

# Low-flow anaesthesia in infants and children

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During the past 10 yr, there has been a revival of interest in low-flow anaesthesia in adult practice. This appears to reflect a desire to minimize wastage of expensive volatile anaesthetic agents and reduce atmospheric pollution. However, paediatric anaesthetists have been more cautious about adopting low-flow methods. The aim of this review is to examine critically some of the concerns about the use of low-flow anaesthesia in infants and children, with a view to encouraging greater use of the method in these patients.

## Definitions of low-flow and closed system anaesthesia

White and Baum separately defined low-flow anaesthesia in terms of the fresh gas flow rate at which a given level of rebreathing occurs in an absorber system (onset of rebreathing and rebreathed fraction of 50%, respectively).<sup>3,69</sup> These definitions appear somewhat cumbersome and fail to specify an exact flow below which 'low flow' may be said to occur, as the degree of rebreathing at any given flow depends on the precise arrangement of the breathing system. Accordingly, I suggest that low-flow anaesthesia should be defined as the use of a flow rate less than the patient's alveolar ventilation, the latter being the minimum flow required to ensure adequate carbon dioxide elimination during spontaneous or controlled ventilation with the most efficient non-absorber breathing system, the enclosed Mapleson A.<sup>48,49</sup> The proposed definition differentiates clearly between high- and low-flow techniques and is applicable to both paediatric and adult patients.

Within this rather broad definition, a large number of specific techniques are possible, depending on the fresh gas flow chosen. However, it seems likely that the major advantages of the method are achieved only when the fresh gas flow is reduced to 1.0 litre min<sup>-1</sup> or less.<sup>4</sup> 'Closed system anaesthesia' is a term reserved for a technique in which significant leaks from the breathing system have been eliminated and maintenance fresh gas flow is just sufficient to replace the volume of gas and vapour taken up by the patient.

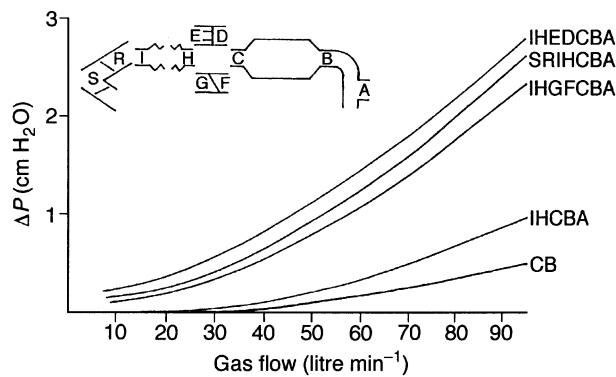
## Advantages and disadvantages

The major advantages of a carbon dioxide absorption technique were summarized by Waters as reduced loss of heat and moisture, economical use of anaesthetic gases and reduced operating theatre pollution.<sup>68</sup> It is also apparent that the use of low-flow anaesthesia promotes greater understanding of the function of anaesthetic equipment and the pharmacokinetics of inhalation anaesthesia<sup>38</sup>; this, and the extra vigilance required during low-flow anaesthesia, should benefit patient safety.<sup>11,15</sup> The ability to use standard equipment for patients of all ages is a further advantage of the low-flow method. This ability has been enhanced recently by the development of microprocessor-controlled ventilators capable of delivering pre-set tidal volumes to 20 ml (e.g. Dräger Cicero and Cato).<sup>55</sup> Disadvantages of the low-flow method include reduced ability to predict inspired oxygen and anaesthetic concentrations and the potential for carbon dioxide accumulation in the event of soda lime exhaustion.

Specific reservations of the use of low-flow anaesthesia in children can be divided into concerns about the use of circle systems *per se* and doubts about the feasibility and effectiveness of low-flow methods. The attitude of many paediatric anaesthetists to circle systems is reflected in the following quotation: 'They are much bulkier than the T-piece system . . . and have greater resistance due to the presence of inspiratory and expiratory valves. They are also complicated and have a greater potential for incorrect assembly'.<sup>27</sup> Doubt about the practicality of low-flow anaesthesia in children is evident in the following: 'Because of the difficulty in maintaining a leak free breathing system... children less than 5 years old . . . remain unsuitable candidates for low-flow anaesthesia'.<sup>10</sup> Although attitudes appear to be changing, a recent review of breathing systems for children maintains a bias for non-absorber breathing systems.<sup>42</sup>

## Concerns about the use of circle systems in children

Concerns about the use of circle systems in children seem to have started with two articles which appeared in the



