not in a range expected to be clinically significant. The significantly lower prilocaine concentrations may indicate a greater margin of safety for prilocaine as compared to lidocaine in terms of potential systemic toxicity.

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Minimum Alveolar Concentration of Halothane for Tracheal Intubation in Children

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Deep inhalation anesthesia can be used for tracheal intubation in children when neuromuscular blockade is contraindicated. Gregory *et al.*[1] and Nicodemus *et al.*[2] have found age-related variations in the minimum alveolar concentration (MAC) that prevents movement after skin incision. Yakaitis *et al.*[3] found that the minimum alveolar concentration of halothane permitting tracheal intubation in 50% of children between the ages of 2 and 6 yr (MAC-EI) was greater than the MAC for skin incision (MAC-EI = 1.33%, MAC = 0.91%).[1,3] Although MAC is known for various age groups, there are no data on MAC-EI except for children between 2 and 6 yr.[3] Knowledge of MAC-EI is important for predicting the level of anesthesia that will permit laryngoscopy and tracheal intubation without patient movement or coughing. We, therefore, determined the MAC-EI in the age groups from 6 months to 12 yr. Patients under age 6 months were excluded from the study because of our inability to obtain precise and reproducible measurements of end-tidal gas concentrations.

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Materials and Methods

After obtaining institutional approval and written informed consent from the parent or legal guardian of the child, we studied 148 healthy ASA 1 and 2 children undergoing general endotracheal anesthesia for elective surgery. Patients were excluded if they had a history of prematurity or central nervous system disorders, or if they were receiving any drugs preoperatively.

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None of the children received premedications. Patients were divided into two groups: phase 1 (30 patients) to assess the accuracy of pharyngeal gas sampling; and phase 2 (118 patients) to determine MAC-EI.

Patients were anesthetized with halothane in 100% oxygen, using a Bain modification of a Mapelson D circuit in children below 20 kg, and a circle absorber system in others. Heart rate, arterial blood pressure, temperature, and oxygen saturation were monitored by standard methods. After induction of anesthesia, ventilation was controlled with large tidal volumes to achieve a plateau on the capnogram and an end-tidal carbon dioxide tension of 32–45 mmHg. Gas samples were aspirated from an 8 French suction catheter placed in the oropharynx. Inspired and end-tidal halothane, carbon dioxide, oxygen, and nitrogen concentrations were measured by a mass spectrometer (Perkin Elmer Mass Spectrometer MGA 1100®, Perkin-Elmer, Pomona, CA) that had been calibrated with gases analyzed to ±0.02% accuracy (Scott Medical Products, Plumsteadville, PA). If the end-tidal nitrogen concentration exceeded 0.5%, the oropharyngeal catheter and the seal around the face mask were adjusted to exclude contamination of gas samples by ambient air.

The inspired anesthetic concentration (Fi) was reduced after induction of anesthesia so that only a small gradient occurred between the inspired and end-tidal halothane concentrations. Before tracheal intubation was attempted, the end-tidal halothane concentration was maintained at a steady state for at least 10 min.

In phase 1 (the first 30 patients), we tested the accuracy of the gas sampling technique and performed tracheal intubation with neuromuscular blockade. Following intubation, a premeasured 19 gauge Deseret Intracath® catheter was inserted into the endotracheal tube until the hub fitted tightly at a modified elbow connector and the tip was within 1 cm of the distal end of the tracheal tube. Concentrations of gas from the first sample drawn through the catheter were compared with oropharyngeal concentrations drawn just prior to intubation. In children below 5 kg, mean tracheal and oropharyngeal values differed significantly (table 1). In patients weighing more than 5 kg, there were no significant differences in mean oropharyngeal and tracheal gas concentrations (table 2). We, therefore, excluded children below 6 months of age and 5 kg body weight from the next phase of the study.

In phase 2, 118 patients were studied to determine MAC-EI. Neuromuscular blocking agents were not used and conditions during tracheal intubation were reported as an all-or-none phenomenon of adequate or inadequate anesthesia. Adequate anesthesia was defined as the absence of laryngospasm, coughing, bearing down on the tracheal tube, or body movement during intubation. Individual data are presented in figure 1. MAC-EI calculations were based on the oropharyngeal concentrations and response to tracheal intubation.

