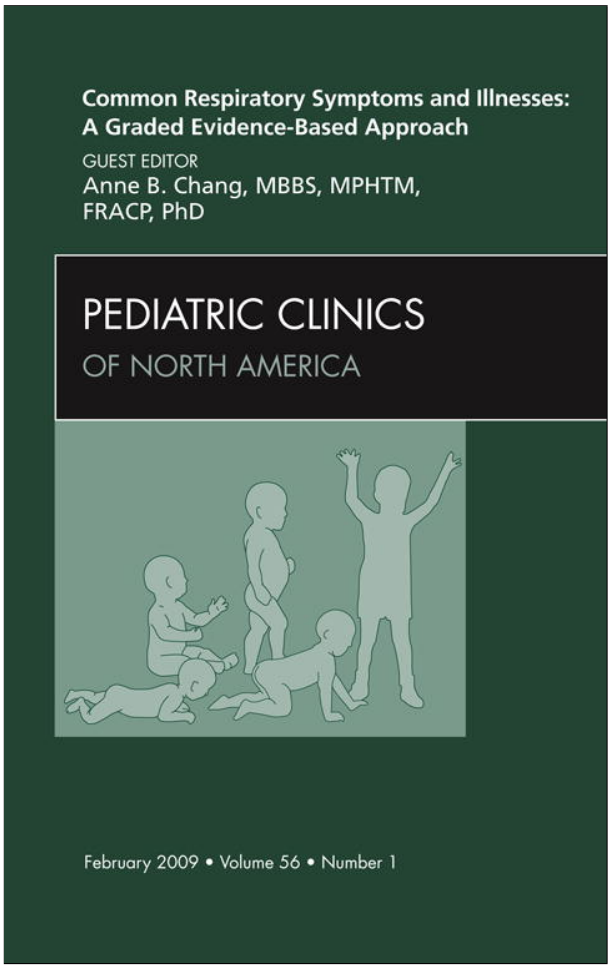

Domiciliary Oxygen for Children

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KEYWORDS

• Oxygen • Domiciliary • Home • Neonatal lung disease

The pediatric use of domiciliary oxygen (supplemental oxygen delivered in the home) has been steadily increasing since its first reported use in children in the 1970s.[1] Like much pediatric practice, because of a scarcity of good evidence to inform clinicians, there is a lack of consensus over many issues. Most available evidence relates to infants discharged home with chronic neonatal lung disease (CNLD), which is easily the largest patient group receiving domiciliary oxygen. Because this article is part of a series on ''evidence-based management,'' much of it relates to CNLD; however, other conditions are also covered, remembering the adage ''lack of evidence of benefit is not the same as evidence for lack of benefit'' (**Box 1**). Nevertheless, whenever possible, recommendations are accompanied by a grade indicating quality of evidence and strength of the recommendation using the GRADE system.[2]

DEFINITIONS

Although domiciliary refers to the home, in the context of oxygen therapy, it refers to delivery of supplemental oxygen outside the hospital because it may also be used outside the home, especially by children. Modes of delivery fall into three categories. Long-term oxygen therapy (LTOT) is defined as the provision of oxygen for continuous use at home for patients who have chronic hypoxemia (attributable to any cause) to maintain oxygen saturation (SaO_2) at or greater than 92% (depending on the type of oximeter) or PaO_2 greater than 8 kPa.[3] It may be required 24 hours per day or during periods of sleep only; thus, the adult definition that includes a requirement for more than 15 hours per day is not relevant. Ambulatory oxygen therapy (AOT) refers to the provision of portable oxygen that can be used outside the home. In adult patients, this is not always necessary because many are house-bound (although they may still need to attend hospital appointments). All children on LTOT require facilities for portable AOT unless they only use nighttime oxygen. This particularly applies to the infant age group (who spend periods during the day sleeping) because parents need to be able to take the baby outside the home to lead as normal a life as possible. Short burst oxygen therapy (SBOT)

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Box 1
Principal pediatric conditions that may require long-term oxygen therapy

- CNLD (bronchopulmonary dysplasia)
- Other neonatal lung conditions (eg, pulmonary hypoplasia)
- Congenital heart disease with pulmonary hypertension
- Pulmonary hypertension secondary to pulmonary disease
- Interstitial lung disease
- Obliterative bronchiolitis
- Cystic fibrosis and non-cystic fibrosis bronchiectasis
- Obstructive sleep apnea syndrome and other sleep-related disorders
- Neuromuscular conditions requiring noninvasive ventilation
- Disorders of the chest wall (eg, thoracic dystrophy, severe kyphoscoliosis)
- Sickle cell disease
- End-of-life palliative care

refers to acute use of short-term oxygen, and there are few indications specific to children, although it is undoubtedly used that way in many families (eg, during seizures).

NORMAL OXYGEN LEVELS

Painful arterial stabs result in a crying (and sometimes hypoxic) child, which gives unreliable results; thus, studies of oxygen levels in children are invariably performed using pulse oximetry. The issue here, however, is that pulse oximeters do not all give equivalent readings of SaO_2; thus, it is necessary to know which oximeter was used when comparing studies. A group of investigators have studied children at varying ages using the same equipment (**Table 1**). Their study of healthy term infants in the first month of life measured by pulse oximetry found in the first week of life that the baseline SaO_2 ranged from 92% to 100% (median of 97.6%), whereas in weeks 2 through 4, it ranged from 87% to 100% (median of 98.0%).[4] Episodes of desaturation (SaO_2 $\leq$80% for $\geq$4 seconds) occurred in 35% of recordings in week 1 and in 60% in weeks 2 through 4. These investigators also studied 67 older healthy full-term infants aged 4 to 8 weeks and found that their baseline SaO_2, measured by pulse oximetry, ranged from 97% to 100% (median of 99.8%).[5] Short

Table 1
Normal oxygen saturation levels in healthy children, measured by the same group of investigators using pulse oximetry

