

Beecher, MD, was at the forefront of identifying ethical problems with human experimentation; he reported his findings and opinions in several prominent journals, including this one.<sup>5,6</sup> Finally, although not relevant to Domino's experiments, the Belmont Report was published in 1979.\* Therefore, I would argue that the definitions and obligations were available before the 1980s; the problem was that they were being ignored.

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## In Reply:

Although I thank Dr. Butterworth for his comments concerning my commentary,<sup>1</sup> I do not agree with his opinion that US medical researchers consistently obtained informed consent from human subjects before the 1980s. The Nuremberg Code (1947), the Declaration of Helsinki (1964), and Beecher (1966)<sup>2</sup> describe research without consent from human subjects and were all published before the 1980s. However, printed copies of these documents were not readily available to US physicians. Until the 1980s, even fewer physicians thought that the Nuremberg Code or Helsinki Declaration had much to do with medical research or clinical practice within the United States.

The Nuremberg Code was composed subsequent to the conviction of Nazi physicians who defended their horrific research, claiming it was similar to medical research being done all over the world.<sup>3</sup> That code stated as its very first basic principle that human experimentation should involve the "voluntary consent of the subject."

The World Medical Assembly meeting in Helsinki published what became known as the Declaration of Helsinki. It

contained 22 "basic principles" for guiding human subject research. The Declaration was later revised in 1975 and 1983.

The medical community did not develop sanctions for researchers who disregarded the Nuremberg Code or the Helsinki Declaration.

Beecher's<sup>2</sup> comments in the *New England Journal of Medicine* were not welcomed by some in the medical research community because prominent researchers thought his ideas about obtaining informed consent from human subjects would stifle medical research. His article was originally refused publication in *JAMA*<sup>4</sup> and the *New England Journal of Medicine* agreed to publish it only after more than half of the cases he described were removed.

I agree with Butterworth that Beecher—along with many of his distinguished anesthesiologist colleagues—rightly deserves a place of honor in the development of the understanding of clinical research ethics. However, I certainly did not know specifically of Beecher's *New England Journal of Medicine* article<sup>2</sup> when I started doing human subject research in 1976. It was not until I took the time and effort to research ethical issues in anesthesiology practice that I began to understand the development of medical ethics in the United States.

The medical literature of the 1970s is, unfortunately, replete with clinical studies that did not meet the standards of the Declaration of Helsinki.<sup>5</sup> Even today, many physicians do not value the study of medical ethics because they do not believe it is an academic discipline. Many surgeons believed that consent was not routinely required and that medical ethics was a waste of time that served only to "raise doubts where there were none before."<sup>6</sup> Multidisciplinary panels that composed Federal regulations for human research had more ethicists and members of the public than physicians because US society wanted consistent treatment of human subjects of research.

The community of professional physicians failed to agree on required elements of consent or enforce consistency in obtaining patient consent. Beecher<sup>2</sup> himself stated that achieving truly "informed consent" was probably not possible. He acknowledged the pressure on researchers to publish combined and an explosion of research funds to coerce researchers to proceed without trying too hard to fully inform research subjects.<sup>2</sup>

Federal standards were defined in the late 1970s, published in 1981, and enforced thereafter. They defined the requirements for informed consent for research subjects, which, until that time, were pretty much up to individual researchers—some of whom had more defensibly ethical practices than others.

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\* National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. 1979. Available at: <http://ohsr.od.nih.gov/guidelines/belmont.html>. Accessed February 3, 2011.

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## Anesthesiologists as Genetic Counselors?

To the Editor:

We wish to comment on the editorial by Drs. Lee and Raja "Should Anesthesiologists be Equipped as Genetic Counselors?"<sup>1</sup>

Although Drs. Lee and Raja highlight pharmacogenetics and molecular genetic factors that might influence patients' response to pain medication, the omission of a discussion of certain pharmacogenetic disorders specifically related to anesthesiology is baffling and a significant oversight. In particular, there are two classic pharmacogenetic disorders of special interest to anesthesiologists: the response to succinylcholine due to mutations in the gene that elaborates pseudocholinesterase (butyrylcholinesterase), and malignant hyperthermia syndrome.

Anesthesiologists who are expert in understanding malignant hyperthermia already use molecular genetic testing to guide patients in the selection of anesthetics and to determine the risk of developing malignant hyperthermia. A sophisticated knowledge of the significance of the more than 200 mutations associated with the ryanodine receptor gene<sup>2</sup> is necessary for advising patients with malignant hyperthermia. In fact, at one of the two DNA testing laboratories for malignant hyperthermia (the University of Pittsburgh, Division of Molecular Genetics, Pittsburgh, Pennsylvania) a genetic counselor is employed to help evaluate and advise patients.

The issue of understanding let alone counseling patients on the direct-to-consumer tests for evaluating a patient's risk for disease or response to medication, is exceedingly complex because phenotype may be influenced by several genes and gene products. The Food and Drug Administration at recent hearings has cited concerns for risks to public health imposed by the trend toward increasingly complex tests brought to market primarily through the Internet and without Food and Drug Administration review.

As the authors point out, the functional significance of a mutation is complicated by the genetic background of the

patient as well as environmental factors. The question concerning these tests is not "Are people buying them?" but rather how does one interpret these tests and provide meaningful advice to patients?

Genetic counseling has become increasingly complex as the collaboration between pathogenic mutations and contributing genetic variants generates sometimes unpredictable phenotypes and patterns of heredity. Without in-depth education and training, anesthesiologists should not be giving advice on the response to pain and pain medication based on a DNA profile. Physicians in all specialties should develop a working relationship with centers that have medical genetics divisions or departments that include board-certified genetic counselors to provide the necessary genetic counseling.

It is entirely appropriate for anesthesiologists to focus research activities on the molecular genetic basis of drug response and take an active interest in education concerning molecular genetic research. This is a far cry from being "equipped" as a genetic counselor.

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In Reply:

We thank Rosenberg *et al.* for their interest in our editorial<sup>1</sup> on the potential role that anesthesiologists may have to play as genetic counselors in light of developments in the direct-to-consumer genetic testing market. We also appreciate these researchers noting the importance of malignant hyperthermia when discussing genetics in anesthesiology. The focus of the editorial was on pain genes; it was not meant to be comprehensive.

It is undeniable that most anesthesiologists have little to no formal training in genetics and genetic counseling; therefore, it would be to the patient's benefit to seek consultation with a genetic counselor for answers concerning his or her genetic predispositions. We agree that all specialists, including anesthesiologists, should develop a working relationship with a medical genetics department to respond appropriately to patients' concerns based on their genetic profile and to provide optimal care to their patients.

Unfortunately, such communication between anesthesiologists and genetic counselors is not the norm. For example, although patients with a suspected malignant hyperthermia crisis or a suspected susceptibility to malignant hyperthermia are advised to undergo *in vitro* contracture testing and ge-