The Relationship between Age and Halothane Requirement in Man

George A. Gregory, M.D.,* Edmond I. Eger, II, M.D.,† Edwin S. Munson, M.D.‡

The minimum alveolar concentration (MAC) values for halothane in eight age groups were determined. MAC was found to be highest in newborns and lowest in the elderly. These changes in anesthetic requirement with age parallel changes in cerebral oxygen consumption, cerebral blood flow and neuronal density.

AN INVERSE RELATIONSHIP between age and anesthetic requirement is suggested by clinical experience. Cullen[1] and Guedel[2] wrote that anesthetic requirement decreased with age. Guedel related this to decreased reflex irritability, metabolic rate and oxygen consumption. Reynolds[3] stated that "the inspired concentration of halothane necessary to maintain anesthesia seems to be higher in pediatric patients than adults." Deming[4] measured cyclopropane concentrations in blood of adults and children at constant EEG levels and found the concentrations highest in the newborn and lowest in adults. Except for Deming's study, none of the clinical impressions of the relationship between age and anesthetic requirement have been substantiated by measurement of the anesthetic dose in equilibrium with the brain. None has utilized an objective measurement of anesthetic depth.

We proposed to determine whether anesthetic requirement changes with age, and if so, to quantify the magnitude of the change. To define this and compare anesthetic doses required to produce the same depth of anesthesia in different age groups, we used the minimum alveolar concentration (MAC).

Methods

Healthy patients about to undergo elective surgery were premedicated with atropine 30 to 60 minutes prior to the induction of anesthesia with halothane–oxygen. The trachea was intubated, and respiration was controlled with an Air Shields ventilator. All patients were hyperventilated to reduce the differences between end-tidal and inspired concentrations of halothane. Bridges and Eger[5] previously found hyperventilation to have no effect on MAC. In patients under 6 years of

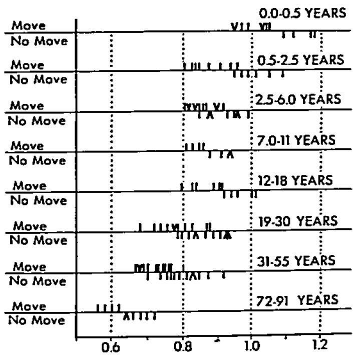

FIG. 1. Data for determining MAC. Each line above or below the horizontal represents one patient. A line above the horizontal represents movement and a line below represents no movement to skin incision. A "V" indicates two patients at the same alveolar concentration.

* Clinical Instructor (San Francisco).
† Professor (San Francisco).
‡ Assistant Professor (Davis).

Received from the Department of Anesthesia, University of California Medical Center, San Francisco, California, and the Department of Anesthesia, University of California Medical Center, Davis, California. Accepted for publication December 12, 1968. Supported in part by U. S. Public Health Service grants 5T1 GM-00063-01 and 5R01 HE-07946-05.

TABLE 1. Means and Standard Deviations of Various Parameters

No. of Patients	Age (Years)	Hemoglobin (g/100 ml)	Esophageal Temperature at Time of Incision (°C)	100 F_I/F_E*	Minutes at Test Concentration	Total Minutes Halothane	MAC (per cent)
12	0.2 ± 0.18 (0–0.5)	12.2 ± 2.5	36.3 ± 0.5	105.50 ± 3.9	19.1 ± 5.4	44 ± 15	1.08
14	1.5 ± 0.75 (.5–2.5)	11.53 ± 0.85	36.7 ± 0.4	109.15 ± 5.4	26.6 ± 16.1	50 ± 15	0.97
19	4.1 ± 1.0 (2.5–6)	12.1 ± 1.05	36.6 ± 0.6	111.1 ± 5.5	21.9 ± 7.2	47 ± 10	0.91
8	8.4 ± 1.0 (7–11)	12.6 ± 1.0	35.9 ± 0.5	110.96 ± 5.5	34.9 ± 16.2	55 ± 19	0.87
11	15.5 ± 1.8 (12–18)	13.9 ± 1.0	36.3 ± 0.4	111.1 ± 6.5	23.1 ± 13.8	42 ± 17	0.92
22	24.9 ± 3.0 (19–30)	14.0 ± 1.6	36.1 ± 0.5	114.08 ± 8.9	24.2 ± 9.8	50 ± 17	0.84
24	42 ± 7 (31–55)	—	36.1 ± 0.4	112.69 ± 5.8	27.0 ± 11.0	42 ± 7	0.76
10	81.4 ± 6.2 (70–96)	12.3 ± 1.5	35.7 ± 0.07	—	56.0 ± 31.0	86 ± 47	0.64

* F_I is inspired and F_E is end-tidal halothane concentration.