Age	n	Median	Range	Reference
Ex-preterm babies at term	66	99.4	89–100	6
1 week	50	97.6	92–100	4
2–4 weeks	50	98.0	87–100	4
4–8 weeks	67	99.8	97–100	5
2–16 (mean 8) years	70	99.5	96–100	8

episodes of desaturation to 80% or less were found in 81% of infants, occurring at a median of 0.9 per hour, with a median duration of 1.2 seconds (97% were for less than 4 seconds). They studied 66 preterm infants born at a gestational age of 25 to 36 weeks (median of 34 weeks) when they had reached term.[6] Their baseline SaO_2 ranged from 89% to 100% (median of 99.4%). Desaturations were more frequent (median of 5.4 per hour) and longer (median of 1.5 seconds) than in the term infants, however.[5] High altitude affects SaO_2 and may need to be taken into account when interpreting normal values (and publications).[7] Finally, they studied 70 healthy older children with a mean age of 8 years (range: 2–16 years) using a pulse oximeter.[8] Baseline SaO_2 was a median of 99.5% (range: 95.8%–100%, fifth centile = 96.6%). The number of desaturations of 90% or less decreased with age, with episodic decreases seen in 47% of 2- to 6-year-olds and in 13% of 13- to 16-year-olds. A more recent study in 100 third-grade primary school children (mean age = 9.3 years) recorded overnight SaO_2 measured by pulse oximetry.[9] The median SaO_2 was 97% (range: 94%–100%), and a baseline SaO_2 less than 97% was uncommon. Furthermore, although intermittent desaturations by 4% or more were frequent, the SaO_2 rarely decreased to 90% or less.

WHAT ARE THE ADVERSE EFFECTS OF CHRONIC LOW OXYGEN SATURATION?

This, of course, depends on the degree and duration of the low SaO_2 levels, and it is likely that mild hypoxemia has no adverse effects. Newborns and infants younger than 1 year of age, however, have an increased tendency to ventilation-perfusion mismatch, making them particularly susceptible to hypoxemic episodes, especially if they are ill or in the presence of airway hypoxia.[7] There are several factors that contribute to this greater risk for developing hypoxemia: the presence of fetal hemoglobin (with the oxygen dissociation curve shifted to the left), tendency to pulmonary vasoconstriction in the presence of airway hypoxia, tendency to bronchoconstriction in the presence of airway hypoxia, relatively fewer alveoli, compliant rib cage, and smaller airway diameter.[7] In addition, in the first 2 months of life, infants may show a paradoxical inhibition of the respiratory drive causing apnea or hypoventilation in response to hypoxia or infection.[7] Some of the more recognized adverse effects are outlined in this article.

Pulmonary Arterial Hypertension

Chronic alveolar hypoxia leads to an increase in systolic pulmonary artery pressure resulting from pulmonary vasoconstriction and increased pulmonary vascular resistance. There is adaptation of the pulmonary endothelium with pulmonary artery remodeling.[10] This can lead to right ventricular hypertrophy and dysfunction, and eventually to right heart failure.

Acute Life-Threatening Events and Sudden Infant Death

It is known that hypoxia can cause apnea and hypoventilation; thus, the greatest concern is that a period of hypoxia may lead to an acute life-threatening event or actual sudden infant death (SID).

Neurodevelopmental Problems

Intermittent oxygen desaturations are associated with significant learning difficulties in animal studies.[11] Chronic or intermittent hypoxia has been shown to affect cognitive and behavioral outcomes adversely, particularly in some children with congenital cyanotic heart disease and sleep-disordered breathing.[12]

- **Suboptimal growth**
  In infants with chronic hypoxemia, this is best demonstrated by the fact that growth velocities improve when the babies are given supplemental oxygen. This may relate to the effects of hypoxemia on nutrient absorption from the gastrointestinal tract[13] or may be attributable to changes in growth hormone secretion.[14]
- **Increased airway resistance**
  This may result from hypoxia in infants with CNLD, a finding that was not seen in healthy infants.[15]
- **Increased airway inflammation**
  This can result from hypoxia attributable to up-regulated cytokine expression and neutrophil inflammation in CF.[16]

WHAT ARE THE ADVERSE EFFECTS OF CHRONIC HIGH OXYGEN SATURATION?

The effect of too much oxygen on the developing retina is well established, although less relevant at the stage at which the baby is being considered for hospital discharge. Oxygen toxicity, particularly in premature infants, can inhibit lung healing and contribute to ongoing lung injury through the formation of reactive oxygen intermediates and peroxidation of membrane lipids.[17] The Benefits of Oxygen Saturation Targeting (BOOST) study showed a nonsignificant excess) of deaths from pulmonary causes in the babies kept at a higher SaO_2.[18] The Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP) study found an increased rate of adverse pulmonary sequelae (pneumonia and exacerbations of CNLD), although not deaths, in the high-saturation group; this group also had more infants still requiring supplemental oxygen at 3 months.[19] Oxidative stress from a high oxygen concentration may also be a contributing factor to the development of bronchopulmonary dysplasia (BPD),[20] and it is suggested that a fraction of inspired oxygen (F_IO_2) of 0.8 to 1.0 for 24 hours is associated (but not necessarily causative) with the occurrence of BPD.[1] In addition, animal work has shown a possible permanent blunting of the ventilatory response to hypoxia after exposure to high oxygen concentrations during a critical developmental period.[11] This could lead to an increase in sleep-disordered breathing and even sudden death.

WHAT IS THE EVIDENCE THAT SUPPLEMENTAL OXYGEN IS BENEFICIAL TO PATIENTS AND THAT DOMICILIARY OXYGEN IS PREFERABLE TO HOSPITAL BASED OXYGEN?

These questions are answered for a variety of conditions outlined in this article, accepting that evidence is often lacking. Benefit is considered in terms of symptoms (eg, breathlessness, respiratory distress, exercise tolerance), growth and neurodevelopment, school attendance and hospitalization rates, quality of life, psychologic impact, and survival. Obviously, these parameters are not applicable to all patient groups.

This section deals with the issues of LTOT and AOT because almost all children receiving LTOT should not be confined to their home; thus, equipment for AOT must be provided (unless LTOT is used at nighttime only). The indications for LTOT are therefore identical to those for AOT.

Chronic Neonatal Lung Disease

The definitions of CNLD and BPD keep evolving. CNLD is said to be present in babies born before term who require continuous oxygen at 36 weeks of gestational age, or if they are born at greater than 32 weeks of gestational age, they still require supplemental oxygen at 28 days of age. BPD is defined as the need for supplemental oxygen for at least 28 days after birth, and it is graded according to the oxygen flow rate required

near to term.[21] CNLD is the main indication for LTOT in children; data from the Children's Home Oxygen Record database for England and Wales indicate that CNLD is the underlying cause in 57% of cases. Data from surviving babies (born between 1997 and 2002) weighing less than 1500 g showed that 22% developed BPD.[22] They often require a prolonged period of mechanical ventilation and continued to need supplemental oxygen once extubated. With increased survival of extremely low birth weight premature infants, the incidence of CNLD is also likely to increase,[23] as is the need for LTOT.