**Fig 1** Variation in pressure with flow in various parts of a circle system. The arrangement of the circle system is shown in the diagram above the curves; the letters next to the curves indicate the direction and path of gas flow. Three different sets of valves were tested: SR=Y piece valves; ED=mushroom valves; GF=Adriani valves. IH=Flexible tubing; CB=absorber unit.<sup>53</sup>

American literature in the early 1950s. In the first, Stephen and Slater described 'early fatigue . . . and undesirable upset in body metabolism' in children breathing from an adult circle system, which they attributed to resistance in the tubing, valves and soda lime, and excessive deadspace under the face mask.<sup>62</sup> A short time later, Adriani and Griggs noted that the breathing of infants anaesthetized with an adult circle system was 'usually laborious and deep' which they attributed to hypercapnia secondary to excessive deadspace, ineffective absorption of carbon dioxide and breathing system resistance.<sup>1</sup> Neither of these early reports includes capnographic or acid-base data and it seems likely that their conclusions were based largely on clinical impression.

### Resistance to breathing

Resistance to breathing during anaesthesia occurs in the breathing system and in the tracheal tube. Traditionally, it is measured in terms of the pressure decrease across the equipment at a given flow rate. A study by Orkin, Siegal and Rovenstein revealed that in a typical circle system the tubes and absorber have about equal resistance and together account for about one-third of the total resistance of the system (Fig. 1).<sup>53</sup> Three sets of valves tested had practically the same resistance and accounted for two-thirds of the total resistance. Their data indicated that for an average adult, whose peak flow under anaesthesia is approximately 35 litre min<sup>-1</sup>, the pressure decrease across the complete system should be less than 0.75 cm H<sub>2</sub>O, while that across the valves should be less than 0.5 cm H<sub>2</sub>O. Contrary to a widely held belief that the resistance imposed by older anaesthetic breathing systems was unduly high, these values appear to be quite acceptable.<sup>52 70</sup> For an infant of 9 months, whose peak flow is approximately 10 litre min<sup>-1</sup>, the pressure decrease across the systems tested by Orkin, Siegal and Rovenstein should be less than 0.25 cm H<sub>2</sub>O. In contrast, the pressure decrease across a 3.5-mm tracheal tube in a 3-month-old infant with a peak flow of approxi-

mately 6 litre min<sup>-1</sup> should be approximately 2.5 cm H<sub>2</sub>O.<sup>7</sup> These values suggest that the resistance of the tracheal tube in a young infant is at least 10 times that of the circle system.

Anaesthetized infants cope remarkably well with acute increases in airway resistance, as shown by Graff and colleagues.<sup>25</sup> After a moderate increase in airway resistance in 10 anaesthetized infants, there was an immediate increase in the force of breathing, as reflected by oesophageal pressure, so that tidal and minute volumes were maintained for the duration of the test (10 min). The speed of the response suggested a reflex mediated by muscle spindles in the diaphragm. However, the authors also noted that ventilation was maintained at the cost of a three-fold increase in the work of breathing, which could lead eventually to hypercapnia and acidosis as a result of muscle fatigue.

### Apparatus deadspace

The response of paediatric patients to an increase in apparatus deadspace has been investigated by Charlton, Lindahl and Hatch.<sup>8</sup> These authors found that increasing the deadspace produced an immediate increase in end-tidal carbon dioxide concentration in anaesthetized infants and children. However, tidal and minute volumes increased by 40–50% over the next 10 min so that end-tidal carbon dioxide partial pressures returned to baseline values. They concluded that the short-term ventilatory response to an increased deadspace was adequate; nevertheless, apparatus deadspace should be minimized in equipment designed for children and controlled ventilation should be used liberally in infants.

### Paediatric circle systems

In adapting the circle system for paediatric use, it was originally assumed that all components of the apparatus should be reduced in proportion to the size of the patient in order to minimize deadspace and resistance.<sup>61</sup> Several miniaturized circle systems were produced, of which the Bloomquist Paediatric and Ohio Infant Circle Systems are possibly the best known.<sup>14</sup> However, the assumption that smaller valves would result in less resistance proved to be in error, as resistance is inversely proportional to the diameter of the valve.<sup>28</sup> Furthermore, being non-standard apparatus, all paediatric circle systems involved a considerable nuisance factor, requiring complete changeover from adult systems. Although some authors reported favourably on these systems, they did not gain wide acceptance and are little used today.<sup>17 63</sup>

### Anatomical and physiological differences

The respiratory system of the infant is disadvantaged in various ways compared with that of the adult.<sup>50</sup> The ribs in the infant are almost horizontal and contribute very little to respiration which is almost entirely diaphragmatic. Also, the infant diaphragm has fewer type I muscle fibres rendering it susceptible to fatigue.<sup>32</sup> Increased metabolism on a

weight basis in the infant is reflected in an increase in ventilation; but as tidal volume remains relatively constant throughout life ( $7 \text{ ml kg}^{-1}$ ), the increase is caused by an increase in ventilatory frequency. This is an inefficient way of increasing ventilation as a large proportion of the increase is wasted ventilating respiratory deadspace. The infant's chest wall is also relatively compliant compared with the lungs, so that FRC is reduced and small airways closure tends to occur at end-expiration.<sup>43</sup> This can lead to atelectasis and hypoxaemia. Anaesthesia with tracheal intubation probably aggravates these problems by preventing 'laryngeal braking', a important mechanism by which infants tend to maintain FRC above its true resting value.

