Domino KB, Dudman AJ, Hamilton WK, Kampine J, Kotrly KJ, Maltby JR, Mazloomdoost M, MacKenzie RA, Melnick BM, Motoyama E, Muir JJ, Munshi C: Multicenter study of general anesthesia: I. Design and patient demography. ANESTHESIOLOGY 72:252–261, 1990

2. Forrest JB, Cahalan MK, Rehder K, Goldsmith CH, Levy WJ, Strunin L, Bota W, Boucek CD, Cucchiara RF, Dhamee S, Domino KB, Dudman AJ, Hamilton WK, Kampine J, Kotrly KJ, Maltby JR, Mazloomdoost M, MacKenzie RA, Melnick BM, Motoyama E, Muir JJ, Munshi C: Multicenter study of general anesthesia: II. Results. ANESTHESIOLOGY 72:262–268, 1990
3. Forrest JB, Rehder K, Cahalan MK, Goldsmith CH: Multicenter study of general anesthesia: III. Predictors of severe perioperative adverse outcomes. ANESTHESIOLOGY 76:3–15, 1992
4. Brown BW Jr: An application of health services research to Anesthesiology. ANESTHESIOLOGY 76:1–2, 1992
5. Prentice RL: Surrogate endpoints in clinical trials: Definition and operational criteria. Stat Med 8:431–440, 1989
6. Mangano DT: Perioperative cardiac morbidity. ANESTHESIOLOGY 72:153–184, 1990

(Accepted for publication April 17, 1992.)

Anesthesiology
77:395–396, 1992

In Reply:—Burke points out that certain risk factors in a univariate chi-square analysis increase the probability of outcome occurrence while there is an apparent decrease in the probability for the same risk factors in a logistic regression. "Any severe respiratory outcome" (ASRO) refers to patients with at least one of the sixteen types of severe respiratory outcomes that were studied.[1] The relative risk (cf. Table A3)[2] of ASRO in 5,965 smokers in the study population of 17,201 patients was 1.77 times the risk in 11,236 nonsmokers ($P = 3.2^{-4}$). Also the risk of ASRO in 523 patients with chronic obstructive pulmonary disease (COPD) was 3.00 times the risk in 16,678 patients without COPD ($P = 1.2^{-4}$), and the risk of ASRO in 6,014 male patients was 1.75 times the risk in 11,187 female patients ($P = 4.4^{-4}$). Since a relative risk greater than 1 is an increased risk (and less than 1 is a reduced risk), we conclude that patients who smoke, or who have COPD, or who are male, have an increased risk of perioperative ASRO. This is in accord with what we would have expected from clinical experience.

We next tested the importance of these risk factors and all others with a significant chi-square statistic, as independent predictors of severe adverse outcomes, using a series of different stepwise logistic regressions (SLR). We reported the findings for the final model (table 1)[2]; the findings were similar in each of the sequential models tested. Burke's question prompted us to request another audit of the coding used by the Data Management Center for these SLRs. An error was found in the coding. In table 1, male should be female, obesity should be nonobese, and smoking should be nonsmoking. To calculate the probability of an outcome for male, obesity, and smoking the logistic coefficients for these predictors should have a negative sign. We are grateful to Burke for pointing this out to us. There were six significant predictors for ASRO, each with a negative logistic coefficient. These were, with percent probability (Pr) in parentheses: history of cardiac failure (Pr = 6.6%), history of COPD (Pr = 4.1%), obesity (Pr = 3.6%), male (Pr = 3.3%), abdominal surgical procedures (Pr = 3.2%), and smoking (Pr = 2.8%). To the extent that there were only certain risk factors entered in the final SLR, these findings represent the important factors contributing to the risk of ASRO. We conclude from this that a history of COPD is a more important predictor of ASRO than smoking status in this SLR model.

A positive logistic coefficient for a risk factor should not be interpreted as protective for an outcome, as Burke suggests. Rather, the relative importance of each factor can be assessed in terms of its contribution to the overall probability for that outcome within the algorithm that now defines the model. For example, the probability of severe hypertension in patients with a history of hypertension is 0.3% (b = −0.75); in patients having cardiovascular surgical procedures the probability is 1.0% (b = −1.18); and in patients having gynecologic surgical procedures the probability is <0.1% (b = 1.08). Thus, cardiovascular surgery is a more important predictor of severe hypertension than either a history of hypertension or gynecologic surgery. Obviously there are likely to be influential relationships between certain risk factors (*e.g.*, COPD and smoking, coronary artery disease and age, hypertension and diabetes). We did not specifically test for such interactions in detail, but it would be of interest to do so.