There have been no controlled studies on the effects of mild hypoxemia on mortality in infants who have CNLD. It has been suggested that the use of supplementary oxygen may reduce mortality from SID, however.[24] This may be because oxygen therapy reduces the number of apneic and cyanotic episodes, in addition to the frequency of intermittent desaturations.[24] Certainly, supplemental oxygen significantly reduces pulmonary arterial hypertension in infants who have CNLD, and this effect is achieved at an oxygen concentration that is deliverable at home (2–3 L/min by nasal cannulae).[25] Measurement of infant lung function has shown that supplemental oxygen reduced total pulmonary resistance and increased compliance in babies who had severe BPD and reversible obstructive lung disease.[26] The effect of oxygen on sleep quality is difficult to interpret, but it seems that although desaturations are reduced, this is at the cost of sleep disruption.[27–29]

Home oxygen has been shown to improve growth to the level of healthy term infants, and premature discontinuation of the supplementation (against medical advice) caused a significant deceleration in weight gain.[30–32] The effect of supplemental oxygen on neurodevelopment is difficult to assess, but it is likely to be beneficial.[33] Further, it reduces the risk for nosocomial infection and it is believed to be good for parent-child bonding.[33] Although there have been no randomized trials of babies on LTOT, it is suggested that caring for babies on supplementary oxygen at home is preferable to a prolonged hospital stay.[34] Finally, it is beneficial in terms of freed resources for neonatal units and reduces the total cost of care for an infant.[34–37]

Recommendation: Domiciliary LTOT should be considered for infants who have CNLD and are otherwise ready for hospital discharge. Recommendation B, quality of evidence: moderate.

Other (Oxygen-Dependent) Neonatal Lung Conditions

Other relevant neonatal lung conditions include pulmonary hypoplasia, congenital pneumonia, and meconium aspiration syndrome; however, compared with CNLD, these cases are rare. Survivors of congenital diaphragmatic hernia repair not uncommonly develop chronic lung disease, mainly attributable to pulmonary hypoplasia or lung damage resulting from mechanical ventilation. Some require domiciliary oxygen, but this is unusual beyond 2 years of age.[38] Randomized controlled trials have not been (nor could they be) conducted; hence, the low-level recommendation, Nevertheless, it is likely that outcomes from receiving LTOT at home would be no different from those in babies with CNLD.

Recommendation: Domiciliary LTOT should be considered for infants with other oxygen-dependent neonatal lung conditions who are otherwise ready for hospital discharge. Recommendation I, quality of evidence: poor.

Congenital Heart Disease: Acyanotic and Cyanotic

It is likely that only those with pulmonary hypertension (without Eisenmenger syndrome) need to be at home on long-term oxygen. In cyanotic congenital heart disease, oxygen has little effect in raising SaO_2 and is not indicated, although the degree of

polycythemia may be reduced.[39] In some cases with chronic left-to-right shunting, however, irreversible pulmonary vascular disease can develop and cause right-to-left shunting (Eisenmenger syndrome). The resulting pulmonary hypertension is not responsive to oxygen. However, in a small but important controlled study, 100% oxygen given for a minimum of 12 hours per day for up to 5 years significantly improved survival in children with pulmonary vascular disease too severe to have corrective surgery.[40] This was not the case in a recent 2-year study of adults with advanced Eisenmenger syndrome, however, in which nocturnal oxygen had no impact on survival, exercise capacity, or quality of life.[41] Some children with congenital heart disease who are awaiting corrective surgery (without Eisenmenger syndrome), and who have raised pulmonary artery pressure that is oxygen responsive, may benefit from LTOT, as can some children after surgery.[42] In addition, children with severe right ventricular failure and resting hypoxemia need long-term oxygen, but are unlikely to be at home.[39] Decisions in these cases should be made by a specialist pediatric cardiologist.

Recommendation: Domiciliary LTOT should be considered for children with pulmonary hypertension accompanying Eisenmenger syndrome (if they have symptomatic relief) and in children who have pulmonary vascular disease too severe for corrective surgery, who are otherwise ready for hospital discharge. Recommendation B, quality of evidence: low.

Pulmonary Hypertension (Secondary and Primary)

Pulmonary hypertension resulting from pulmonary disease (secondary) is caused by chronic hypoxia and considerably worsens the overall prognosis of the underlying disease.[10] There are several associated pulmonary disorders (reviewed by Roy and Couriel).[43] Acute hypoxia causes smooth muscle contraction in pulmonary arteries, and chronic hypoxia leads to pulmonary vasoconstriction and endothelial dysfunction. Children have a more reactive pulmonary circulation in response to hypoxemia than adults, and oxygen is the most important vasodilator for maintenance of pulmonary vascular tone.[43] LTOT reverses or at least slows the progress of the hypoxic-induced changes to the pulmonary vascular bed and can contribute to improved survival.[10]

Primary pulmonary hypertension has a poor prognosis in children (median survival <1 year). Some of the children desaturate during sleep (especially during the early morning hours) because of mild hypoventilation, which may lead to severe dyspnea, and the resulting hypoxemia can be eliminated by supplemental oxygen.[39] These children also need oxygen available at home for emergency use (eg, when they have viral upper respiratory tract infections) because some tend to desaturate.

Recommendation: Domiciliary LTOT should be considered for children with pulmonary hypertension who are otherwise ready for hospital discharge. Recommendation B, quality of evidence: low.

Interstitial Lung Disease

Interstitial lung disease represents a spectrum of rare conditions with a variable but often poor outlook (eg, chronic pneumonitis of infancy, nonspecific interstitial pneumonitis, desquamative interstitial pneumonitis, immunodeficiency) in which oxygen exchange is impaired. Drug therapy (usually systemic corticosteroids or hydroxychloroquine) is sometimes beneficial. Many of the children are hypoxic and require LTOT. The European Respiratory Society Task Force on Chronic Interstitial Lung Disease reported that 26% of all children with interstitial lung disease were on long-term oxygen, including 55% of those younger than 2 years of age.[44] There has been a single unpublished adult study (reported in a Cochrane review) with the finding that domiciliary

oxygen had no effect on mortality after 3 years.[45] A randomized controlled trial of domiciliary oxygen can never be conducted; hence, the low level of the evidence-based recommendation. Nevertheless, in reality, the recommendation is to offer it.