Considerations such as these led Jackson Rees, in 1950, to recommend the use of controlled ventilation whenever anaesthesia was required in infants.<sup>31</sup> The rapid ventilatory frequencies and short expiratory times used with his T-piece technique may also have provided a measure of positive end-expiratory pressure (PEEP) necessary to counter the tendency to atelectasis in infants (Rees, personal communication). Acceptance of the need for controlled or assisted ventilation in infants appears to have occurred much later in the USA (around the mid 1960s)<sup>20 57 60</sup> but with it many of the arguments against the use of circle systems in paediatric anaesthesia disappeared, and by 1980 the use of adult circle systems with controlled or assisted ventilation was considered acceptable for patients of all ages.<sup>61</sup> To this should be added that controlled (rather than assisted) ventilation is the preferred option in neonates; indeed, it may be considered mandatory in this age group.<sup>17 44 56</sup> Also, while controlled or assisted ventilation is desirable in infants managed either with a circle system or a T-piece, spontaneous ventilation is permissible in children over 1 yr of age.<sup>9 59</sup>

In recent years, the use of an adult circle system for paediatric anaesthesia has become increasingly common in the USA,<sup>17 64</sup> although most paediatric anaesthetists do not use flow rates less than  $2 \text{ litre min}^{-1}$ .<sup>21</sup> When using adult circle systems for paediatric patients, connectors should be of minimal deadspace and it is advisable to substitute the standard 22-mm breathing tubes with 15-mm flexible lightweight plastic tubes (e.g. DAR SpA, 41307, Mirandola, Italy) to reduce bulk. In addition, the use of a smaller reservoir bag (800–1000 ml) enables better visual assessment of spontaneous ventilation possible in children aged more than 1 yr.

## Concerns about low-flow techniques in children

Concerns about the use of low-flow techniques in children include the problem posed by leaks in the breathing system, questionable economy and the problem of predicting inspired anaesthetic and oxygen concentrations. More recently, there has been anxiety about the possible accumulation of degradation products of sevoflurane, a promising alternative to halothane for paediatric anaesthesia.

## Leaks in the breathing system

Routine use of uncuffed tracheal tubes for airway maintenance in children is a potential source of leakage from the breathing system. Similarly, leaks may occur in a high proportion of cases managed with a laryngeal mask airway (LMA).<sup>45</sup>

The suggestion that there should be a leak around the tracheal tube during anaesthesia in children comes from the work of Koka and colleagues,<sup>37</sup> although a link between excessive tube size and tracheal stenosis in paediatric patients undergoing long-term ventilation had been established several years earlier.<sup>65</sup> In a large prospective series, Koka and colleagues found that 40 of 80 children who developed post-intubation croup had no leak around the tube at approximately  $25 \text{ cm H}_2\text{O}$ ; accordingly, they suggested that an appropriately sized tube should allow a leak at  $20\text{--}25 \text{ cm H}_2\text{O}$ . However, it is clear from their results that the presence of a leak around the tube failed to prevent croup occurring after operation in 50% of the observed cases. Contributing factors in these cases included trauma during intubation, coughing on the tube, change in position of the head and prolonged surgery.

In my view, the importance of a leak around the tube during anaesthesia has been exaggerated; there appears to be no basis for the commonly held belief that tubes should allow a leak in the usual working range  $0\text{--}20 \text{ cm H}_2\text{O}$ . Accordingly, my practice is to select the smallest tube which passes easily into the trachea and does *not* leak in the working range. Having used this approach for several years, I have not experienced an increase in problems with postoperative croup.