We have already discussed the possible limitations and potential bias in our study. It should be noted also that not all patients in the study were included in the SLR models. Thus, although there were 5,965 smokers, 6,223 obese patients, and 6,014 males in the study, there were only 4,761 smokers (79.8%), 5,530 obese patients (88.9%), and 4,537 males (75.4%) entered in the final SLR model. In large studies such as ours it is inevitable that in some patients, some data are missing. This leads to their rejection from entry in the SLR. We cannot be sure that this did not exclude patients in a nonuniform way. Because the result was very similar in each of the SLR models, we believe that this possibility is remote.

One further difficulty in interpreting our findings is that some of the severe perioperative adverse outcomes as we defined them[1] may be in themselves risk factors, as we[1] and Pace have stated. This seems most likely with severe hemodynamic disturbances, which he argues should be classified as "process variables" rather than outcomes, citing our example of severe tachycardia in patients with cardiac disease as a risk factor for perioperative myocardial ischemia. For the purpose of our study, we defined an "outcome" simply as a result or consequence of the care provided to our patients. This definition includes mortality, serious morbidity, and dysfunction (mild, moderate, or severe). Although there is no consensus on the preferred terminology, our definition of outcome agrees with others.[3,4] In large multiinstitutional studies, it is essential that every effort is made to ensure consistency and completeness in the reporting of outcomes. We agree that our criteria for changes in blood pressure and heart rate reported as outcomes were quite modest, but we considered this to be mandated by the objective of the study in testing our hypothesis—that there are differences among the four anesthetics for adverse outcomes such as arrhythmia, hypotension and vomiting.[1] The process we used to verify our data was extensive, and when we discuss severe outcomes we have already excluded all patients with minor or moderate hemodynamic disturbance. For example, there were 5,275 patients with hypotension (30.7%)[5] and 6,969 patients with tachycardia (40.5%), but of these there were only 191 patients with severe hypotension (3.6% of the patients with hypotension) and only 153 patients with severe tachycardia (2.2% of the patients with tachycardia). In addition to rating outcomes for severity, each outcome was given an "occurred with" and "treated with" subcode and these were reviewed in detail to ensure the inclusion of only those patients with clinically important severe adverse outcomes.

In previous papers[5] we reported significant differences among the study anesthetic groups for severe outcomes (tachycardia, hypertension, ventricular arrhythmia, and bronchospasm) and found essentially the

same result in our most recent analysis. Whether these findings of mainly severe intraoperative hemodynamic disturbance may be risks for clinically important postoperative morbidity is not known. The thorough review of perioperative cardiac morbidity by Mangano[6] presented "preliminary findings" on dynamic predictors, and he concluded that "a casual relationship between hypotension and ischemia may exist; however, neither the degree nor the duration of hypotension necessary to precipitate ischemia has been determined." Also, in several studies, ischemic events have been reported in patients with decreases in intraoperative blood pressure of 20% or less.[7,8] For all of these reasons we are confident that the criteria used for these hemodynamic outcomes were appropriate for our study since we wished all episodes to be reported. Also, it was necessary to minimize as far as possible any observer bias as to their clinical importance.

We would like to extend the concluding statement by Pace by observing that our study could not demonstrate a difference among the anesthetic agents for mortality, myocardial infarction, and stroke because of insufficient sample size. We agree that the importance of differences in severe hemodynamic disturbance in the context of mortality or serious morbidity is not known. Clearly this should be investigated.

It should be remembered that most of our patients were healthy, and thus the statistical safety net of a large denominator may have obscured our ability to focus on those patients in most need of our expertise and vigilance. Despite this, we hope our study will stimulate questions, such as Burke and Pace ask as a basis for future study. We are most grateful for their interest and thoughtful comments.