Recommendation: Domiciliary LTOT should be considered for hypoxic children who have interstitial lung disease and are otherwise ready for hospital discharge. Recommendation I, quality of evidence: poor.

Obliterative Bronchiolitis

Obliterative bronchiolitis leads to severe obstructive lung disease, and although it may occur after a viral infection (eg, adenovirus), the cause is often unknown. There is no specific therapy, and, again, the outlook is variable. Many of the children are hypoxic and require LTOT, although, again, there is no evidence base to back this up. In a recent large review, there is no mention of oxygen in the section on treatment.[46] In one study of 18 children in Chile who had postadenoviral bronchiolitis obliterans, 28% children required home oxygen but it could be discontinued after 1 year in all the children.[47] A smaller study from Malaysia of children on home oxygen found that those with bronchiolitis obliterans required a longer duration, with a median of 28 months (interquartile range: 14–66 months).[48]

Recommendation: Domiciliary LTOT should be considered for hypoxic children who have obliterative bronchiolitis and are otherwise ready for hospital discharge. Recommendation I, quality of evidence: poor.

Cystic Fibrosis and Non-Cystic Fibrosis Bronchiectasis

As therapy improves, there are fewer children with cystic fibrosis (CF) who are hypoxic and require supplemental oxygen, and pulmonary hypertension is uncommon in children who have CF. Hypoxemia may be associated with infective chest exacerbations when ventilation-perfusion mismatch is worsened. It is estimated that 1% to 2% of children who have CF receive LTOT.[3] There is, however, no clear-cut definition of hypoxia in CF, and little evidence to guide when supplemental oxygen is indicated.[16] Oxygenation problems are not limited to those who have severe disease; a study of 24 children (median age of 9.5 years) showed that 96% of children with normal lung function or mild to moderate lung disease (defined as forced expiratory volume in 1 second, percentage predicted of 40%–60% and 60%–80%, respectively) had desaturation events during sleep, although they would not be classified as having nocturnal hypoxia (SaO_2 <90% for >5% of the time).[49] There was a degree of correlation of nocturnal oxygenation with clinical, radiographic, and growth parameters. Although the proportion of children who had CF and had desaturations was similar to that in a study of normal children,[9] the children who had CF had a lower mean and minimum SaO_2 and more desaturation events.

There is surprisingly little evidence for the benefit of LTOT in CF, and although it led to an improvement in school or work attendance, there was no effect on mortality, frequency of hospitalization, or disease progression in a small study (n = 28).[50] A problem with that study was that nocturnal oxygen was titrated to normalize daytime SaO_2, which is not necessarily predictive of nocturnal hypoxemia; thus, some of the patients may have been undertreated. It is not clear how many of the subjects were children, although all were older than 12 years of age; two of four of the recruiting hospitals were children's CF units. It is recommended that LTOT be reserved for those patients who have CF who obtain symptomatic relief,[51] particularly because adherence to treatment is usually poor if the child feels no benefit. The potential adverse psychologic effect of starting oxygen at home must be also considered. It is often taken as an indicator of a serious deterioration in the child's condition and has rightly been

described as an ''emotional life event'' for a patient who has CF.[52] It is yet another burden of treatment; thus, the patient and family must be motivated and convinced of the need.

In two small adult studies comparing noninvasive ventilation (NIV) with supplemental oxygen, it was noted that in those receiving supplemental oxygen alone, the improvement in oxygenation was accompanied by an increase in transcutaneous carbon dioxide (CO_2), which caused morning headaches in a few patients.[53,54] Studies have not been performed in children, but there is no reason to suggest that this would be different in adolescents having severe lung disease, who are the ones likely to be receiving home oxygen. It is therefore recommended that monitoring of transcutaneous CO_2 levels be performed when oxygen therapy is initiated.

A Cochrane systematic review has summarized the effects of supplemental oxygen on exercise from three studies (which included a few children only); there was an improvement in exercise duration and peak performance.[55] In reality, use of supplemental oxygen for exercise would not be an indication for domiciliary oxygen in children. There are other causes of bronchiectasis in children (although in approximately 50% cases, no underlying cause is found), and LTOT is occasionally necessary for those with severe disease.

Recommendation: Domiciliary LTOT should be considered for hypoxic children who have CF as a means to improve school attendance and for those who obtain symptomatic relief. Monitoring of transcutaneous CO_2 levels should be performed when oxygen therapy is initiated. Recommendation B, quality of evidence: low.

Obstructive Sleep Apnea Syndrome

In cases in which the obstruction can be relieved, any pulmonary hypertension that may have developed is usually reversible and resolves rapidly.[43] Obstructive sleep apnea syndrome may require NIV if the obstruction cannot be relieved. Occasionally, supplemental oxygen alone is used if the child does not tolerate face mask ventilation (eg, some children with Down's syndrome). As a temporary treatment, it seems to be safe and has a beneficial effect on oxygenation and sleep quality.[56] Oxygen does not suppress the ventilatory drive in most children who have obstructive sleep apnea syndrome, but $PaCO_2$ levels should still be monitored.[57]

Recommendation: Domiciliary LTOT can be considered for children who have obstructive sleep apnea syndrome and do not tolerate NIV as long as $PaCO_2$ levels are monitored. Recommendation B, quality of evidence: low.

Chronic Hypoventilation: Central, Neuromuscular Weakness, Chest Wall Disorders

There are some patients who require long-term NIV because of chronic hypoventilation (to control hypercapnia and hypoxemia). Oxygen alone is inadequate for most children with chronic hypoventilation. A UK survey in 1997 estimated the number of children receiving NIV to be 141, of whom 93 (65%) were at home.[58] The incidence was shown to have increased over the previous decade, and this figure is likely to continue to increase in the future. The children had a variety of conditions, principally neuromuscular disorders (46%), congenital central hypoventilation syndrome (13%), spinal injury (12%), craniofacial syndromes (7%), and BPD (4%). There was a variety of other less frequent causes (18%). In 35% of cases, they had access to supplemental oxygen at home as well (E. Jardine, personal communication, 2004). It is likely that these children have other problems affecting the lungs (eg, recurrent infection attributable to aspiration from swallowing difficulties and gastroesophageal reflux) that lead to the oxygen requirement. In one UK series of children with neuromuscular and skeletal disease requiring NIV, 5 of 40 children required supplemental oxygen at night (to

maintain SaO_2 >90%), and 2 of the children stopped the oxygen after 6 months of NIV.[59] Core guidelines have suggested that children on home ventilation should have a stable oxygen requirement with an FIO_2 requirement of less than 40%.[60]

Recommendation: Domiciliary LTOT can be considered for children with chronic hypoventilation who remain hypoxic despite NIV with optimal CO_2 control. Recommendation I, quality of evidence: low.

