

REVIEW

Oxygen administration in infants

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The main methods of oxygen administration to infants are reviewed. Some methods are more economical and therefore more useful in developing countries. All the methods have potential complications and therefore need to be carefully supervised.

There are several different methods of non-invasive oxygen administration: head box oxygen, holding an oxygen source close to the infant's face, facemask, nasal prongs, nasal catheter, and nasopharyngeal catheter (fig 1). Oxygen administration is a routine procedure in the care of ill neonates and infants and therefore it is important to know the efficacy, the risks, and the impact on lung function of the methods used.

Arterial oxygen saturation is one of the determinants of oxygen transport. Pulmonary diseases with ventilation-perfusion inequalities lead to diminished arterial oxygen saturation and are amenable to oxygen treatment—that is, administration of an increased fraction of inspired oxygen (F_{iO_2}). In neonates and infants, such diseases include hyaline membrane disease, pneumonia, bronchopulmonary dysplasia, bronchiolitis, and pulmonary oedema.

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World wide, acute infections of the lower respiratory tract kill more than 4 million children every year, most of them less than 5 years of age. They are the leading cause of death in that age group and 99% of the deaths occur in developing countries.¹ Oxygen therapy is often life saving. There is a substantial reduction in mortality when oxygen is given to hypoxic patients with very severe pneumonia, as shown for children in Papua New Guinea.^{2,3} Looked at from this world-wide perspective, the safety and cost of oxygen therapy are most important. In developing countries, safe, simple, effective, and inexpensive methods of oxygen administration are favoured. The World Health Organisation (WHO) recommends nasopharyngeal catheters and nasal cannulae as safe and efficient means of oxygen administration.² These methods are also useful in the industrialised world because they have the potential to reduce the risks of treatment. Therefore, the present review applies to the practice in developing and developed countries equally.

There are few infant data on headbox and facemask oxygen, although these methods are regularly used in practice in developed countries. Therefore, this review concentrates on oxygen

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delivery by nasal cannula, nasal catheter, and nasopharyngeal catheter. The studies on the latter methods were performed in infants weaned from ventilation for respiratory distress syndrome and heart surgery, and in infants requiring supplemental oxygen flow for apnoea of prematurity, bronchopulmonary dysplasia, and pneumonia.

HEADBOX OXYGEN (FIG 1A)

Of the methods discussed, this is the only one that allows the F_{iO_2} to be determined precisely. The oxygen concentration should be measured by an oxygen analyser placed near the baby's mouth. There is no increased risk of airway obstruction by mucus and gastric distension. Humidification is not necessary.² Headbox oxygen is generally well tolerated, although the limitations placed on mobility are undesirable when prolonged oxygen treatment is required. Furthermore, the enriched oxygen environment is disturbed when feeding or suctioning is required.⁴ Giving oxygen by headbox needs relatively high flows to achieve adequate concentrations of oxygen and avoid carbon dioxide accumulation. Carbon dioxide toxicity may occur with low flows of oxygen caused by kinking or disconnection of the oxygen tubing and inappropriate tight seal of the box around the infant's neck. A gas flow of 2–3 litres/kg/min is necessary to avoid rebreathing of carbon dioxide (J Tibballs and M Hochmann, Royal Children's Hospital, Melbourne, unpublished).

FACEMASK (FIG 1B)

As with headbox administration, there is a danger of carbon dioxide accumulation if the flow of gas into the facemask is too low. If spontaneous inspiratory flow rates exceed the delivered oxygen flow rate, then there is room air entrainment through the perforations of the mask. The oxygen concentration delivered varies, depending on the infant's inspiratory flow rate and the oxygen flow into the system. The effective oxygen fraction (hypopharyngeal oxygen fraction, F_{HO_2}) is difficult to predict, but it is rarely above 40%.⁵ However, there are no data in newborns and infants. Small children will often refuse to keep a mask over their face. The mask also interferes with feeding.