TABLE 2. Data from the Eight Patients Equilibrated at More than One Concentration of Halothane

Patient	Age (Years)	Procedure	End-tidal Halothane Concentration (per cent)	Move with Incision of Skin
1	0.10	(l) inguinal hernia;	0.95	yes
		(r) inguinal hernia;	1.07	yes
		umbilical hernia	1.19	no
2	0.25	(l) inguinal hernia;	0.95	yes
		(r) inguinal hernia	1.075	yes
3	28 hours	anoplasty	0.99	yes
			1.01	no
4	0.75	(l) inguinal hernia;	1.01	no
		(r) inguinal hernia	0.80	yes
5	1.5	(r) inguinal hernia;	0.88	no
		(l) inguinal hernia;	0.80	no
		umbilical hernia	0.70	yes
6	1.5	(l) inguinal hernia;	0.85	yes
		(r) inguinal hernia	0.85	no
7	4.5	pyeloyrethroplasty;	0.89	yes
		pyeloyrethroplasty	1.04	no
8	5.5	(l) inguinal hernia;	0.88	no
		(r) inguinal hernia	0.81	yes

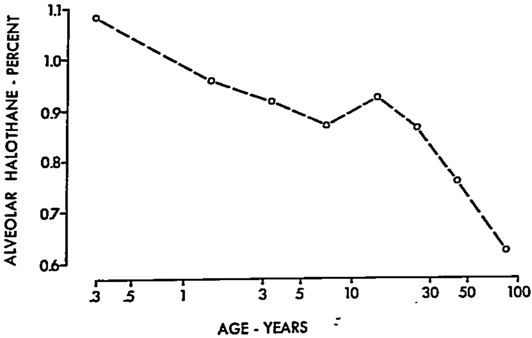

FIG. 2. Mean alveolar halothane concentration *vs.* age.

age, end-tidal samples were obtained with a Rahn sampler, and in those 6 years old and older, by intermittent suction through a nylon catheter placed at the tracheal end of the endotracheal tube. Halothane concentrations were determined with a Beckman infrared halothane analyzer in all age groups except the elderly, whose concentrations were determined with an ultraviolet halothane analyzer. Each patient was observed at the time of incision of the skin and any movement noted.

Eight age groups were studied: 0 to 6 months, 7 months to 2.5 years, 2.6 years to 6 years, 7 to 10 years, 11 to 18 years, 19 to 30 years, 30 to 55 years, and 72 to 92 years. Eight patients studied received multiple incisions and were equilibrated at different end-tidal concentrations for each. Only the response to the first incision was used in the determination of MAC.

Results

The data obtained for all groups are shown in figure 1 and table 1. In figure 1 a line above the horizontal represents movement following incision, a line below, no movement. Hemoglobin concentrations, body temperatures, the percentage ratios of inspired to end-tidal halothane concentrations (100 F_I/F_E), and the minutes of stability at the test concentration are presented (table 1).

Data from the eight patients who had more than one incision are given in table 2. All of these patients were less than 6 years of age. The ranges of end-tidal halothane concentrations over which they did and did not move were narrow.

Discussion

The highest anesthetic requirement was in patients newly born to 6 months of age and the lowest in those 70 years old and older. There may have been a small increase in anesthetic requirement at puberty. The most striking change occurred between birth and 6 months of age. During this period the anesthetic requirement for halothane was reduced by nearly a fourth of the total decrease found over the age range studied (fig. 2).