Sickle Cell Disease

It is important that children who have sickle cell disease and upper airway obstruction do not become hypoxemic during sleep because it can lead to debilitating episodes of sickling.[61] Low overnight SaO_2 has been linked to cerebrovascular disease and frequent episodes of acute pain.[62] In addition, in a recent study of 75 children aged older than 6 years, the prevalence of elevated pulmonary artery pressure was 30%, which was similar to that in adults.[63] This was significantly associated with a low SaO_2 documented in the clinic. Because pulmonary hypertension confers a high risk for death in sickle cell disease (at least in adults),[64] it is obvious that chronic hypoxemia must be prevented. For this reason, domiciliary oxygen should be provided for children with persistent nocturnal hypoxia after other causes (eg, adenotonsillar hypertrophy) have been treated. It is recommended in the UK guideline for sickle cell disease in childhood that overnight SaO_2 should be measured if there is a history of snoring, or nocturnal enuresis after the age of 6 years.[62] The UK guideline also recommends an annual measurement of SaO_2 when the child is well and is in outpatient treatment; if it is less than 95%, overnight monitoring should be undertaken.[62] Furthermore, home oxygen is suggested as one of the therapies for chronic sickle lung, although the UK guideline gives no evidence to back up this recommendation.

Recommendation: Domiciliary LTOT should be considered for children who have sickle cell disease and nocturnal hypoxia. Recommendation I, quality of evidence: low.

Palliative Care and End-of-Life Care

There are no data on the management of terminal dyspnea in patients who have neuromuscular disorders and CF.[65] Most published data are on adult patients who have terminal cancer; a double-blind crossover trial in 14 adults showed that oxygen at a rate of 5 L/min delivered by mask improved the subjective sensation of dyspnea.[66] A recent meta-analysis, however, found that oxygen did not provide symptomatic benefit for patients who had cancer with refractory dyspnea and were mildly or nonhypoxemic.[67] It has been suggested that supplemental oxygen may be effective in relieving dyspnea in children who cannot tolerate NIV (especially when they are not hypercapnic).[68] With chronic hypercapnia, the hypercarbic drive to breathe may be blunted, and in these circumstances, when the primary drive to breathe is hypoxemia, this may be removed by supplemental oxygen. Although this may lead to hypopnea or even apnea, this is less of a concern in an end-of-life situation.[68] It may also be important for the family to have a full view of their child's face; thus, nasal cannulae may be preferable to a NIV face mask.[68] Clinical experience shows that some children do get a degree of symptomatic relief from supplemental oxygen, although, of course, it does not affect the final outcome. In addition, reversing hypoxemia can cause pulmonary vasodilation and prevent the intracranial vasodilation that can be a cause of headaches.[68] For these reasons, oxygen can be offered, but children are likely to continue with it only if they find it helpful.

Recommendation: Domiciliary LTOT can be considered for children undergoing palliative care who obtain symptomatic relief from supplemental oxygen. Recommendation I, quality of evidence: low.

INDICATIONS FOR ACUTE USE OF DOMICILIARY OXYGEN

Neurodisability: Recurrent Seizures

It is apparent that some children with seizures are receiving home oxygen, which is administered at the time of the seizure. There has been a study of respiratory function observed during 101 seizures in 37 children.[69] An increase in respiratory rate was noted in 66% of the 21 generalized seizures, but this was not associated with apnea or hypoxemia (measured by pulse oximetry). No respiratory abnormalities were seen during the 40 absence seizures. Nevertheless, the 40 focal seizures were often associated with respiratory abnormalities, 70% by frequent respiratory pauses and 30% by apnea, and significant hypoxemia (defined as SaO_2 <85%) was observed in 40% of seizures. Supplemental oxygen is unlikely to be beneficial because the brief period of hypoxia does not respond to oxygen while the child is not breathing, and the hypoxia is self-limited and brief anyway. The UK guideline referred to on the National Institute for Clinical Excellence Web site does, however, suggest that oxygen be administered to patients in the hospital having generalized tonic-clonic status epilepticus.[70]

Recommendation: domiciliary acute oxygen therapy is not recommended for children with neurodisability who have recurrent seizures. Recommendation I, quality of evidence: low.

Acute Asthma

Any child with an acute asthma episode severe enough to require oxygen should be in the hospital and not at home. There are, however, a few children who have such severe asthma that they need supplemental oxygen while waiting for an ambulance to take them to the hospital; thus, it must be available at home. In addition, these severely asthmatic children may need an oxygen supply to drive their nebulizer while waiting for the ambulance. Generally, spacer devices are preferred for administering bronchodilators,[71] but there are occasions when the child is only able to use a nebulizer. Home nebulizers are usually driven by room air, but nebulized salbutamol can cause an initial decrease in SaO_2 in asthmatic children and wheezy infants, more commonly with air- than with oxygen-driven nebulization.[72,73] This may be clinically significant if the child is already hypoxemic and on the steep part of the oxygen dissociation curve from the acute bronchoconstriction. For those children with recurrent severe life-threatening episodes, it is better to have oxygen available in the home for use with their nebulizer before transfer to the hospital.

Recommendation: domiciliary acute oxygen therapy is recommended for children with recurrent episodes of severe acute asthma as a temporary therapy before ambulance transfer to the hospital. Recommendation B, quality of evidence: moderate.

Acute Bronchiolitis

The need for supplemental oxygen in an infant with acute bronchiolitis has generally been regarded as an indication for hospital admission. The recommendation in the Scottish Intercollegiate Guideline Network (SIGN) guideline is that infants with an SaO_2 of 92% or less require inpatient care, and they can be considered for discharge when their SaO_2 is greater than 94%.[74] Nevertheless, there has since been a randomized trial of 92 infants aged 2 to 24 months presenting with acute bronchiolitis and hypoxia, defined as an SaO_2 of 87% or less.[75] After an 8-hour observation period, 70% of those randomized for discharge with home oxygen could be discharged (some no longer required oxygen, and some failed to meet the discharge criteria). Of those sent home, 97% were treated successfully with oxygen at a rate of 1 L/min by means of

nasal cannulae as outpatients; 1 infant, however, had to be admitted after a cyanotic spell that occurred after 24 hours at home. This certainly opens up a potential alternative to hospital admission, but if financial considerations were excluded, the author's suspicion is that most parents would opt for a short hospital stay. It must also be remembered that these patients presumably had the US definition of bronchiolitis (it is not defined in the paper) and that some of them would have been diagnosed outside the United States as having acute viral wheeze or infantile asthma.