Recent studies challenge not only the need for a leak around the tube, but the apparent myth that cuffed tubes are contraindicated during anaesthesia in children. Thus, Khalil and colleagues found no correlation between the presence or absence of a leak at  $20\text{--}25 \text{ cm H}_2\text{O}$  and the severity of post-intubation croup in 159 healthy children undergoing anaesthesia for strabismus surgery.<sup>33</sup> Khine and colleagues allocated randomly 488 infants and children to undergo intubation with either a cuffed or an uncuffed tube.<sup>35</sup> Cuff pressure was regulated by use of a blow-off device to  $25 \text{ mm Hg}$  ( $34 \text{ cm H}_2\text{O}$ ). They found no difference in the incidence of postoperative complications, including croup, but there was a significant reduction in the need for repeated laryngoscopy, lower levels of operating theatre pollution and an increased ability to use low fresh gas flows in patients managed with a cuffed tube. However, a reduction in size of 1 mm internal diameter was necessary in order to pass a cuffed rather than an uncuffed tube. The resulting increase in resistance could be a disadvantage in smaller children undergoing anaesthesia with spontaneous ventilation.

In another study, Fröhlich and colleagues compared the seal obtained using an uncuffed tracheal tube selected according to the formula: internal diameter =  $16 + \text{age (yr)}/4$  (mm) or a size 2 LMA in 30 children aged

**Table 1** Mean (SD) [range] fresh gas flows used in infants (0–12 months), pre-school children (1–4 yr) and school-aged children (5–16 yr) managed either with an enclosed Mapleson A system or a circle system. \*\*\* $P < 0.0001$  between subgroups managed with the enclosed Mapleson A

	Infants 0–12 months (litre min <sup>-1</sup> )	Pre-school 1–4 yr (litre min <sup>-1</sup> )	School-age 5–16 yr (litre min <sup>-1</sup> )
Enclosed Mapleson A	1.4 (0.1) [1.2–1.6] (n=5)	2.2 (0.3) [2.0–2.4] (n=12)	3.2 (0.8)*** [2.9–3.6] (n=20)
Circle system	1.2 (0.4) [1.0–1.8] (n=10)	1.2 (0.3) [0.9–2.1] (n=19)	1.3 (0.2) [0.9–1.6] (n=11)

2–6 yr undergoing closed system anaesthesia with controlled ventilation.<sup>24</sup> Loss of gas from the system was less than 100 ml min<sup>-1</sup> in 13 (87%) children managed with a tracheal tube and in 12 (80%) children managed with the LMA. Maximum gas loss was approximately 700 ml min<sup>-1</sup> in the tracheal tube group and 350 ml min<sup>-1</sup> in the LMA group. The authors concluded that airway sealing with both devices was adequate to perform low-flow or closed system anaesthesia in young children.

#### *Economics of low-flow anaesthesia in children*

The question of the economy of low-flow anaesthesia in children has been examined in a study from this hospital.<sup>54</sup> We measured consumption of isoflurane and fresh gas flows in 77 infants and children aged 1 month–16 yr during 20, all-day operating lists. Patients were allocated to receive anaesthesia with controlled ventilation using an enclosed Mapleson A system (MIE Carden 'Ventmasta', A mode) or an adult circle system modified as described above. Fresh gas flows for the enclosed Mapleson A system were determined by the formula  $\dot{V}_F = 0.6 \times \sqrt{\text{weight (kg)}}$  litre min<sup>-1</sup>, approximating to normal alveolar ventilation.<sup>2 48</sup> Fresh gas flow for the circle system was initially set at 3 litre min<sup>-1</sup> for 5 min, followed by 1.5 litre min<sup>-1</sup> for a further 5 min before being reduced to a maintenance flow of 0.8 litre min<sup>-1</sup>. The initial periods of high flow were necessary to denitrogenate the system and to ensure adequate uptake of anaesthetic gas and vapour<sup>18 67</sup>; they were taken into account when calculating the mean fresh gas flows for the circle system.

The mean consumption rate of isoflurane for the enclosed Mapleson A group was 11.1 g h<sup>-1</sup> while that of the circle system group was 4.7 g h<sup>-1</sup>, a saving of 58% with the circle. Mean fresh gas flow for the enclosed Mapleson A group was 2.6 litre min<sup>-1</sup> compared with 1.2 litre min<sup>-1</sup> for the circle group, a saving of 54% with the circle. When mean fresh gas flows were stratified by age, the percentage saving with the circle was less in infants than those for pre-school and school-aged children (14% vs 45% and 59%), reflecting the fact that flow rates for the enclosed Mapleson A increased with age (Table 1). Under the conditions of the study, the use of low-flow anaesthesia resulted in substantial savings in volatile anaesthetic vapour

and gases in pre-school and older children. However, we found no contraindication to using the low-flow technique in infants who may benefit most from conservation of heat and moisture. As flow requirements for the more commonly used T-piece systems are at least one-third greater than those for the enclosed Mapleson A system during controlled ventilation,<sup>48</sup> it is apparent that greater savings would have been shown with the circle system in all age groups if one of the former had been used as our control. Not having to determine individual fresh gas flows using a complex formula was a further advantage of the low-flow method.