A falsely high MAC value would be obtained if end-tidal gas were contaminated by that inspired.[8] In patients with ventilation/perfusion abnormalities such that areas of ventilated but poorly perfused lung are present, gas coming from poorly perfused areas of lung would contribute essentially unchanged inspired gas to the end-tidal sample, thus raising end-tidal halothane concentrations and the MAC value. This could occur in the very young and the elderly. To reduce the impact of this, if present, we reduced the end-tidal-to-inspired halothane concentration differences to low levels in all patients. That is, the end-tidal value was only slightly below the inspired value as indicated by 100 (F_I/F_E) in table 1. While we have no 100 (F_I/F_E) data for the older age group, the lengths of time at constant end-tidal concentrations suggest that the ratios were near 100.

Part of the increased anesthetic need in children less than 6 months of age may be related to compositional differences of the brain.[6] Although no causal relationship may exist, the decrease in anesthetic requirement with aging is associated with decreased cell density in the central nervous system, decreased cerebral oxygen consumption, and decreased cerebral blood flow.[7]

Clinically, these data imply that there is not a standard dose of halothane applicable to all ages. A dose adequate for a 40-year-old patient may be too low for the newborn and too high for the octogenarian.

The halothane for this study was supplied by Ayerst Laboratories.

References

1. Cullen, S. C.: Anesthesia. Chicago, Yearbook Publishers, 1961.
2. Guedel, A.: Inhalation Anesthesia. New York, The Macmillan Company, 1937.
3. Reynolds, R. N.: Halothane in pediatric anesthesia, Int. Anesth. Clin. 1: 209, 1962.
4. Deming, M.: Agents and techniques for induction of anesthesia in infants and younger children, Anesth. Analg. 31: 113, 1952.
5. Bridges, B., and Eger, E. I., II: The effect of hypocapnia on the level of halothane anesthesia in man, ANESTHESIOLOGY 27: 634, 1966.
6. McIlwain, H.: Biochemistry and the central nervous system. London, J. and A. Churchill Ltd., 1959.
7. Kety, S. S.: Human cerebral blood flow and oxygen consumption as related to aging, J. Chronic Dis. 3: 478, 1956.
8. Saidman, L. J., Eger, E. I., II, Munson, E. S., Babad, A. A., and Muallem, M.: Minimum alveolar concentrations of methoxyflurane, halothane, ether, and cyclopropane in man: Correlation with theories of anesthesia, ANESTHESIOLOGY 28: 994, 1967.

Obstetrical Anesthesia

FETAL BRADYCARDIA The relationships of fetal bradycardia to fetal and maternal blood levels of mepivacaine were examined in 15 unmedicated, healthy multiparous patients following the bilateral paracervical injection of 300 mg of 1.5 per cent mepivacaine. Mepivacaine was present in significant levels in the maternal blood by five minutes. Peak concentrations, evident by 10 to 20 minutes, varied from 4.7 to 17.2 μg/ml. Mepivacaine was detectable in significant concentrations in fetal samples obtained at 5 or 10 minutes. Peak concentrations occurred before 30 minutes and varied from 3.4 to 15 μg/ml. Fetal blood levels were consistently lower than maternal levels, and averaged 79 per cent of concentrations measured in simultaneously-drawn maternal blood. Fourteen of the 15 infants had Apgar scores of 8 or 9; the remaining infant scored 4. Fetal bradycardia was encountered in three cases. Two episodes of bradycardia were associated with Apgar scores of 8. In the third, bradycardia persisted and was associated with an Apgar score of 4. The only significant pH variation was in the infant with persistent bradycardia. The fetal bradycardia frequently encountered with this type of anesthesia appears to be related to concentrations in the fetal blood of 12.8 to 15 μg/ml. Although such levels might result in fetal depression, they do not appear high enough to cause death of a healthy fetus. These data stress the importance of distinguishing fetal bradycardia induced by drug toxicity from that resulting from asphyxia, and suggest that paracervical block is contraindicated when placental insufficiency is anticipated. *(Gordon, H. R.: Fetal Bradycardia After Paracervical Block: Correlation with Fetal and Maternal Blood Levels of Local Anesthesia (Mepivacaine), N. Eng. J. Med. 279: 910 (Oct.) 1968.)*