References

1. Palmer SK: Preserving patients' health curing WWII: Commentary. ANESTHESIOLOGY 2010; 113:685–6
2. Beecher HK: Ethics and clinical research. N Eng J Med 1966; 274:1354–60
3. Vollmann J, Winau R: Informed consent in human experimentation before the Nuremberg code. BMJ 1996; 313:1445–9
4. Harkness J, Lederer S, Wikler D: Laying ethical foundations for clinical research. Bull World Health Organization 2001; 79: 365–72
5. Belsey A: Patients, doctors and experimentation: Doubts about the Declaration of Helsinki. J Med Ethics 1978; 4:182–5
6. Editorial: Ethics, surgery and clinical research. J Med Ethics 1980;6:51–2

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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"?[1]

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[2] 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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References

1. Lee FH, Raja SN: Should anesthesiologists be equipped as genetic counselors? ANESTHESIOLOGY 2010; 113:507–9
2. Stowell K: Malignant hyperthermia: A pharmacogenetic disorder. Pharmacogenomics 2008; 9:1657–72

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In Reply:

We thank Rosenberg *et al.* for their interest in our editorial[1] 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-

netic counseling at a certified malignant hyperthermia center,[2] it is not uncommon for anesthesiologists to counsel and anesthetize such patients. Often, patients are advised of their possible genetic disposition and a trigger-free general or regional anesthetic technique is used, with safe results.[2]

Anesthesiologists are often in the difficult position of meeting a patient for the first time minutes before the start of a procedure and do not have all of the patient's relevant medical information. There is a clear need for assistance when it comes to genetic counseling. We hope that in the days of personalized medicine, anesthesiologists will better educate themselves in genetics as it relates to anesthetic practice, seek the expertise of colleagues in medical genetics departments, and foster a pragmatic relationship for the benefit of patients.

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References

1. Lee FH, Raja SN: Should anesthesiologists be equipped as genetic counselors? Anesthesiology 2010; 113:507–9
2. Wappler F: Anesthesia for patients with a history of malignant hyperthermia. Curr Opin Anaesthesiol 2010; 23:417–22

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The Discovery of Chloroform: Has David Waldie's Role Been Exaggerated?

To the Editor:

It is now commonly accepted that James Y. Simpson, (1817–1870), professor and chairman of the Department of Midwifery at Edinburgh University (Scotland), tried chloroform after it was suggested to him in October 1847 by David Waldie, L.R.C.S. (Edinburgh; 1813–1889), pharmacist in Liverpool. Likewise, it is commonly accepted that Simpson was ungenerous in acknowledging his friend's contribution to the discovery.

Indeed, a brief footnote in Simpson's first account of the discovery[1] stated, "Waldie had mentioned the perchloride of formyle (chloroform) among others as worthy of a trial." In the same footnote, Simpson warmly thanked his assistants, J. Matthews Duncan, F.R.C.S. (1826–1890), and George Keith, as well as William Gregory (1803–1858), who had suggested the chloride of hydrocarbon (Dutch liquid) and given him samples of various compounds to try. Gregory was chairman of the Chemistry Department at Edinburgh University. Duncan and Keith had studied midwifery under Simpson.

However, a review of the facts surrounding the discovery of chloroform leads us to question the importance of Waldie's contribution and the extent of Simpson's ingratitude. The reminiscences of Duncan and James Miller (1812–1854), professor of surgery at Edinburgh University, never mention Waldie. In addition, throughout the years after the discovery, Simpson repeatedly thanked Waldie.

In early 1848, Miller, who was a professor of surgery at Edinburgh University and neighbor of Simpson, described the evening of November 4, 1847, as it was reported to him by participants.[2] Although Simpson initially discarded the chloroform as "too heavy," he later changed his mind and retrieved it from the wastebasket. Miller does not mention Waldie.

Duncan, who was then a lodger and one of Simpson's assistants (later becoming a renowned obstetrician in Edinburgh then in London), gave a different and more detailed version of the events in a March 6, 1870, letter to Robert Christison (1797–1880), a professor of toxicology and medical jurisprudence at Edinburgh University.[3] A copy of that letter was sent by Duncan's widow to the *British Medical Journal* in 1896.[4] The letter indicates that, a few days before the discovery, Simpson and Duncan visited Gregory, who gave them samples of various compounds. Duncan inhaled several of them on the morning of November 4, 1847. He found chloroform to be "the most interesting of them" and brought it to Simpson's dining room that evening. He reported that he had forgotten the name given to the compound, but that "it certainly was not chloroform." It probably was perchloride of formyle.[1]

Duncan's sister Isabella, in two short posthumous biographies of her brother,[5–7] added that he had been unconscious for 15 min after he had inhaled chloroform. It was this response that prompted him to suggest it to Simpson. She indicated that her brother had been hurt when Simpson ignored his important role in the discovery although he had never complained. Duncan, too, never mentioned Waldie.

Thus, both Miller and Duncan ignored Waldie.

In a lecture given to the Liverpool Literary and Philosophical Society on November 29, 1847,[8] Waldie complained of Simpson's lack of acknowledgment. Possibly encouraged by family and friends, he was more emphatic in a pamphlet published in 1870 after Simpson's death.[9] But Waldie was unfair to his late friend who had profusely thanked him in a letter accompanying his account of the discovery[1] he had sent him in 1847.[10] Simpson also frequently mentioned Waldie's name in his lectures to medical students.[9]

In a letter to his Liverpool colleague John Abraham (1813–1881), pharmacist at Clay & Abraham Co., Waldie admitted that Simpson's acknowledgment "had been handsome."[11] Waldie was thus amply thanked for a mere suggestion he had offered in October 1847.

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References

1. Simpson JY: Account of a New Anaesthetic Agent as a Substitute for Sulphuric Ether in Surgery and Midwifery. Edinburgh, Sutherland & Knox, 1847, pp 8–9
2. Miller J: Experience with Chloroform. Edinburgh, Sutherland & Knox, 1848, pp 9–11

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