OXYGEN ADMINISTRATION BY HOLDING AN OXYGEN SOURCE NEAR THE INFANT'S FACE (FIG 1C)

This kind of oxygen administration is widely used for short periods—for example, after extubation

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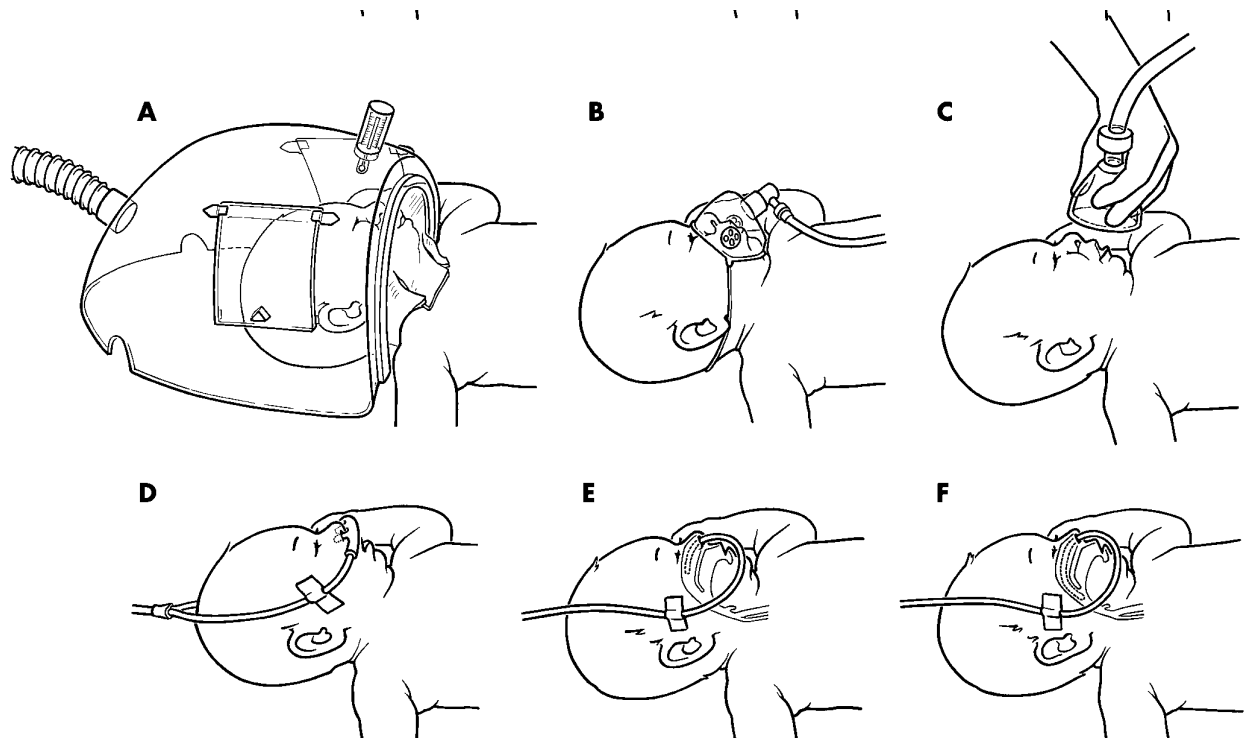


Figure 1 (A) Headbox oxygen; (B) facemask; (C) oxygen administration by holding an oxygen source near the infant's face; (D) nasal cannulae; (E) nasal catheter; (F) nasopharyngeal catheter.

or when breast feeding an infant who is on headbox oxygen. Owing to the dilutional effects of ambient air, the effective F_{IO_2} —that is, the hypopharyngeal F_{IO_2} —may be low and is unpredictable. Infants dependent on supplemental oxygen should be given oxygen by nasal catheter when they are fed; this allows a more predictable and stable oxygen delivery.⁴

NASAL CANNULAE (FIG 1D)

Nasal cannulae, nasal catheters, and nasopharyngeal catheters are more invasive methods of giving oxygen, and questions arise about airway obstruction, gastric distension, the need for humidification, and changes in lung function.

Nasal cannulae are a device ending in two short tapered tubes (about 1 cm in length) that are designed to lie just within the nostrils. They are also called nasal prongs. This is the preferred method of home oxygen therapy in infants.⁶⁻⁸ Older infants with chronic lung conditions may find it difficult to keep nasal cannulae on, particularly at night.

