TABLE 1. Unit Doses (ml of Liquid) of Isoflurane Calculated by Three Methods

Weight (kg)	0.0287 × kg$^{3/4}$	1/100 × (0.9 × kg + 9)	1/100 × (kg + 9)
10	0.16	0.18	0.19
20	0.27	0.27	0.29
30	0.37	0.36	0.39
40	0.46	0.45	0.49
50	0.54	0.54	0.59
60	0.62	0.63	0.69
70	0.70	0.72	0.79
80	0.77	0.81	0.89
90	0.84	0.90	0.99
100	0.91	0.99	1.09

Hence:

$$\text{unit dose (vapor)} = 2 \times 1 \times 1.48 \times 2 \times kg^{3/4} = 5.92 \times kg^{3/4} \quad (2)$$

To convert to ml of liquid anesthetic, where 1 ml liquid = 206 ml vapor, the equation becomes:

$$\text{unit dose (ml of liquid)} = 1/206 \times 5.92 \times kg^{3/4} = 0.0287 \times kg^{3/4} \quad (3)$$

If the Frenette substitution is employed, then unit dose (ml of liquid) = $0.0287 \times (0.3 \times kg + 3) = 0.0086 \times kg + 0.086$; represented more simply as:

$$\text{unit dose (ml of liquid)} = 1/100 \times (0.9 \times kg + 9) \quad (4)$$

An approximation is given by:

$$\text{unit dose (ml of liquid)} = 1/100 \times (kg + 9), \quad (5)$$

which is a calculation that can be rapidly and easily performed.

The calculated unit dose, applying equation 5 above, gives a reasonable approximation of the correct unit dose, as determined by the more traditional calculation represented by equation 3, but tends to slightly overestimate the correct unit dose in larger patients. For example, in a 100-kg patient, the true unit dose is overestimated by approximately 0.18 ml. A comparison of the unit doses determined by equations 3, 4, and 5 appears in table 1. We routinely use equation 5 because of the simplicity of the arithmetic, and have been able to measure end tidal anesthetic concentrations corresponding quite closely to the concentrations predicted by equation 5.

Correct application of equation 5 will give a unit dose of isoflurane (in ml of liquid) that, when injected into the circuit, produces an alveolar concentration of 1%. As discussed above, unit doses are injected according to a schedule determined by squared intervals of time. Doses are adjusted up or down according to clinical needs. For example, a 70-kg patient requiring 2% alveolar concentration of isoflurane would receive a double unit dose, or approximately $0.79 \times 2 = 1.58$ ml of liquid isoflurane. The calculation is rapid, and allows the practice of closed-circuit anesthesia without requiring a slide rule or complex dosage tables.

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REFERENCES

1. Frenette L, Baillargeon R, Perreault L: Closed-circuit anesthesia made easier. ANESTHESIOLOGY 65:704, 1986
2. Lowe HJ, Ernst EA: The Quantitative Practice of Anesthesia: Use of the Closed Circuit. Baltimore: Williams and Wilkins, 1981

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Is Isoflurane Dangerous for the Patient with Coronary Artery Disease? Another View. I.

To the Editor:—Anesthesia and surgery are dangerous for patients with coronary artery disease.[1–3] However, careful monitoring and control of the determinants of myocardial oxygen balance can markedly decrease this danger.[4] In my opinion, potent inhaled anesthetics are uniquely suited for this purpose for the following reasons: 1) they can control all the major determinants of myocardial oxygen demand; heart rate, myocardial contractile performance, and ventricular wall stress (arterial blood pressure); 2) dangerous increases in heart rate and blood pressure in the clinical situation are most often related to noxious surgical stimulation, and potent inhaled anesthetics can also block this stimulus at the same time that they treat the hemodynamic conse-

