model to an age group, which is outside of the age range of our study population (e.g., to very young patients, where, in fact, the predicted risk can be exaggerated using our model). However, the scope of our current investigation did not include pediatric cases. The increase in the incidence of PONV among pediatric patients and the decrease in the incidence of PONV with increasing adult age means that the association is not linear if we combine pediatric and adult patients. It does not mean that a bimodal distribution exists between PONV and age, in which there should be two peaks in the distribution. There is one peak (i.e., one mode) in late childhood, with a lower incidence of PONV in early childhood and adulthood.

We have developed and validated a mathematical model to calculate the risk of PONV among ambulatory surgical patients. We believe that this model will predict patients’ risk of PONV and promote efforts to reduce the incidence of PONV.

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Perturbation of Lipid and Protein Structure by General Anesthetics: How Little Is Too Little?

To the Editor—Lipid-based theories of general anesthetic action have long endured because numerous studies have shown that the in vivo pharmacology of an anesthetic correlates remarkably well with its ability to perturb the structural properties of simple lipid bilayers. The Meyer-Overton correlation between anesthetic potency and hydrophobicity, the inactivity of nonanesthetic long chain alcohols and highly halogenated volatile compounds (nonimmobilizers), and pressure reversal have all been demonstrated in studies using protein-free lipid bilayers. Nevertheless, a most persuasive and often mentioned argument against lipid-based theories is that at clinically relevant concentrations, anesthetics induce only small perturbations in lipid bilayer structure. For example, halothane reduces the order parameter (increase the ‘fluidity’) of lipid bilayers by only 1% at clinically relevant concentrations. An equivalent reduction in order parameter may be obtained by raising the temperature of the bilayer by less than 1°C. Similarly, halothane reduces the transition temperature between a lipid bilayer’s liquid and gel phases by only 0.5°C at anesthetic concentrations and by only 5°C even at 10 times the minimum alveolar concentration (MAC). I was, therefore, very interested to read the study by Johansson et al. quantifying the effects of isoflurane and halothane on structural properties of bovine serum albumin, a lipid-free protein model used in mechanistic studies of anesthetic action. What did their studies show? At approximately 1 MAC, isoflurane and halothane increased the fluorescence anisotropy of bovine serum albumin by 1%. An equivalent reduction was obtained by raising the temperature of bovine serum albumin by approximately 1°C. Similarly, isoflurane and halothane raised the transition temperature between the folded and unfolded states of bovine serum albumin by less than 1°C at anesthetic concentrations and by only 3–4°C even at 10 times MAC. Studies of anesthetic binding to other protein models have been similarly unable to demonstrate significant anesthetic-induced changes in protein structure. Thus, anesthetics induce similarly small changes in the structural properties of lipids and proteins. For consistency, shouldn’t we now conclude that such insensitivity argues strongly against a protein site of anesthetic action?

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The inability to detect significant anesthetic-induced structural changes in either lipid or protein model systems highlights the practical (and obvious) limitations of such studies: we can only measure what we can measure. Fluorescence anisotropy, denaturation temperature, phase transition temperature, and order parameter have been used by biophysicists for many years as indicators of lipid bilayer and protein structure in large part because they are easily quantitated. There is no compelling theoretical reason to believe that changes in these properties directly accounts for the functional effects of anesthetics on relevant targets in the central nervous system. In fact, it seems quite likely that the anesthetic state results from changes in other lipid and/or protein physical properties that are not so easily measured.

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In Reply.—Dr. Raines correctly points out that the effects of either 1 MAC isoflurane or 1 MAC halothane on tryptophan side-chain mobility in bovine serum albumin are comparable to what follows from a 1°C reduction in temperature. Changes in lipid fluidity in the presence of anesthetic molecules can be mimicked by small variations in temperature, and this has been argued to indicate that lipids are an implausible site of anesthetic action. By analogy then, as noted by Dr. Raines, the same line of argument would suggest that a protein target would be an equally unlikely in vivo site of anesthetic action.

If anesthetics interact directly with protein targets and alter their function, then binding must influence either the structure of the protein or its dynamics. Alternatively, anesthetics may compete with native ligands for their binding sites. The latter mode of action does not appear to apply in the case of ligand-gated ion channels, since anesthetics increase the affinity of the native neurotransmitter. If anesthetics interact directly with proteins not amenable to experimental analysis at present are responsible for the clinical effects of inhaled anesthetics. One example of this is the lipid-based mechanism of general anesthetic action proposed by Cantor. However, until such theories can be experimentally tested, we remain optimistic that currently available biophysical tools will provide useful information, and generate testable hypotheses, regarding how these important clinical agents may exert their effects on the central nervous system.

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Is the System at Fault, or Its Players?

To the Editor:—We read with great interest the article and accompanying editorial describing the mismatch between potential and actual claims and remedies in anesthesia malpractice litigation. The authors conclude that the discrepancy resides either in the peer review process of the study or in the legal system. Despite use of residents in training as peer reviewers, the authors argue for the latter. Both pairs of writers decry the existing tort system and put forward proposals for its overhaul. As a third interpretation, we suggest that the problem lies not so much in the system of litigation society has adopted, as in the training and credentialing of its practitioners. To scrap a system that has accomplished much good (handicap access, gender equity, the moment in time when the personal injury tort system and its incentives must be part of every medical student's education as a requisite to ongoing legal education to retain the credential. Precedent for such a scheme may be found in the successful operation of the Intellectual Property Bar. Factual arguments before a jury selected from the community must be preserved, but with courts controlled by a specifically skilled and experienced judiciary.

Third, efficient execution of the existing system obliges the legal profession to create a corresponding Medical Malpractice Bar, with documentation of an undergraduate degree in the life sciences, specialty training during law school, passage of a rigorous exam, and continuing legal education to retain the credential. Precedent for such a scheme may be found in the successful operation of the Intellectual Property Bar. Factual arguments before a jury selected from the community must be preserved, but with courts controlled by a specifically skilled and experienced judiciary.

In the survey, 13 individuals were harmed by deviations from standard care determined by peer review, yet none resulted in legal action. Were the circumstances of disclosure to these patients at the time of injury investigated? Did the injured patients seek legal counsel but

Anesthesiology, V 92, No 5, May 2000