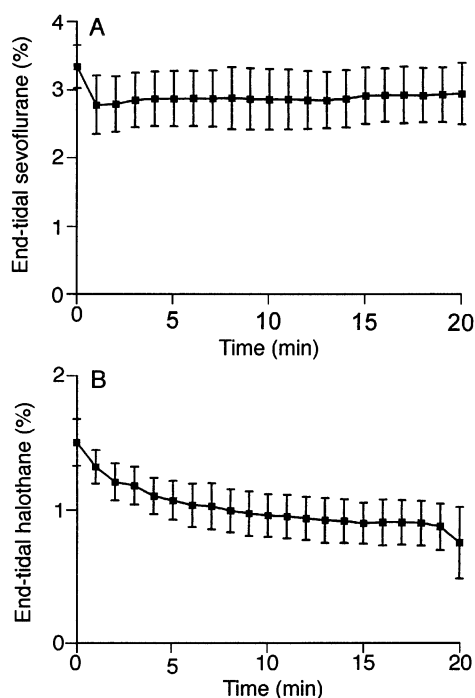
#### *Predicting volatile anaesthetic concentration*

Low-flow anaesthesia, as commonly practised with the vaporizer outside the circuit, carries the risk of accidental under-dose of volatile anaesthetic if there is failure to appreciate that there may be a significant difference between the inspired anaesthetic concentration and the concentration delivered from the vaporizer. The difference between fresh gas concentration and inspired–expired concentrations of inhaled anaesthetics is inversely related to the blood solubility of the individual agents; thus, predictable levels of anaesthesia may be achieved and maintained more easily at low-flow rates when the newer, less soluble, volatile anaesthetic agents, desflurane and sevoflurane, are used.<sup>39 51</sup> The use of volatile agent monitors permits precise control of the inspired anaesthetic concentration and is regarded as mandatory when fresh gas flows of less than 1 litre min<sup>-1</sup> are used.<sup>3 4</sup>

There is little information on the predictability of anaesthetic concentrations during low-flow anaesthesia in children. In a recent study at this hospital, 40 healthy children were randomized for maintenance of anaesthesia of short duration with sevoflurane or halothane using a low-flow technique.<sup>47</sup> Induction of anaesthesia was with 33% oxygen 6 litre min<sup>-1</sup> in nitrous oxide and either 8% sevoflurane or 5% halothane. After intubation, inspired concentrations were reduced to 4% and 2%, respectively. In the operating room, patients were connected to a circle system with a fresh gas flow of 6 litre min<sup>-1</sup> until the ratio of the expired and inspired anaesthetic concentrations ( $F_E/F_I$ ) was 0.8; at this point fresh gas flow was reduced to 0.6 litre min<sup>-1</sup>.  $F_E$  and  $F_I$  were then measured for another 20 min.

Mean time to low-flow in patients who received sevoflurane was 1.7 min while the time to low-flow for patients who received halothane was 2.8 min. After flow reduction, there was an initial rapid decline in sevoflurane concentration followed by a very gradual increase (Fig. 2A). Halothane concentration declined initially and then continued to decline to 20 min (Fig. 2B). These results suggest that the end of the initial rapid increase in  $F_E/F_I$  (signified by  $F_E/F_I = 0.8$ ) is an appropriate end-point to institute flow reduction with sevoflurane, which may therefore be regarded as a suitable agent for low-flow anaesthesia of short duration. In contrast, the progressive decline in halothane concentration after





**Fig 2** Variation in mean (SD) end-tidal concentrations of sevoflurane (A) and halothane (B) with time after flow reduction.<sup>47</sup>

flow reduction indicates significant continuing uptake after  $F_E/F_I$  0.8.

These results are in agreement with the analysis of Lin and colleagues<sup>40 41</sup> which emphasizes that the initial rapid rate of increase in  $F_E/F_I$  ratio demonstrated by Eger<sup>16</sup> reflects mainly FRC washin and not uptake of anaesthetic by the blood. According to Lin and colleagues, body uptake of anaesthetic agents should be maximal after the washin phase is complete; this will clearly have a greater impact on a relatively soluble agent such as halothane than on sevoflurane. In practice, the satisfactory performance of low-flow anaesthesia with moderately soluble anaesthetic agents such as halothane, enflurane or isoflurane, requires a fairly long initial period of high flow (approximately 15–20 min) together with a significant increase in the vaporizer setting after flow reduction (60–130%).<sup>3 18</sup> This being the case, it is clear that any subsequent change from low to high flow may result in serious overdose unless accompanied by a reduction in the vaporizer setting.