quences; and 3) perhaps most importantly, these drugs can be titrated both in and out of the patient, unlike any other type of drug. Consequently, many of us (anesthesiologists) believe that potent inhaled anesthetics are valuable agents for producing anesthesia in patients with ischemic heart disease. However, by definition, they are dangerous drugs. In high-risk patients, they must be administered *cautiously*, utilizing knowledge of the pharmacology of the drugs and the pathophysiology of the disease process in the patient. As Dr. Becker has indicated, the well-documented coronary vasodilating properties of isoflurane can result in diversion of myocardial blood flow from ischemic areas toward non-ischemic areas, at least in animal models, and perhaps in humans.[5] However, in my opinion, Buffington's experiments demonstrate that the cardiac effects of isoflurane are about halfway between those produced by halothane (dose-related myocardial depression and minimal coronary vasodilation) and adenosine (minimal myocardial depression and dose-related coronary vasodilation).[6] Consequently, isoflurane should not produce as predictable maldistribution of coronary blood flow in the ischemic heart as does adenosine. I believe that the comparison is not unlike that shown for nifedipine and adenosine by Gewirtz *et al.*[7] Moreover, practically all the documented human data suggesting that isoflurane has caused or increased ischemia in patients with coronary artery disease can be explained by either decreased coronary perfusion pressure (oxygen supply) or increased heart rate and blood pressure (oxygen demand).[8-10]

In many clinical circumstances, the combination of central nervous system depression, systemic vasodilation, and moderate myocardial depression may be the ideal pharmacologic effects to balance myocardial oxygen supply and demand. In addition, the other available potent inhalation anesthetics indeed do have "adverse effects on other organ systems."[5] Both halothane and enflurane are more potent myocardial depressants. Halothane can produce hepatitis in rare patients, and the FDA has determined (wrongly, I believe)[11] that enflurane is also hepato- as well as reno-toxic. Several authors have documented that isoflurane can have beneficial effects in a patient with ischemic heart disease[12-14] and, conversely, that halothane can have deleterious effects.[15,16] Therefore, I believe that, rather than indicating that isoflurane is "dangerous for some patients with ischemic heart disease," as are all potent inhalation anesthetics, I would have preferred that Dr. Becker give us (anesthesiologists) the same advice as he has given his colleagues (cardiologists) concerning the use of potent coronary vasodilators: "In summary, this study suggests that if vasodilators are to be used in acute myocardial infarction they should be used *cautiously*."[17] Hopefully, we all use all our anesthetics *cautiously* in patients with coronary artery disease.

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REFERENCES

1. Topkins MJ, Artusio JF: Myocardial infarction and surgery—A five year study. Anesth Analg 43:716–720, 1964
2. Tarhan S, Moffitt EA, Taylor WF, Giuliani ER: Myocardial infarction after general anesthesia. JAMA 220:1451–1454, 1972
3. Steen PA, Tinker JH, Tarhan S: Mycardial reinfarction after anesthesia and surgery. JAMA 239:1566–1570, 1978
4. Rao TK, Jacobs KH, El Etr AA: Reinfarction following anesthesia in patients with myocardial infarction. ANESTHESIOLOGY 59:499–505, 1983
5. Becker LC: Is isoflurane dangerous for the patient with ischemic heart disease? ANESTHESIOLOGY 66:259–261, 1987
6. Buffington CW, Romson JL, Levine A, Duttlinger NC, Huang AH: Isoflurane induces coronary steal in a canine model of chronic coronary occlusion. ANESTHESIOLOGY 66:280–292, 1987
7. Gewirtz H, Gross SL, Williams DO, Most AS: Contrasting effects of nifedipine and adenosine on regional myocardial flow distribution and metabolism distal to a severe coronary arterial stenosis: Observations in sedated closed-chest, domestic swine. Circulation 69:1048–1057, 1984
8. Reiz S, Balfors E, Sorenson MB, Ariola S, Friedman A, Truedson H: Isoflurane—A powerful coronary vasodilator in patients with coronary artery disease. ANESTHESIOLOGY 59:91–97, 1983
9. Moffitt EA, Barker RA, Glenn JJ, Imrie DD, del Campo C, Landymore RW, Kinley CE, Murphy DA: Myocardial metabolism and hemodynamic responses with isoflurane anesthesia for coronary arterial surgery. Anesth Analg 65:53–61, 1986
10. Larsen R, Hilfiker O, Philbin DM, Sonntag H: Isofluran: Koronardurhblutung und Myokardstoff weschel bie Patienten mit koronarar Herzkranеit. Anaesthesist 35:284–290, 1986
11. Eger EI II, Smuckler EA, Ferrell LD, Goldsmith CH, Johnson BH: Is enflurane hepatotoxic? Anesth Analg 65:21–30, 1986
12. Bastard OG, Carter JC, Moyers JR, Vross BA: Circulatory effects of isoflurane in patients with ischemic heart disease: A comparison with halothane. Anesth Analg 63:635–639, 1984
13. Hess W, Arnold B, Schulte-Sasse U, Tarnow J: Comparison of isoflurane and halothane when used to control intra-operative hypertension in patients undergoing coronary artery bypass surgery. Anesth Analg 62:15–20, 1983
14. Tarnow J, Markschies-Hornung A, Schulte-Sasse U: Isoflurane improves the tolerance to pacing induced myocardial ischemia. ANESTHESIOLOGY 64:147–156, 1986
15. Kistner JR, Miller ED, Lake CL, Ross WT: Indices of myocardial oxygenation during coronary artery revascularization in man with morphine versus halothane anesthesia. ANESTHESIOLOGY 50:324–330, 1979
16. Wilkinson PL, Hamilton WK, Moyers JR, Graham BG, Ports TA, Ullyot PJ, Chatterjee K: Halothane and morphine-nitrous

