Editorial Comment

The Art and Science of Mixing and Matching*

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In this issue of the Journal, Natale et al. (1) report clinical advantages of a hybrid biphasic nonthoracotomy defibrillating system compared with their earlier experience using a monophasic device with a congenitally designed transvenous defibrillating lead system. This involved preliminary clinical results in patients receiving a standard CPI monophasic implantable cardioverter-defibrillator versus a biphasic implantable cardioverter-defibrillator (Cadence, Ventritex) using the same CPI Endotak (C-60) transvenous lead system with both devices. The authors report lower defibrillation thresholds and improved clinical efficacy and utility (decreased implantation time, shorter patient recovery time and higher implantation rate) based on a retrospective comparison of a new hybrid defibrillating system with an earlier clinical investigational experience.

The art of medicine reflects individual innovation. The science of medicine reflects identifiable variables and measurable outcomes. Clinical efficacy and safety (clinical utility) encompasses both science and art from the diverse perspectives of the public, the regulatory agencies responsible for public safety, competing manufacturers and the medical community. It is the physician's role to responsibly advance the art and science of medicine for patient benefit. Natale et al. recognized some of the uncertainties surrounding the use of hybrid defibrillating systems, but they may be creating more controversy instead of advancing the art and science of medicine.

The present study. Natale et al. (1) failed to address the starting and termination dates of both series, the investigational protocol status of the nonhybrid implantable cardioverter-defibrillator system, differences in implantation protocol, the "learning curve" influence and available alternative therapies while advancing the advantages of biphasic hybrid use. The report lacks data and description with regard to sensing. It only addresses the value of biphasic versus monophasic defibrillation. There are no comments about inappropriate shocks, nor in fact is there a specific comment with regard to observed or potential sensing problems with the Endotak (C-60) lead with its designed matched device or in a "mix and match" configuration. The primary safety issue with an Endotak (C-60) lead in a "mix and match" configuration is sensing (2,3). The authors provide no observations in their report with respect to the safety and efficacy of sensing; however, they infer that the hybrid biphasic system is safer and more clinically efficacious. Only through careful inspection of the report does it become apparent that the observations are limited to improvement in biphasic compared with monophasic defibrillation thresholds (p = 0.03). Proper antitachycardia system function is dependent on both accurate tachycardia recognition and effective termination response. The rate-sense signal from the Endotak integrated bipolar has characteristics different from the standard dedicated bipolar. If the Endotak lead, with its integrated bipolar rate signal, is combined with other manufacturers' devices, their sensing schemes might lead to detection abnormalities and misdirected therapy.

Implications and problems. When addressing the issue of "mixing and matching" devices for arrhythmia management that have not been formally tested in such a combination, one should assume that a patient who is refractory to approved therapy and has no other alternatives is likely to benefit according to the expertise of the physician ("taking the high road"). One could also take the "low road" and assume that for marketing purposes and "leapfrogging" technology around the Food and Drug Administration (FDA)," clinicians, in concert with manufacturers, are trying to advance certain technology independent of the specific needs of an individual patient. The specific patient may benefit, or the patient may not experience beneficial or adverse results, or the patient may be harmed. Unfortunately, this type of clinical experience (clinical data) currently does not contribute to the regulatory decision process. Furthermore, even data from sound clinical investigations do not influence the regulatory device evaluation process. This frustrates physicians and encourages them to circumvent the FDA. Also, reports such as that of Natale et al. enable biased parties to inform, misinform or disinform the medical community with regard to the efficacy and safety of a mixed and matched system.

The physician should follow the guidelines for safety and efficacy for a specific patient unless or until the patient's particular and peculiar clinical presentation necessitates innovation. Then it is up to the physician to improvise in a manner that is most likely to benefit the patient and least likely to cause harm. The obligation of the physician is to gain knowledge, to educate colleagues and always to provide continuously improved patient care. If Natale et al. are directly or indirectly supporting the hybrid use of this particular combination as a standard or an acceptable norm,
they therefore should clearly address the efficacy and safety issues of defibrillation as well as the efficacy and safety issues of sensing because both aspects are equally important for effective defibrillation therapy. The specific issues of sensing were well known at the time of the preparation of this report. Certainly, it is the prerogative of the authors to take their limited approach; however, they then should state to the reader that there are other issues involved and that they can be found by consulting various references. The dilemmas of pursuing continuous improvement in clinical practice. The FDA has encouraged industry to do the following: 1) avoid device marketing for out of label use; 2) police and discourage the use of out of label devices by the medical community; 3) apply for investigational device exemption to formally test mixing and matching of implantable cardioverter-defibrillator systems. The FDA is also encouraging physicians and researchers, in cooperation with manufacturers, to apply for individual investigational device exemptions to test innovative technologies in a manner that facilitates subsequent FDA data analysis. Unfortunately, the process of obtaining this type of investigational device exemption is cumbersome. Fortunately, the FDA is committed to streamlining this process in the near future. The use of mixing and matching should depend on relative risk. Mixing and matching in pacing is more readily tolerated because of less critical electromechanical interfaces and much less critical clinical sequelae. Mixing and matching of implantable cardioverter-defibrillator systems is potentially more dangerous. The CPI device and the CPI Endotak lead were “tuned” to function as a system. The use of one company’s device with another company’s lead system presents greater risk and more potential difficulty. This type of mixing and matching also provides the potential for achieving the best system. The only way to tell is to acquire sound scientific data. Physicians should have the right to mix and match when it is to the patient’s benefit and when alternative, approved systems are not available. One steps into an uncertain, vulnerable position when mixing and matching without clear clinical indication for the specific patient: The risks of mixing and matching exist and may prove not to be significant; however, they are currently unknown. Physicians should follow the rules of what is safe and effective until the patient becomes refractory to established therapies; then it is up to the physician to improvise for the best therapy according to his or her judgment. The only solution is continuous dialogue between the medical provider, the manufacturer and the regulatory body to achieve the common mission of improved patient care that includes access to new technology. It is unfortunate that Natale et al. and others are forced to pursue this mix and match approach of third-generation ICD technology, whereas our colleagues in Europe are now successfully applying fourth- and fifth-generation ICD technology that was designed in the United States but transported overseas because of regulatory barriers. Concurrent with these regulatory barriers are the recent attempts by Medicare and the Office of the Inspector General to limit use of certain medical procedures and devices that physicians believe have been shown to be safe, effective and superior to other therapies but are not yet FDA approved (New York Times, Saturday, June 18, 1994). Les Aspin, our former Secretary of Defense, received a pacemaker outside of labeled indication, yet the same type of application would now not be reimbursed by Medicare. Further government controls and cost savings may well limit access for the poor and elderly to the latest and best medical options. In addition, these controls will likely stifle U.S. advances in clinical research that have set our medical system apart from others worldwide. This type of two-class medical delivery system is the rule rather than the exception worldwide, where long lines and inferior medical care are the norm for all but those who can afford access to a private system. We must avoid a system that provides first-rate modern therapy for only those who can afford the best U.S. technology applied in foreign lands but limits access to the best medical care for the less fortunate, including the elderly and the poor. A reformed national health care system that functions under government rules similar to Medicare will certainly ration the best technology and medical care for everyone when cost is the primary issue.

References