#### Oxygen concentration during low-flow anaesthesia

During low-flow anaesthesia, using a mixture of gases, an allowance must be made for the amount of oxygen consumed by the patient when calculating maintenance fresh gas settings. Failure to do this may result in unacceptably low levels of oxygen in the inspired gas (i.e.  $F_{I_{O_2}} < 0.3$ )<sup>13</sup> and possibly lead to oxygen desaturation. Foldes, Cervaolo and Carpenter's<sup>19</sup> solution to this problem was to calculate the oxygen consumption of the patient and subtract this from the desired fresh gas flow. The remainder of the fresh gas flow was then divided between nitrous oxide and oxygen

**Table 2** Oxygen ( $O_2$ ) and nitrous oxide ( $N_2O$ ) flowmeter settings for use with low-flow anaesthesia in paediatric patients. The flowmeter settings were calculated to provide an  $F_{I_{O_2}}$  of 0.33 with total fresh gas flows ( $\dot{V}_F$ ) of 1000 ml  $\text{min}^{-1}$  or 600 ml  $\text{min}^{-1}$  based on the upper limit of each weight range. Percentage oxygen concentration is provided for use with machines fitted with fresh gas mixing valves. All values are approximate

Age group	Wt (kg)	Flowmeter settings for $\dot{V}_F$ 1000 ml $\text{min}^{-1}$			Flowmeter settings for $\dot{V}_F$ 600 ml $\text{min}^{-1}$		
		$O_2$	Air	$O_2$ (%)	$O_2$	Air	$O_2$ (%)
Infants (< 1 yr)	3–10	400	600	40	250	350	40
Children (1–12 yr)	11–40	450	550	45	300	300	50
Adolescents (> 12 yr)	41–70	500	500	50	350	250	60

in the desired ratio and added to the calculated oxygen consumption to give the final flowmeter settings. The following formula was used to facilitate calculation of the oxygen flowmeter setting:

$$\dot{V}_{F_{O_2}} = \dot{V}_{O_2} + (\dot{V}_F - \dot{V}_{O_2}) \times F_{I_{O_2}} \quad (1)$$

where  $\dot{V}_{F_{O_2}}$  = oxygen flowmeter setting;  $\dot{V}_{O_2}$  = calculated oxygen consumption;  $\dot{V}_F$  = total fresh gas flow; and  $F_{I_{O_2}}$  = desired inspired oxygen concentration.

The nitrous oxide flowmeter setting ( $\dot{V}_{F_{N_2O}}$ ) was then obtained by subtracting the oxygen flowmeter setting from the total fresh gas flow:

$$\dot{V}_{F_{N_2O}} = \dot{V}_F - \dot{V}_{F_{O_2}} \quad (2)$$

Using this method, reliable guidelines for the control of oxygen concentration with flow rates less than 1.0 litre  $\text{min}^{-1}$  were drawn up for use in adults<sup>19 67</sup>; however, no comparable guidelines have been published for paediatric patients. Table 2 shows oxygen and nitrous oxide flowmeter settings calculated from the above formulae to provide a minimum  $F_{I_{O_2}}$  of 0.33 in three groups of paediatric patients (infants, children and adolescents) with total fresh gas flows of 1000 or 600 ml  $\text{min}^{-1}$ .

Oxygen consumption was calculated from body weight using a modified version of Brody's formula<sup>6 36</sup>:

$$\dot{V}_{O_2} = 10 \times \text{wt}(\text{kg})^{0.75} \quad (3)$$

The flowmeter settings shown in Table 2 have been rounded to 50 ml, being the usual limit of accuracy of the fine flow tubes used in clinical practice. In most cases this has resulted in increased oxygen flows, but where oxygen flows were decreased, this did not exceed 10 ml or 3% of the calculated setting. Percentage oxygen concentration has also been calculated for use with machines fitted with fresh gas mixing valves (e.g. Dräger Julian). In practice, fresh gas flows of both 1000 and 600 ml  $\text{min}^{-1}$  can be used satisfactorily in paediatric patients, although the use of the lower flow provides less room for error in setting the flowmeters. For reasons of safety, it is a requirement that  $F_{I_{O_2}}$  and  $Sa_{O_2}$  are monitored continuously when fresh gas flow is reduced to 1 litre  $\text{min}^{-1}$  or less.<sup>26</sup> Fresh gas flows

**Table 3** Oxygen ( $O_2$ ) and air flowmeter settings for use with low-flow anaesthesia in paediatric patients. The flowmeter settings are calculated to provide an  $F_{I_{O_2}}$  of 0.33 with total fresh gas flows ( $\dot{V}_F$ ) of 1000 ml  $\text{min}^{-1}$  or 600 ml  $\text{min}^{-1}$  based on the upper limit of each weight range. Percentage oxygen concentration is provided for use with machines fitted with fresh gas mixing valves. All values are approximate