There is no risk of gastric distension, as it is not possible to push them in too far. Humidification is not required with nasal cannulae.⁹ The natural nasal mechanisms are heating and humidifying the inspired gases. There is only a slight risk of airway obstruction by mucus.² Weber *et al*¹⁰ observed complete nasal obstruction in eight out of 62 children (age range seven days to five years) with nasal cannulae.

The F_{IO_2} reaching the patient's airway is not easy to determine. Vain *et al*¹¹ measured the F_{HO_2} . F_{HO_2} is almost identical with the tracheal oxygen concentration, and is therefore a reliable measure of the actual F_{IO_2} the infant is breathing.¹²⁻¹³ Ten infants receiving 0.5 or 1 litre/min oxygen through nasal cannulae were examined (table 1).¹¹ In a recent study, the same oxygen delivery system produced lower F_{HO_2} values with the same flows (table 1).¹⁴ F_{HO_2} was inversely related to respiratory rate and therefore probably minute ventilation. Whether the mouth was open or closed did not affect F_{HO_2} . The authors were concerned about possible oxygen toxicity associated with the high F_{HO_2} values they found. However,

these levels were measured with exceedingly high oxygen flows not mentioned in any other paper. Fan and Voyles¹⁵ used an indirect method to determine the "true" F_{IO_2} . They measured the transcutaneous P_{O_2} for a given nasal cannula flow, and then placed the infants into a headbox to evaluate the F_{IO_2} necessary to reach the same transcutaneous P_{O_2} (table 1). In infants > 3500 g, 1 litre/min 100% nasal cannula oxygen produced an actual F_{IO_2} of 30%, which is considerably less than the value obtained by Vain *et al*. However, Fan and Voyles used a different nasal cannula system (a 10 F Hudson oxygen catheter was secured under both nares) and the infants studied were larger. In fact, they found that smaller infants (< 3500 g) required lower flow rates to deliver a given F_{IO_2} (table 1). Wilson *et al*¹⁶ measured F_{HO_2} in very premature infants (table 1). The 0.5 litre/min value is comparable to the finding of Vain *et al*¹¹ in larger infants. Wilson *et al* observed wide variation in the F_{HO_2} readings for any given infant (however, no measure of distribution is given). Finer *et al*¹⁷ measured F_{HO_2} in newborn infants receiving low flow nasal cannula oxygen (table 1). They found weight dependent values.

The F_{HO_2} studies show that the actual F_{IO_2} depends on the cannula flow rate, the F_{IO_2} in the cannula gas flow, the relation between prong and nasal diameters, and the patient's body weight. F_{HO_2} may further depend on minute ventilation and the relative duration of inspiration and expiration.¹⁸ Whether the amount of mouth breathing affects F_{HO_2} is controversial.^{14, 18} Sedated infants may have compromised upper airway patency with decreased minute ventilation.¹⁹ Therefore, sedated infants on nasal cannula oxygen may have a lower F_{HO_2} than unsedated infants. On the other hand, nasal cannula flow has been shown to produce positive distending airway pressure,^{20, 21} and Hammer *et al*¹⁹ showed that the application of continuous positive airway pressure (CPAP) in sedated infants improved minute ventilation. Thus, nasal cannula oxygen of sufficient flow may increase the actual F_{IO_2} , even in sedated infants. The actual F_{IO_2} may decrease with mouth breathing.² Even neonates are not exclusive nose

Table 1 Hypopharyngeal oxygen concentrations (F_{HO_2}) generated with different methods of oxygen administration

Method	Reference	Weight (g)	Cannula/catheter diameter*	Oxygen flow (litres/min)	Mean F_{HO_2} (%)
Headbox					$F_{HO_2} = F_{IO_2}$ in box
Facemask					No data
Oxygen line to face					No data
Nasal prongs	Wilson <i>et al</i> ⁶	932 (mean)	1 mm	0.2	42
			1 mm	0.3	40
			1 mm	0.5	45
	Finer <i>et al</i> ¹⁷	590–1315	1 mm	0.2	83
		1580–4020	1 mm	0.2	47
	Vain <i>et al</i> ¹¹	1780–4090	1 mm	0.5	45 (SD 10)
			1 mm	1	65 (SD 9)
	Kuluz <i>et al</i> ¹⁴	3000–10000	1 mm	0	20 (SE 0.4)
			1 mm	0.5	35 (SE 1.7)
			1 mm	1	45 (SE 1.8)
			1 mm	2	57 (SE 3.7)
			1 mm	3	70 (SE 2.5)
			1 mm	4	73 (SE 2.7)
	Fan & Voyles ¹⁵	<3500	10 F	0.5	35†
		>3500	10 F	0.5	28†
			10 F	1	31†
			10 F	2	35†
Nasal catheter					No data
Nasopharyngeal catheter	Shann <i>et al</i> ¹	1400–1000	8 F	150 ml/kg	50†