TABLE 1. Demographic Data and Comparison of Oropharyngeal and Distal Tracheal End-tidal Halothane Concentrations in Phase 1 Subjects Below 5 kg Weight and Below 6 Months Age

Case #	Age	Weight (kg)	Temp (°C)	$\frac{(Fi-FA)}{FA} \times 100$ (%)	End-tidal Halothane Concentrations Samples from	
					Oropharynx (%)	Distal Trachea (%)
1	6 weeks	3.1	36.2	14.0	1.13	0.99
2	2 weeks	3.6	36.5	12.1	1.32	1.10
3	7 weeks	4.2	36.5	21.0	1.21	1.14
4	3 weeks	3.7	36.3	18.6	1.19	1.08
5	10 weeks	4.5	36.0	14.1	1.57	1.49
6	12 weeks	4.2	35.9	16.5	1.39	1.27
Mean		3.9	36.2	16.1	1.30	1.17*
±SD		±0.5	±0.3	±3.1	±0.16	±0.18

Fi = inspired halothane concentration; FA = end-tidal halothane concentration measured at the distal trachea.

* $P < 0.05$ for oropharyngeal *vs.* tracheal end-tidal halothane concentration.

The technique used to determine MAC-EI was adapted from Dixon's "Up-and-Down" method.[4] In each age group, the first patient was anesthetized to an arbitrary end-tidal halothane concentration. For each succeeding patient in that group, this concentration was decreased or increased by 0.1 ± 0.05%, depending on the adequacy or inadequacy of anesthesia during intubation in the previous patient. A logit transformation of the dose-response curve permitted the calculation of the MAC-EI and the ED95 at which 50% and 95% of patients, respectively, had adequate anesthesia for intubation. The standard error of MAC-EI was calculated by the method described by Stevens *et al.*[5] and subsequently used by others.[6,7]

The mean differences between oropharyngeal and tracheal concentrations, between MAC-EI in various groups, and between MAC-EI and MAC from Gregory *et al.*,[1] were analyzed by a one-way analysis of variance, by paired and unpaired *t* tests, and by the Student-Newman-Keuls multiple range test. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 provides demographic data and compares the end-tidal oropharyngeal and tracheal gas concentrations in phase 1 infants below 5 kg body weight and 6 months of age. Table 2 provides this data for other children in phase 1 of the study. The individual halothane concentrations and responses to tracheal intubation in the 118 phase 2 patients are shown in figure 1. The mean MAC-EI (±SEM) was 1.65 ± 0.01% for in-

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TABLE 2. Demographic Data and Comparison of Oropharyngeal and Distal Tracheal End-tidal Halothane Concentrations in Phase 1 Subjects Above 5 kg Weight and 6 months of Age

Case #	Age	Weight (kg)	Temp (°C)	$\frac{(Fi-FA)}{FA} \times 100$ (%)	End-tidal Halothane Concentrations Sampled from: Oropharynx (%)	Distal Trachea (%)
Group 1: 6–12 months						
7	6 months	6.6	35.9	15.0	1.35	1.33
8	6 months	6.9	36.0	18.7	0.71	0.69
9	7 months	5.8	36.1	15.4	1.34	1.36
10	8 months	8.9	35.7	9.4	1.01	1.02
11	10 months	6.4	36.2	18.1	0.72	0.70
12	12 months	10.3	35.8	8.4	1.33	1.37
Mean		7.4	35.9	14.2	1.07	1.08
±SD		±1.7	±0.2	±4.3	±0.31	±0.32
Group 2: 12–24 months						
13	13 months	9.1	36.7	14.1	1.12	1.15
14	16 months	9.9	36.0	15.5	1.34	1.35
15	18 months	10.4	35.9	12.8	1.44	1.46
16	21 months	11.7	36.1	11.9	1.27	1.25
17	22 months	10.9	35.7	18.3	1.04	1.09
Mean		10.4	36.1	14.5	1.24	1.26
±SD		±0.99	±0.3	±2.5	±0.16	±0.15
Group 3: 2–6 yr						
18	3 yr	14.5	35.7	15.8	1.21	1.22
19	4½ yr	18.0	35.9	19.3	1.46	1.43
20	5 yr	17.8	35.6	16.9	1.37	1.35
21	5¼ yr	18.8	36.9	19.4	1.59	1.60
22	6 yr	24.1	36.2	22.1	1.27	1.32
Mean		18.7	36.0	18.7	1.38	1.38
±SD		±3.5	±0.5	±2.5	±0.15	±0.14
Group 4: 6–12 yr						
23	8 yr	37.0	35.7	15.0	1.26	1.24
24	8¼ yr	32.7	36.3	18.5	1.44	1.43
25	9 yr	35.2	35.7	11.7	1.62	1.64
26	10 yr	39.2	35.5	17.5	1.45	1.47
27	11 yr	35.5	37.0	19.3	1.54	1.53
28	10 yr	41.1	35.2	12.6	1.73	1.71
29	11 yr	40.1	35.8	18.2	1.29	1.31
30	12 yr	42.4	35.1	11.8	1.66	1.64
Mean		37.9	35.8	15.6	1.50	1.50
±SD		±3.3	±0.6	±3.2	±0.17	±0.17