Age group	Wt (kg)	Flowmeter settings for $\dot{V}_F$ 1000 ml $\text{min}^{-1}$			Flowmeter settings for $\dot{V}_F$ 600 ml $\text{min}^{-1}$		
		$O_2$	Air	$O_2$ (%)	$O_2$	Air	$O_2$ (%)
Infants (< 1 yr)	3–10	200	800	40	150	450	40
Children (1–12 yr)	11–40	300	700	45	250	350	50
Adolescents (> 12 yr)	41–70	350	650	50	300	300	60

should be adjusted, if necessary, to maintain acceptable  $F_{I_{O_2}}$  and  $Sa_{O_2}$  levels.

Occasionally, air may be preferred to nitrous oxide as a carrier gas for oxygen administered with or without a volatile anaesthetic agent. Air is indicated relatively often in infants as bowel distension caused by nitrous oxide can exacerbate surgical difficulty during abdominal closure and premature and sick neonates may not tolerate the depressant effects of nitrous oxide on the heart.<sup>58</sup> In older children and adults, air may be used similarly to avoid distension of air-containing cavities, or simply to avoid denitrogenation.<sup>66</sup> In calculating the flowmeter settings of air and oxygen for a given  $F_{I_{O_2}}$  during low-flow anaesthesia, it is probably simplest to start by calculating the air flowmeter setting from the known amount of pure nitrogen in a manner similar to that described for high-flow systems<sup>12</sup>:

$$\dot{V}_{F_{\text{air}}} = (\dot{V}_F - \dot{V}_{O_2}) \times (1 - F_{I_{O_2}}) / 0.79 \quad (4)$$

The flow of oxygen is then obtained by subtraction from total fresh gas flow:

$$\dot{V}_{F_{O_2}} = \dot{V}_F - \dot{V}_{F_{\text{air}}} \quad (5)$$

Table 3 shows the oxygen and air flowmeter settings required to provide a minimum  $F_{I_{O_2}}$  of 0.33 in three groups of paediatric patients with total gas flows of 1000 or 600 ml  $\text{min}^{-1}$ . It was constructed using the above formulae and Brody's formula for oxygen consumption (3). The error associated with rounding flows to 50 ml was similar to that for Table 2. Again, it is emphasized that fresh gas flows should be varied, if necessary, to maintain acceptable  $F_{I_{O_2}}$  and  $Sa_{O_2}$  levels.

Only one study has addressed the problem of ensuring adequate inspired oxygen concentration during low-flow anaesthesia in paediatric patients.<sup>55</sup> In this study, 20 infants weighing 2.2–6.0 kg were anaesthetized using standard i.v. or inhalation methods; tracheal intubation was facilitated with neuromuscular blocking agents and ventilation was controlled using a Dräger Cicero or Cato ventilator. Anaesthesia was maintained with isoflurane and 33–40% oxygen in nitrous oxide ( $n=14$ ) or air ( $n=7$ ). During the first 10 min of anaesthesia, the flowmeters were set to deliver a

high fresh gas flow of 4–6 litre  $\text{min}^{-1}$ . Thereafter, flow rate was reduced to 600 ml  $\text{min}^{-1}$  which was calculated as follows: the infant's oxygen consumption was set at 60 ml  $\text{min}^{-1}$  and the remaining fresh gas flow of 540 ml was split into 180 ml  $\text{min}^{-1}$  of oxygen and 360 ml  $\text{min}^{-1}$  of nitrous oxide or, 90 ml  $\text{min}^{-1}$  of oxygen and 450 ml  $\text{min}^{-1}$  of air, to ensure a minimum  $F_{I_{O_2}}$  of 0.33. (The theoretical basis for these calculations has been outlined above; the resulting flowmeter settings are similar to those shown for infants in Tables 2 and 3.) Duration of mechanical ventilation was 60 (30–115) min during which mean  $F_{I_{O_2}}$  remained greater than 0.33 (range 0.32–0.49) in all patients. Oxygen flow was increased in two infants with a post-conceptual age <31 weeks because of  $Sa_{O_2} < 95\%$ ; no increase in fresh gas flow was required to maintain the volume of the system. The authors concluded that low-flow anaesthesia was a safe technique in infants providing oxygen consumption of the patients was taken into account when calculating fresh gas flow.