JAMES B. FORREST, M.D., PH.D.
Department of Anaesthesia
McMaster University
1200 Main Street West
Hamilton, Ontario
Canada 18N 3Z5

KAI REHDER, M.D.
Department of Anesthesiology
Mayo Clinic
Rochester, Minnesota 55905

MICHAEL K. CAHALAN, M.D.
Department of Anesthesiology
University of California, San Francisco S436
San Francisco, California 94143

CHARLES H. GOLDSMITH, PH.D.
Department of Clinical Epidemiology and Biostatistics
McMaster University
1200 Main Street West
Hamilton, Ontario
Canada 18N 3Z5

REFERENCES

1. Forrest JB, Rehder K, Goldsmith CH, Cahalan MK, Levy WJ, Strunin L, Bota W, Boucek CD, Cucchiara RF, Dhamee S, Domino KB, Dudman AJ, Hamilton WK, Kampine J, Kotrly KJ, Maltby JR, Mazloomdoost M, MacKenzie RA, Melnick BM, Motoyama E, Muir JJ, Muschi C: Multicenter study of general anesthesia I. Design and patient demography. ANESTHESIOLOGY 72:252–261, 1990
2. Forrest JB, Rehder K, Cahalan MK, Goldsmith CH: Multicenter study of general anesthesia III. Predictors of severe perioperative adverse outcomes. ANESTHESIOLOGY 76:3–15, 1992
3. Brown DL: Anesthesia risk: A historical perspective, Risk and Outcome in Anesthesia. Edited by Brown DL. Philadelphia, JB Lippincott, 1988, p 2
4. Tuman KJ: Evaluating anesthetic outcome, Advances in Anesthesia. Volume 8. Edited by Stoelting RK, Barish PG, Gallagher TJ. St Louis, Mosby-Year Book, 1991, pp 311–331
5. Forrest, JB, Cahalan MK, Rehder K, Goldsmith CH, Levy WJ, Strunin L, Bota W, Boucek CD, Cucchiara RF, Dhamee S, Domino KB, Dudman AJ, Hamilton WK, Kampine J, Kotrly KJ, Maltby R, Mazloomdoost M, MacKenzie RA, Melnick BM, Motoyama E, Muir JJ, Munshi C: Multicenter study of general anesthesia II. Results. ANESTHESIOLOGY 72:262–268, 1990
6. Mangano DT: Perioperative cardiac morbidity. ANESTHESIOLOGY 72:153–184, 1990
7. Lieberman RW, Orkin FK, Jobes DR, Schwartz AJ: Hemodynamic predictors of myocardial ischemia during halothane anesthesia for coronary revascularization. ANESTHESIOLOGY 59:36–41, 1983
8. Kotter G, Kotrly K, Kalbfleisch H, Vucins E, Kampine J: Myocardial ischemia during cardiovascular surgery as detected by an ST segment trend monitoring system. J Cardiothorac Anesth 1:190–199, 1987

(Accepted for publication April 17, 1992.)

Anesthesiology
77:396–397, 1992

A Few Details Regarding Tonometric Measurement of Blood Pressure

To the Editor:—A long-time student of techniques of blood pressure measurement, I am disturbed by several aspects of the paper by Kemmotsu and colleagues on arterial tonometry.[1]

Why did the authors use a 22-G cannula for intraarterial pressure measurement? The norm in this country has been an 18-G cannula, although the emerging fashion is to use a 20-G. A cannula of still smaller bore may serve only to sanitize (by damping) the derived traces, perhaps contributing to the otherwise implausible damping coefficients of up to 0.5. By smoothing the direct arterial trace, one might then expect to have better concordance between direct and indirect systolic readings.

The authors' selection of citations would imply that "major problems such as infections and thromboembolic and traumatic complications" *commonly* follow intraarterial cannulation for pressure measurement. The literature, however, supports the view that arterial cannulation is a remarkably benign procedure insofar as major circulatory problems are considered,[3,4] and that infection is rare even in the critically ill, chronically cannulated patient.[5]

In their discussion, the authors aver that "the technique of arterial tonometry was invented in the early 1960's." Not so! Etienne Jules Marey demonstrated his "sphygmograph" at the court of Napoleon III; this sphygmograph was a portable device, applied to the wrist, that would record on a moving, smoked glass plate "the pulsebeats of an artery, not only with their frequency, regularity, and relative intensity, but also with the individual shape of each one."* The device was available from Charles Verdin, instrument maker in Paris, about 1890. A