Fi = inspired halothane concentration; FA = end-tidal halothane concentration measured at the distal trachea.

fants between 6 and 12 months of age, 1.48 ± 0.06% for children between 12 and 24 months of age, 1.40 ± 0.05% in children between 2 and 6 yr of age, and 1.37 ± 0.04% in children between 6 and 12 yr of age. The mean MAC-EI was significantly higher for infants compared to all other age groups (table 3). The mean MAC-EI for children between 12 to 24 months was significantly higher than that for older children. The mean MAC-EI for children between 2 and 6 yr and 6 and 12 yr were not statistically different.

Linear regression analysis of the relationship between MAC-EI in the age groups we studied and MAC from the study of Gregory *et al.*[1] revealed a correlation of 0.995 ($r^2 = 0.989$) for the equation:

$$\text{MAC-EI} = 1.37\text{MAC} + 0.167$$

The ED95 of halothane for tracheal intubation was 2.25% for infants between 6 and 12 months of age, 1.88% for children 12 to 24 months of age, 1.85% for children between 2 and 6 yr of age, and 1.79% for children between 6 and 12 yr of age. Linear regression analysis of the relationship between ED95 and MAC-EI revealed a correlation of 0.974 ($r^2 = 0.949$) for the equation:

$$\text{ED95} = 1.62(\text{MAC-EI}) - 0.44$$

DISCUSSION

The consistency of a MAC-EI to MAC ratio for halothane in the age groups studied confirms the usefulness of MAC as a measure of relative anesthetic potency.

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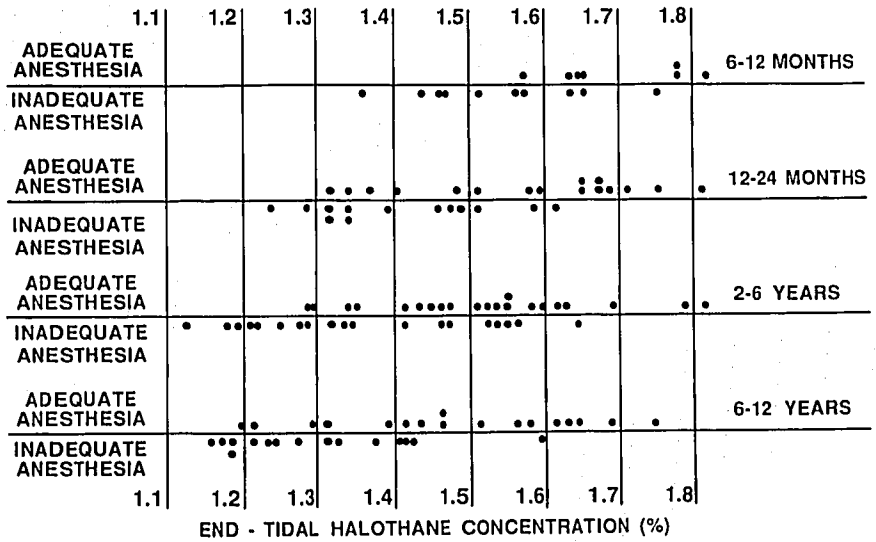

FIG. 1. Data for individual patients in phase 2. Each dot represents one patient. The position of the dot on the horizontal axis indicates the end-tidal halothane concentration. The position of the dot above or below the line indicates whether anesthesia for intubation was or was not adequate, respectively.