#### *Degradation of sevoflurane by carbon dioxide absorbents*

The use of sevoflurane in low-flow systems has been the subject of controversy following the demonstration that a breakdown product, fluoromethyl-2,2-difluoro-1-(trifluoromethyl) vinyl ether (compound A), formed by a reaction with carbon dioxide absorbents, is nephrotoxic in rats. The concentration of compound A found in absorber breathing systems increases with decrease in gas flow, increased sevoflurane concentration, increased carbon dioxide production, increase in absorbent temperature and drying of the absorbent.<sup>5</sup> These increases are greater with the use of barium hydroxide lime (Baralyme) than with soda lime. Although inhaled concentrations of compound A sufficient to cause nephrotoxicity in rats (50 ppm) have been found during low-flow (0.5–1.0 litre  $\text{min}^{-1}$ ) sevoflurane anaesthesia in humans (67 ppm),<sup>23,34</sup> they are generally much lower and there have been no reports of compound A nephrotoxicity. Nevertheless, the Food and Drug Administration of the USA prohibited the use of sevoflurane in rebreathing systems with flow rates less than 2 litre  $\text{min}^{-1}$ .<sup>46</sup> In contrast, the Medicines Control Agency of the UK has not considered it necessary to impose such restrictions.

The nephrotoxic potential of sevoflurane in low-flow systems is of special concern to paediatric anaesthetists as the drug has several physical characteristics (e.g. low blood:gas solubility, non-pungent odour) making it attractive for use in paediatric patients. In a study of 19 infants and children undergoing 4 h of sevoflurane anaesthesia with a fresh gas flow of 2 litre  $\text{min}^{-1}$ , the mean maximum compound A concentration was 5.4 ppm, while the maximum concentration in a single patient was 15 ppm.<sup>22</sup> There was no evidence of abnormal renal or hepatic function up to 24 h after operation. Interestingly, maximum compound A concentration correlated with both maximum absorbent temperature and patient body surface area. These findings

probably reflect an increase in carbon dioxide production with increasing body size, and suggest that lower concentrations of compound A should be produced in paediatric patients compared with adults for a given absorbent and fresh gas flow.

Results of laboratory studies suggest that biotransformation of compound A–glutathione and cysteine conjugates by renal  $\beta$ -lyase may be important in the development of compound A nephrotoxicity in rats.<sup>30–34</sup> For example, in one study, inhibition of renal uptake of glutathione and cysteine conjugates and of their metabolism by renal  $\beta$ -lyase significantly reduced biochemical markers of renal injury in rats treated with intraperitoneal compound A.<sup>34</sup> Mediation of compound A nephrotoxicity by renal  $\beta$ -lyase may have implications regarding interspecies differences in the effects of compound A. Most importantly, renal  $\beta$ -lyase activity and  $\beta$ -lyase metabolism of compound A cysteine conjugates are approximately 8–30 times less in human than in rat kidney.<sup>29</sup> Accordingly, low human kidney  $\beta$ -lyase activity together with generally low concentrations of compound A in breathing systems during low-flow sevoflurane anaesthesia may explain the lack of compound A nephrotoxicity in humans.

## Conclusion

Low-flow anaesthesia offers several advantages in paediatric practice. The main impediments to its greater use appear to be persisting concerns about circle system resistance and deadspace, and the feasibility and safety of low-flow techniques in younger patients.

This review provided little support for the opinion that older circle systems imposed an excessively high resistance to breathing in infants and children, although it appears that the mechanical deadspace imposed by some Y-piece connectors was excessive.<sup>1</sup> Physiological factors such as muscle fatigue, inefficient ventilation and a tendency to lung collapse were probably responsible for some of the respiratory problems observed in young patients breathing spontaneously from these systems.<sup>1–31–62</sup> Current evidence suggests that if ventilation is controlled in neonates, and either controlled or assisted in infants, an adult circle system fitted with small bore tubing and a reduced capacity reservoir bag is suitable for paediatric patients of all ages.<sup>9–17–59–61</sup> Although experience with flow rates less than 1 litre min<sup>-1</sup> is limited in infants and children, recent studies have shown that the use of such flow rates can be both practical and safe. Airway sealing with both uncuffed tracheal tubes and the LMA is sufficient to perform low-flow anaesthesia in paediatric patients<sup>24–55</sup> and substantial savings in anaesthetic gases and vapours can be made.<sup>54</sup> It is important to recognize that there may be substantial differences between the oxygen and volatile anaesthetic agent concentrations in the fresh gas supply and the inspired gases. However, with the use of appropriate techniques and monitoring devices potential problems can be avoided.<sup>47–55</sup> Renewed interest in low-flow anaesthesia in adult practice and the development of

improved anaesthetic and monitoring equipment seem likely to encourage greater use of the method in paediatric patients.

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