*External diameter at distal portion of cannula/catheter; 1 mm cannula: Infant Nasal Cannula, Salter Labs, Arvin, California, USA.
†Indirect measurement (owing to positive end expiratory pressure production, the measured value may be higher than the real F_{HO_2} ; see text).
SD, standard deviation; SE, standard error of mean.

breathers; they are preferential nose breathers. The high position of the larynx and consequent close apposition of the tongue to the palate contribute to the difficulty the newborn finds in breathing through the mouth.²² However, they may use the mouth for ventilation, both spontaneously and in response to complete nasal occlusion, and this ability increases with postconceptional age.^{23, 24} In healthy, awake neonates, reducing the cross sectional area of nasal dimensions by 50% (by occlusion of one nostril) did not affect tidal flow loops or passive respiratory mechanics.²⁵

How should the amount of oxygen applied be regulated: by changing the flow rate or the oxygen concentration, or both? Removing the need for an oxygen blender would definitely simplify oxygen delivery. Finer *et al*¹⁷ were able to deliver a wide range of F_{HO_2} values to premature and full term newborns using 100% oxygen and a low range flowmeter (25–200 ml/min). Benaron and Benitz¹⁸ analysed the theoretical impact of different weaning strategies on the stability of the actual inspired oxygen concentration. Variability in oxygen delivery is minimal when nasal cannula flow is reduced to the lowest possible flow by using undiluted (100%) oxygen; only then should the cannula oxygen concentration be reduced below 100%. This strategy requires microcalibrated flowmeters. The data of Vain *et al*¹¹ suggest that reducing the F_{IO_2} below 60% has little utility, because of the minimal change in the F_{HO_2} that occurs with a flow change from 1 litre/min to 0.25 litre/min.

When administering supplemental oxygen, the relevant end point is not the F_{HO_2} but the arterial oxygen tension (P_{aO_2}) or the arterial oxygen saturation. F_{HO_2} may not be the only determinant of arterial oxygenation. Nasal cannula oxygen application may produce positive end expiratory pressure (PEEP), which by itself is known to increase P_{aO_2} .^{26–28} There are three studies measuring PEEP production in infants on nasal cannula oxygen (table 2).^{20, 21, 29} In all of these studies, oesophageal balloon manometry was used. Oesophageal pressure is an indirect measure of pleural pressure.³⁰ Therefore, if there is an increase in end expiratory oesophageal pressure when nasal cannulae are applied, this suggests that PEEP is being applied. Locke *et al*²¹ examined premature infants. With 1 mm cannulae there was no change in oesophageal pressure, and therefore no PEEP, on all analysed flows. However, the wider cannulae (3 mm) produced PEEP (table 2). In another study, examining larger infants, 1 litre/min oxygen adminis-

tered through cannulae with an outer diameter of 2 mm generated no significant PEEP (table 2).²⁹ However, Sreenan *et al*²⁰ showed that high flows of oxygen administered through 1 mm cannulae generated PEEP: in 1000 g babies, the mean flow required to produce a PEEP of 4.5 cm H_2O was 1.6 litres/min, and in 2000 g babies, the flow for the same PEEP was 2.3 litres/min (table 2). The same authors showed that high flow nasal cannulae were as effective as conventional nasal CPAP in the management of apnoea of prematurity.

NASAL CATHETERS (FIG 1E)

A nasal catheter is a thin, flexible tube which is passed through the nose and ends with its tip in the nasal cavity. A catheter passed for a distance that is equal to the distance from the side of the nostril to the inner margin of the eyebrow usually reaches the posterior part of the nasal cavity. In infants, this distance is about 2.5 cm. Nasal catheters are usually well tolerated, and they are unlikely to be dislodged. Humidification of the oxygen is not necessary, because the tip of the catheter lies in the nasal cavity.² They can become blocked with mucus, and accumulation of mucus can cause upper airway obstruction. The risk of displacement into the oesophagus, with a risk of gastric distension, is small. However, a nasogastric tube should be in place at the same time (in the same nostril).