Recommendation: domiciliary acute oxygen therapy can be considered for children who have acute bronchiolitis after a period of hospital observation. Recommendation B, quality of evidence: moderate.

ASSESSMENT OF INITIATION OF LONG-TERM OXYGEN THERAPY (WHEN TO START)

The following sections on assessment and follow-up are mainly concerned with infants who have CNLD. This is the largest patient group and is distinguished by having a good prognosis; there are few other patients who can be weaned off the oxygen over time.

Assessment in Infancy

Suitability for domiciliary oxygen therapy should be assessed by a specialist with appropriate experience in the care of the relevant condition; this is usually a respiratory pediatrician or neonatologist (but may be a pediatric cardiologist, general pediatrician, or palliative care specialist). The family must also be assessed as competent to manage home oxygen therapy and be able to cope with all aspects of the baby's care. In adults, measurement of arterial PaO_2 is considered critical, but this is neither possible nor practical in infants. In pediatric practice, SaO_2 measured by pulse oximetry remains the main form of assessment, because an arterial stab in a crying (hypoxic) child is unreliable, whereas capillary PaO_2 does not correlate well with arterial PaO_2.[76] Single measurements are insufficient, and before discharge, SaO_2 must be measured continuously for at least 6 to 12 hours, including periods of sleep, wakefulness, and activity or feeding (watching for the effects of movement artifact). It is important to include all levels of activity because infants have an increased oxygen requirement when active and infants who have CNLD may develop feeding-related hypoxemia.[77] In addition, some children may only be hypoxemic at night, without daytime hypoxemia. An instrument should be used that has been validated in infants, and although it has been suggested that pulse oximeter readings should be verified by an arterial gas measurement at the start of the study, this is impractical and is not essential. It is important to remember that correlation between SaO_2 and arterial PaO_2 is such that at 94% saturation, the PaO_2 may vary from 9 to 17 kPa.[78] Although correlation is particularly poor in the saturation range of 85% to 90%,[79] this should not matter because all infants with SaO_2 less than 90% should receive LTOT anyway.

Most of the work in infancy relates to CNLD, and there is only limited evidence to recommend a minimally acceptable level of oxygenation; hence, the lack of consensus on who requires home oxygen.[80] Normal SaO_2 is around 96%, and supplemental oxygen is usually considered for infants who cannot maintain SaO_2 at 93% or greater when asleep or quietly awake; oxygen therapy is then given to achieve SaO_2 greater than 92%.[3] Previously, some researchers have recommended keeping SaO_2 at 95% or greater,[24] but there is a trend toward lower levels now. This resulted from concerns over oxygen lung toxicity after two important trials. The first was the BOOST trial of 358 premature infants who still required oxygen at 32 weeks of postmenstrual age.[18] This showed that maintaining SaO_2 at 95% to 98% had no advantage over 91% to 94% in

terms of growth and neurodevelopment at 1 year of age (using oximeters). The study also found that the group with the higher target oxygen level had an excess of deaths from pulmonary causes, albeit not statistically significant. This was in keeping with the second study, the STOP-ROP trial on retinopathy of prematurity.[19] Here, 649 preterm infants were randomly assigned to different target oxygen levels (89%–94% vs. 96%–99%) for at least 2 weeks, using oximeters that are calibrated to display SaO_2 that is 1.6% saturation points lower than other commercial oximeters. The study found an increased rate of adverse pulmonary sequelae (pneumonia and exacerbations of CNLD), although not deaths, in the high-saturation group when assessed at 3 months after the due date of the infant (13.2% versus 8.5%). The high-saturation group also had more infants still requiring supplemental oxygen at 3 months (47% versus 37%). Further studies are underway using lower target saturations (85%–89%), and results of these trials are to be combined in a meta-analysis.[81] It must be remembered that the correct target saturation for a preterm baby who has not yet reached term is likely to differ from that of an infant who is old enough to be at home, albeit with supplemental oxygen.

Recommendation: Oxygen therapy should aim to keep SaO_2 at 92% to 94% in infants, particularly during the preterm period, with no more than 5% of time spent at lower than 90% saturation. Assessment of SaO_2 must be for at least 6 to 12 hours and include periods of sleep, wakefulness, and activity or feeding. Recommendation B, quality of evidence: moderate.

Assessment in Older Children

For older children, adult criteria for oxygen prescription may be acceptable, although specific studies on upper and lower limits of PaO_2 for LTOT are lacking. It is important to include an entire night (with at least 4 hours of uninterrupted sleep) in case the child only develops nocturnal hypoxemia, such as in CF, in which nocturnal hypoxemia usually precedes daytime desaturation. In children with hypoventilation, such as in neuromuscular disease, it is important to check the CO_2 status because in the presence of hypercapnia, NIV is necessary rather than LTOT alone. Measurement of overnight transcutaneous or end-tidal CO_2 is ideal, although capillary CO_2 taken just as the child wakes up may be useful if either of the former is not available. Full polysomnography is not usually required.

DISCHARGE CRITERIA

A multidisciplinary meeting should ensure that discharge planning is achieved properly because extensive collaboration is required between the parents and multidisciplinary team. The goal is to select the infants and families most likely to cope at home and to get the timing of discharge right.[82] Each neonatal unit has its own criteria, but some general principles follow:[3]

- The oxygen requirement must be stable with mean SaO_2 of 93% or greater, without frequent episodes of desaturation. SaO_2 should not drop lower than 90% for more than 5% of the artifact-free recording period.
- No other clinical conditions should preclude discharge, and the child must be medically stable with satisfactory growth. There should be no apneic episodes for at least 2 weeks.
- Immunizations should be up to date. Palivizumab may be considered at the appropriate time of year for infants who have CNLD requiring home oxygen.
- Parents are willing and believed to be capable of taking the baby home while still on oxygen.

