaning versus gradual weaning27 and early versus late weaning28 of infants from supplemental oxygen, each reporting only a single study with very limited parameters, which provided little guidance for clinicians. As a result, there remains a range of practices.6,7,15

The following is our recommendation for weaning an infant with CNLD from supplemental oxygen (E4). The infant should receive continuous (24-hour) supplemental oxygen and achieve adequate growth and have no evidence of pulmonary hypertension while maintaining a minimum mean target SpO₂ of 93%–95%, estimated by continuous overnight oximetry or documented by polysomnography (E4). The target SpO₂ level may be set higher for some infants. Once these criteria are met, the flow of supplementary oxygen can be reduced and the assessment repeated. In most cases, it is recommended to clinically review the infant on a monthly basis (E4).

Long-term outcomes of oxygen supplementation strategies applied in infancy

Infants with CNLD who require home oxygen therapy have been found to use more health care resources and have delayed developmental progress in the preschool years compared with infants with CNLD who did not require home oxygen therapy.20,21 An Australasian register of infants with CNLD is needed to document baseline practice and subsequently study proposed parameters for home oxygen therapy and outcome measures to school age. Ideally, this would incorporate the expertise of neonatologists, respiratory and general paediatricians, and allied health care professionals cooperating in designing appropriate randomised controlled trials of target SpO₂ levels and weaning strategies to assess not only short-term measures like weight and length, but more important long-term outcomes like pulmonary hypertension, respiratory function, exercise capacity and neuro-cognitive function.32,33

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Competing interests

None identified.

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