There is one physiological study of nasal catheters. In 12 infants, the transcutaneous oxygen tension was measured with 1 litre/min nasopharyngeal oxygen (with the tip of the catheter just visible below the soft palate), and again with the catheter withdrawn so that it was only 2.5 cm inside the nostril (nasal catheter).³¹ The mean transcutaneous oxygen tension was substantially lower when the tip of the catheter was placed in the nose rather than in the pharynx (mean difference 56 mm Hg, 95% confidence limits 34 to 78 mm Hg). Thus, nasal catheters require a higher oxygen flow to achieve a given transcutaneous oxygen tension.

NASOPHARYNGEAL CATHETERS (FIG 1F)

Nasopharyngeal catheters are inserted into the nose to a depth equal to the distance from the side of the nose to the front of the ear, so that the tip of the catheter is just visible in the pharynx below the soft palate when the mouth of the

Table 2 Positive end expiratory pressure (PEEP) generated with different methods of oxygen administration

Method	Reference	Weight (g)	Cannulae/catheter diameter*	Oxygen flow (litres/min)	PEEP (cm H ₂ O)
Headbox					0
Facemask					No data
Oxygen line to face					0
Nasal cannulae	Locke <i>et al</i> ²¹	1600 (mean)	1 mm	0.5	0
			1 mm	1	0
			1 mm	2	0
			3 mm	0.5	1.4 (SE 0.5)
			3 mm	1	4.2 (SE 0.5)
			3 mm	2	9.8 (SE 1.0)
	Sreenan <i>et al</i> ²⁰	1000	1 mm	1.6	4.5
			2000	1 mm	2.3
	Frey <i>et al</i> ²⁹	5900–11800	2 mm	1	2.4 (SD 3.4)
Nasal catheter					No data
Nasopharyngeal catheter	Frey <i>et al</i> ²⁹	5900–11800 3900–11800	6 F	1	0.8 (SD 2.3)
			8 F	0.5	1.6 (SD 1.4)
			8 F	1	2.8 (SD 2.7)
			8 F	2	4.0 (SD 2.9)

* 1 mm cannula: Infant Nasal Cannula, Salter Labs, Arvin, California, USA; 2 mm cannula: Pediatric Nasal Cannula, Salter Labs; 3 mm cannula: no 3331, HospTak, Inc, Lindenhurst, New York, USA.

infant is open.² In infants, this distance is about 7 cm. Like nasal catheters, nasopharyngeal catheters can easily be secured in place so that they are unlikely to be dislodged, and there is no danger of hypercarbia if the oxygen is turned off or the tubing disconnects. Nasopharyngeal catheters can also become blocked with mucus, and accumulation of mucus can cause upper airway obstruction. In the study of Weber *et al*¹⁰ in the Gambia, in 24 out of 56 children with nasopharyngeal catheters, complete nasal obstruction was observed. For that reason, the catheter has to be taken out and cleaned or changed regularly. Oxygen given through a nasopharyngeal catheter is bypassing the humidifying and warming properties of the nose. Effective humidification is therefore essential to avoid drying of the pharyngeal mucosa and to reduce the likelihood of inspissated secretions.³² However, it has been shown that a cheap, unheated bubble humidifier gives acceptable results when low flows of oxygen (0.5–1.0 litres/min) are given in warm climates.³³ Removing and cleaning the catheter twice a day is also of importance.³³ There is a risk that the catheter will be displaced downward into the oesophagus and cause gastric distension. A nasogastric tube should therefore be passed to permit rapid decompression of the stomach.³²