- Home conditions must be satisfactory, and, preferably, a landline telephone is installed (in addition to a mobile phone). A visit from a member of the home care team is required before discharge.
- Parents are trained and have written information on the use of home oxygen and also cardiopulmonary resuscitation in the case of infants. Vigilance for an empty oxygen supply, dislodged cannulae, or blocked valve is critical. A structured education program can be useful.[83]
- Advice is given about no smoking in the home. It needs to be strongly discouraged, but help to do so must be offered. In a study of burns affecting 27 adults on home oxygen, 89% were smoking at the time; thus, parents must be aware of the danger.[84] Advice must also be given about open flames (eg, birthday cake candles).[85] Notification to local fire services is recommended.
- Older children also need to have training on how to use their oxygen equipment.
- Parents must be advised about travel with cylinders and inform their home and car insurers.
- Appropriate support must be in place (eg, community nursing, nurse specialists, health visitor, social worker).
- Communication with a general practitioner has taken place, and roles are clarified for delivering clinical care.
- Parents must have a list of telephone numbers for advice and emergency help, including a telephone number for repair of equipment breakdown.
- Arrangements are in place for open access to the local pediatric unit.

Recommendation: Children can be discharged from the neonatal unit when their oxygen requirement is stable with a mean SaO_2 of 93% or greater and without frequent episodes of desaturation. The SaO_2 should not drop to lower than 90% for more than 5% of the artifact-free recording period. There should be no other clinical conditions precluding discharge, and the child must be medically stable with satisfactory growth. Recommendation B, quality of evidence: low.

FOLLOW-UP OF INFANTS ON DOMICILIARY OXYGEN

Arrangements for follow-up after discharge should be coordinated by the hospital specialist who has initiated domiciliary oxygen. Liaison must take place between the specialist, local or community pediatrician, general practitioner, nurse specialists, community pediatric nursing service, occupational therapist, and health visitor. The oxygen requirement is likely to change over time; it should be reduced in infants with CNLD but is likely to increase in most other conditions. Regular home monitoring with pulse oximetry is necessary and should be set up by community or specialist nurses. A visit within the first 24 hours is important to reassure parents. The first formal SaO_2 monitoring should take place within a week; subsequent recordings should occur as clinically indicated but rarely less often than every 3 to 4 weeks.[86] Recorded data can then be discussed with the supervising consultant, although protocols can be in place for experienced nursing teams to initiate changes.

These infants require a lot of input from health care professionals. Emotional support is necessary because parents display marked pre- and postdischarge anxiety, which decreases as they see their baby's oxygen dependency resolving.[87] Mothers have also been reported to show low self-esteem, self-blame, and elements of grief and isolation[88] in addition to less vitality and more mental health problems.[89] A study in Oxford, United Kingdom, on 55 babies with CNLD at home with LTOT looked at health care use in 31 of the babies.[34] It was found that these families received a median

of 43 visits per baby (range: 8–173 visits) from a pediatric community nurse and that these lasted a median of 45 minutes; 83% of families saw a health visitor, with a median of 12 visits (range: 2–82 visits), and the visits were for a median of 30 minutes; 83% of families saw a general practitioner, with a median of 6 visits (range: 1–140 visits), and the visits were for a median of 10 minutes. A lesser proportion of families also saw a hospital consultant (they almost all had hospital clinic visits, however, on a median of four occasions), social worker, physiotherapist, and speech therapist. In addition, infants with CNLD who require home oxygen have more frequent and longer hospital admissions, and more clinic attendances, than those sent home without oxygen; this means that their total cost of care was 40% greater.[90] This is particularly the case if they had been hospitalized in the first 2 years of life with respiratory syncytial virus infection, which had a significant impact on the cost of care.[91] In the Oxford study, 41% of the babies required readmission, on a median of 1 occasion (range: 0–10 occasions), staying for a median 9 days (range: 1–64 days).[34]

The children should be seen regularly by the hospital specialist in the clinic to monitor the underlying condition in addition to growth and neurodevelopment. There must be direct access for the child to be admitted to the hospital in the case of any emergency or acute deterioration in his or her condition, and the parents must have the telephone numbers of the team. Even a simple viral upper respiratory tract infection in a young infant on LTOT may necessitate admission, and winter (particularly the first) can be an anxious time for parents. If the caregivers believe the child requires an increase in oxygen, they can turn up the flow rate but must then seek advice from the home care team. Even when the child comes off oxygen, support must continue because the children may sometimes relapse and require further periods of oxygen therapy after an apparently complete recovery. This is usually related to intercurrent infection.

Recommendation: Regular home monitoring with pulse oximetry is necessary. After an initial visit within the first 24 hours, the first formal SaO_2 monitoring should take place within 1 week; subsequent recordings are done as clinically indicated but usually not less often than every 3 to 4 weeks. Recommendation B, quality of evidence: low.

WEANING INFANTS OFF LONG-TERM OXYGEN THERAPY (WHEN TO STOP)

The issue of weaning off oxygen principally applies to infants with CNLD and some other neonatal lung conditions. In children with congenital heart disease, only those having successful corrective surgery or transplantation no longer require LTOT. Some young children with interstitial lung disease or obliterative bronchiolitis may improve sufficiently to lose their oxygen dependency. The older children with progressive lung disease, such as CF or neuromuscular conditions, usually continue to require oxygen for the remainder of their lives. It is not easy to counsel the parents of children who have CNLD as to how long LTOT is needed. Although group data showed that capillary blood $PaCO_2$ measured near term correlates with length of oxygen dependency in CNLD, oxygen dependency is impossible to predict for an individual.[92] In general, however, those with a higher $PaCO_2$ are more likely to require oxygen for longer. The length of time that infants with CNLD remain on LTOT varies, but it is usually less than 12 months, although some require it for several years.[35,93,94] Persisting symptoms or failure to progress warrants review to rule out such conditions as tracheobronchomalacia, large airway stenosis or granuloma formation, gastroesophageal reflux, recurrent aspiration, or unsuspected congenital cardiac disease.