oxide anesthesia in patients undergoing coronary artery bypass operation—Patterns of intra-operative ischemia. J Thorac Cardiovasc Surg 82:372–382, 1981
17. Becker LC: Conditions for vasodilator-induced coronary steal in experimental myocardial ischemia. Circulation 57:1101–1110, 1978

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Is Isoflurane Dangerous for the Patient with Coronary Artery Disease? Another View. II.

To the Editor:—I am amused, confused, and frustrated by the continuing ability of internists to opine with certainty from their relatively brief exposure to matters anesthestic—in contrast to the profound uncertainty I perceive after nearly four decades of full-time exposure to these concepts and problems. While Dr. Becker[1] adds sufficient caveats to cover his opinions, his statements that isoflurane is "almost certainly dangerous" and ". . . the safest course would therefore appear to be to avoid isoflurane in patients with known coronary artery disease" may be followed and believed by many. If this were really true, as we can seldom rule out coronary artery disease in large segments of our population, isoflurane should be restricted to the young.

I certainly agree with Dr. Becker that isoflurane is dangerous—not just for those with coronary artery disease, but for all patients. *All* anesthetic agents are dangerous, but our options rarely include using no anesthetic at all. Isoflurane is currently widely used as a primary or supplementary anesthetic agent in patients having coronary artery disease. This experience yields no data supporting agent dependent outcome differential. This renders Dr. Becker's certainty most interesting. Extrapolation from models and deductions from groups of patients small in number and lacking outcome data are hardly the basis for definite opinions.

We predicted many responses which "seemed almost certain" over the earlier immature years of our specialty. Experience with such dicta as the ten gram hemoglobin rule, our inability to prove or demonstrate success of one anesthetic agent or technique *versus* another, the widely variant pontifications by highly respected members of our profession, and the cyclical nature of our preference for agents have taught us that predicting the inherent danger of virtue of specific agents is unwise. Such advice must still await proper clinical trials. Absent these, most of us have learned to opine with moderation.

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1. Becker LC: Is isoflurane dangerous for the patient with coronary artery disease? ANESTHESIOLOGY 66:259–261, 1987

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Is Isoflurane Dangerous for the Patient with Coronary Artery Disease? Another View. III.

To the Editor:—The editorial by Becker[1] on isoflurane and the patient with coronary artery disease gives a balanced view of the evidence, but one still comes away with an impression that isoflurane has been found guilty. In my opinion, the verdict is by no means certain, and much of the argument against isoflurane is simplistic and flawed.

In the context of the discussion of coronary vasodilators, a serious omission is made. Isoflurane is done a significant injustice when it is not highlighted that this agent is unique among the coronary vasodilators discussed, in that it has a direct effect on diminishing myocardial metabolic rate. The demand side of the equation cannot be ignored. For this reason, extrapolation of findings with other drugs causing coronary steal to the isoflurane argument becomes very complex.

It is certainly possible for any agent or technique to be abused. Furthermore, in this situation, it is usual for the agent or technique to take responsibility for adverse outcomes (this, the technician seldom does). Given that heart rate, blood pressure, and coronary perfusion pressure are kept close to normal levels, there is no