There are two studies evaluating the flow rates through nasopharyngeal catheters necessary to achieve adequate oxygenation.^{10, 31} Shann *et al*³¹ indirectly measured the effective F_{iO_2} . They showed that, in children less than 2 years old, a flow of 150 ml/kg/min through an 8 F nasopharyngeal catheter resulted in the same transcutaneous oxygen tension as placing the child in a headbox containing 50% oxygen (table 1). Further, they found that the smaller 5 or 6 F catheters were much less effective than 8 F catheters. They recommended 0.5 litres/min oxygen through an 8 F nasopharyngeal catheter in newborn infants with pneumonia, and 1 litre/min in infants up to 12 months, in accordance with the WHO guidelines. Weber *et al*¹⁰ determined in a crossover design (nasopharyngeal catheters and nasal cannulae) the flow rates necessary to achieve a pulse oximeter oxygen saturation of 95% in 60 children with a lower respiratory tract infection. The cannulae needed, on average, 26% higher oxygen flow rates than the nasopharyngeal catheters ($p = 0.003$).

Again, as discussed for nasal cannulae, nasopharyngeal oxygen application could generate PEEP and the improvement in oxygenation may be due to an increase in F_{iO_2} or PEEP or both (table 2). In fact, significant increases in PEEP have been shown in nine infants receiving oxygen through 8 F nasopharyngeal catheters (table 2).²⁹ The highest PEEP achieved was 6.3 cm H₂O at a flow rate of 1 litre/min, and 10.6

cm H₂O at a flow rate of 2 litres/min. In the same study, at a flow rate of 1 litre/min the smaller 6 F catheter did not produce a significant increase in PEEP (table 2).²⁹ The impact of the 8 F nasopharyngeal catheter on lung function was further evaluated.²⁹ There was a significant correlation between the generated PEEP levels and dynamic lung compliance. There was no significant difference in $Paco_2$ at the three flow rates, whereas minute ventilation was significantly less with nasopharyngeal oxygen than at baseline. There was an appreciable flow dependent increase in mean Pao_2 . The mechanisms of action of PEEP on the Pao_2 may be related to an increase in functional residual capacity, alveolar recruitment, reduced work of breathing, or an improvement in the distribution of ventilation to perfusion.^{27, 28}

The PEEP generated by nasal cannulae and nasopharyngeal catheters may be beneficial and a welcome byproduct of this kind of oxygen administration, as long as its magnitude is moderate. CPAP has the potential risk of pneumothorax,³⁴ pulmonary interstitial emphysema,³⁵ and pneumopericardium.³⁶ Pneumothorax may precipitate cerebral haemorrhage in premature infants.³⁷ Therefore, it is very important to know the magnitude of PEEP applied.

CONCLUSION

There are non-invasive means of oxygen administration (headbox oxygen, holding an oxygen line to the infant's face, and facemask oxygen) and methods involving the insertion of cannulae or catheters for a defined distance into the upper airways ("semi-invasive"). In the latter methods, the impact on lung function has to be taken into account. There is uncontrolled PEEP production, which may be beneficial up to a moderate degree of about 5 cm H₂O by altering the viscoelastic properties of the lung, but may be detrimental if higher. The level of the generated PEEP is positively associated with the oxygen flow, the cannula or catheter diameter, and the distance to which the catheter is inserted into the nasopharyngeal airway, and negatively with the infant's weight. In premature infants (1000 g), up to 1 litre/min given through 1 mm nasal cannulae is safe, and in infants (4–12 kg) up to 1 litre/min given through 2 mm nasal cannulae or 8 F nasopharyngeal catheters is safe with regard to the risk of excessive PEEP production.

"Oxygen treatment is often life saving, but medical oxygen is very expensive for developing countries and therefore methods involving low oxygen flow are economically advantageous"

Oxygen treatment is often life saving, but medical oxygen is very expensive for developing countries and therefore methods involving low oxygen flow are economically advantageous. Headboxes and facemasks need high flows to achieve adequate oxygenation. The "semi-invasive" methods (cannulae and nasopharyngeal catheters) need less oxygen, with nasopharyngeal catheters being the most economic method. The use of undiluted oxygen is advantageous: there is no need for a blender, and weaning can be achieved by simply decreasing the oxygen flow.

All methods of oxygen administration need supervision by trained personnel to detect and manage complications appropriately. The main complications are hypercarbia with headbox and facemask oxygen, dislodgement with nasal cannulae, and obstruction of the catheter or upper airway, as well as gastric distension, with nasopharyngeal catheters.

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