Halothane may specifically depress airways and airway sensitivity to tracheal intubation independent of a dose-related central nervous system effect. Enflurane and isoflurane may have a different specific effect on the airways. Since suppression of airway reflexes is not necessary in MAC determinations, the MAC-EI for enflurane and isoflurane may or may not have a consistent relationship to the same multiple of MAC as halothane. Yakaitis *et al.*[8] have demonstrated that the log dose-response curves for tracheal intubation with halothane and enflurane are parallel in children between 2 and 6 yr of age. If the log dose-response curves of halothane, enflurane, and isoflurane in various age groups prove to be parallel for MAC-EI, we can speculate that comparisons based on MAC may also hold true for anesthetic doses that block adrenergic and cardiovascular responses (MAC-BAR) and doses at which a patient is awake (MAC-awake).

In previous determinations of MAC,[1-3,5-8] end-tidal gas concentrations in samples drawn from the distal end of an endotracheal tube were used as representative of alveolar concentrations. Studies of MAC-EI are designed so that tracheal intubation will not be successful in all patients. Since we could not always obtain tracheal gas samples, we used oropharyngeal concentrations as representative of alveolar concentrations. We avoided a possible systematic error in gas sampling by excluding children below 6 months of age and 5 kg body weight in phase 2 of the study. To determine MAC-EI in children below 6 months of age, we suggest that gas be sampled intermittently in small aliquots during the latter half of the expiratory phase of several breaths.[6,7]

Contamination of the end-tidal sample by dead space gas, inspired gas, or gas from poorly perfused alveoli can cause errors in estimating MAC.[9-12] These errors are reduced to acceptable levels if the inspired-to-end-tidal concentration gradient is less than 50% of the alveolar level.[9] In all our patients, the gradients were well below this maximum acceptable level. In a study similar to ours, Yakaitis *et al.*[3,8] found a good correlation between tracheal gas concentrations and values obtained from a sample drawn at a point 5 cm distal to the fresh gas inlet. The variation between their value of 1.33% for MAC-EI for halothane and the value in our study (1.40 ± 0.05%) for the same age group is within the inherent error of the "Up-and-Down" method used to

TABLE 3. Demographic Data, MAC-EI, and MAC* in Phase 2 Subjects

Group	Age Range	Number of Cases	Weight (kg) Mean ± SD	Temp (°C) Mean ± SD	$\frac{(Fi-FA)}{FA} \times 100$ Mean ± SD	MAC-EI (%) ±SE	MAC (%)
1	6–12 months	17	7.8 ± 1.3	36.1 ± 0.3	15.8 ± 2.9	1.65 ± 0.01†	1.08
2	12–24 months	29	11.4 ± 2.1	35.9 ± 0.2	16.3 ± 4.1	1.48 ± 0.06‡	0.97
3	2–6 yr	40	18.6 ± 4.4	36.0 ± 0.2	13.7 ± 3.7	1.40 ± 0.05	0.91
4	6–12 yr	32	36.8 ± 7.3	35.9 ± 0.4	12.6 ± 5.2	1.37 ± 0.04	0.87

Fi = inspired halothane concentration; FA = end-tidal halothane concentration.

* MAC from Gregory *et al.*[1]

† $P < 0.05$ for group 1 *vs.* group 2, 3, or 4.

‡ $P < 0.05$ for group 2 *vs.* group 3 or 4.

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estimate MAC when the end-tidal concentration is varied by 0.1%.[13]

Tracheal intubation can be performed at a lighter level of anesthesia than that required to prevent coughing after intubation.[3,8] Moorthy *et al.*[14] have reported that hypoxemia can occur if a patient coughs or strains when the trachea is intubated. The hypoxemia results from small airway closure at a reduced lung volume, and from intracardiac right-to-left shunting across a probe patent foramen ovale. We, therefore, considered anesthesia to be inadequate if coughing and/or straining followed tracheal intubation.

In this study, the ED95 for tracheal intubation was 25–40% higher than the MAC-EI. This is in keeping with data in adults on the relationship between MAC and the ED95 for surgical stimuli.[15] Since halothane causes a dose-dependent depression of myocardial contractility, the higher alveolar concentrations necessary for tracheal intubation without coughing or patient movement may result in hypotension, particularly in hypovolemic neonates and infants.[16] Atropine can ameliorate some of the bradycardia and hypotension associated with halothane.[17] We recommend caution in the use of this technique and prefer to reserve it for situations where neuromuscular blockade is contraindicated.

We conclude that adequate conditions for tracheal intubation without the use of neuromuscular blockade occur at a minimum alveolar concentration of halothane of 1.37 MAC ± 0.167 in 50% of children aged 6 months to 12 yr.

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