There is enormous variety of practice with regard to criteria used by pediatricians about when to discontinue LTOT in children with CNLD, which reflects a lack of evidence on which to base guidelines.[95] During periods of weaning or withdrawal of oxygen, more frequent monitoring is needed. It is not normally necessary for the child to have a SaO_2 monitor kept in the home because one can be provided for intermittent monitoring. Recording should include monitoring during daytime activity, feeding, and sleep. Short-term awake SaO_2 measurements do not predict prolonged sleeping SaO_2.[32] The same target saturations used to decide on initiation of supplementation are used for weaning purposes (92%–94%). Saturation targets in the physiologic range (95%–98%) may be thought to be desirable in infants with pulmonary hypertension. In a study using 2-hour room air challenges, most infants reached their lowest saturations within 40 minutes of discontinuing oxygen and a level of 92% or greater best predicted readiness for weaning judged by 6 months of follow-up.[96] Furthermore, infants requiring an oxygen flow rate of 0.02 L/min per kilogram of body weight were most likely to be successfully weaned.[96]

Some units wean infants from continuous low-flow oxygen to nighttime and naps only, whereas others maintain continuous oxygen until the child has no requirement at all; there is no evidence to recommend which approach is best. When the oxygen requirement is minimal, the children should have supervised weaning into air with continuous monitoring (including active periods and sleep). The babies tend to be weaned down to an oxygen flow rate of 0.1 L/min using a low-flow meter, and from that level, they can usually be weaned straight to air. Although extremely low (or ultralow) flow meters exist (range: 0.025–0.2 L/min), allowing the flow to be reduced even further before weaning to air, this is usually unnecessary. There is also concern that some caregivers may become confused by the decimal points. Weaning is preferably done at home because this minimizes the chances of nosocomial infection, although a child may sometimes need a brief hospital admission. It is usually prudent to ensure that the child has coped with at least one viral upper respiratory tract infection without problems before the equipment is removed from the home, and it should be left there for a few months, especially in the winter.

Recommendation: The same target saturations used to decide on initiation of supplementation should be used for weaning purposes (92%–94%). Higher saturation targets (95%–98%) may be used in infants with pulmonary hypertension. Recommendation B, quality of evidence: low.

Infants can be weaned from continuous low-flow oxygen to provision of oxygen during nighttime and naps only or remain in continuous oxygen on a 24-hour basis until the child has no requirement at all. Recommendation I, quality of evidence: poor.

EQUIPMENT

Provision of equipment depends on local arrangements and availability, but there are some general principles.[3]

- Oxygen concentrators are usually the preferred devices with large back-up cylinders for breakdown (which must be secured to a wall). They work by filtering room air and removing the nitrogen to increase the oxygen concentration.
- Oxygen concentrators need two outlets, one in the child's bedroom and one in the main living room area.
- Portable cylinders are required for ambulatory use. Although many find lightweight cylinders easier to handle, the standard-weight cylinders last longer outside the home.

- Oxygen cylinders may be more appropriate if initial flow rates are lower than 0.3 L/min and the anticipated duration of oxygen therapy is less than 3 months. A back-up cylinder must be available for those on continuous oxygen. Particular attention must be paid to safety and securing of cylinders in the presence of young children.
- Low-flow meter (0.1–1 L/min) must be available for infants and extremely young children.
- A humidification system is often required for those on flow rates greater than 1 L/min for nasal comfort. Cold bubble humidifiers may be used for this purpose, but they only achieve 40% relative humidity and are inadequate for direct airway humidification (eg, by means of a tracheostomy). Heated humidification is less convenient for domestic use and is only effective at flow rates of 4 L/min or higher delivered by a concentrator because water can block the tubing at lower flow rates.
- Appropriately sized soft twin-prong nasal cannulae (small children rarely tolerate >2 L/min by nasal cannulae), a face mask, and nonkinking extension tubing must be provided. Stomahesive (or equivalent) should also be provided to protect the skin in those using nasal cannulae.
- An oxygen conserver is a device to ensure that oxygen is delivered from the cylinder only during inspiration, which prolongs the cylinder life up to threefold. They are said to be usable in older children (>8 years of age) but are generally not used in pediatric practice because of the often irregular and shallow breathing patterns of children.
- Ambulatory equipment must be available as part of the oxygen delivery systems unless oxygen is only required at night. This must be lightweight so that older children can handle it themselves, and for infants, it must fit on to a pram or push chair. Parents need advice on the type of pram to buy (ie, one with a metal basket underneath that is safe and strong enough to hold the cylinder).
- Children in wheelchairs need to have cylinder fitting provided by their wheelchair service to maintain safety.

Oxygen Saturation Monitor (Pulse Oximeter)

The issue of whether parents should be provided with their own saturation monitor has been an area of debate in the United Kingdom. If a child requires continuous monitoring, it is unlikely that he or she is ready for hospital discharge. There is no evidence that provision of oximeters improves the outcome of babies on home oxygen (or that it does not); however, in practice, they may lead to excessive adjustments of the flow rate by the caregivers.[86] They may also give false reassurance, and SaO_2 is only one aspect of the baby's respiratory status. Some parents, however, request one for spot measurements as a guide to when oxygen needs increasing, during, for example, a viral cold. In fact, the baby should be seen in these circumstances, usually by the home care nurse, who can then make a proper assessment. In addition, the use as an overnight ''alarm'' is often unsatisfactory because of the number of false alarms, mostly from movement artifact. Nevertheless, the American Thoracic Society has supported the provision of oximeters to parents, but their rationale seems to be mostly cost based in terms of reducing hospital and office visits.[97]

OXYGEN OUTSIDE THE HOME

School

There is a small but important demand for oxygen therapy to be available in schools. Liaison is required between the specialist pediatric respiratory team and education

health services, and this is usually coordinated by community pediatric services. The following need particular consideration:

- Oxygen delivery equipment must be lightweight and easy for the child to handle and adjust.
- Safety devices must be in place for stabilizing oxygen cylinders or other equipment.
- Insurance coverage must be obtained by the school for the staff and premises.
- Adequate technical back-up must be available.
- School staff must be trained in the use of oxygen therapy.
- School staff must have easily identified health care contacts.
- Provision must be made for ambulatory oxygen for the journey to and from school.

Holidays and Airplanes

Arrangements can and should be made for oxygen concentrators and cylinders to be in place so that families can go away on holiday. Oxygen-dependent children need an increased flow rate during air flight because of the drop in air pressure, and hence equivalent FIO_2 to 0.15 at cruising altitude; the issue of preflight testing has been reviewed recently.[98]

SUMMARY

The use of domiciliary oxygen is significant, with approximately 3500 children receiving it in England and Wales. The evidence base behind this is poor, although evidence for its use in CNLD (the most common indication) is reasonable. Lack of evidence should not mean, however, that it is wrong to prescribe domiciliary oxygen, and common sense and clinical experience must prevail. Studies are urgently needed because, currently, we are not even sure of the ideal target SaO_2.

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