Deactivating Implantable Cardioverter Defibrillators

TO THE EDITOR: Berger (1) raises the important issue of advances in technology outstripping advances in ethical decision-making practices. His comparison of implantable cardioverter defibrillator (ICD) deactivation with hemodialysis discontinuation is valuable in helping to clarify the issues inherent in decisions to remove active and invasive therapies. I am very concerned, however, about the parallel drawn between deactivation of an ICD and deactivation of a permanent pacemaker. The nature of implanted cardiac devices and their functions related to the dying process are inherently different and must be considered as such. An ICD delivers therapy to terminate a life-threatening arrhythmia by delivering a shock or overdrive pacing. This therapy is most often sensed by the patient and is typically associated with marked discomfort. Conversely, a permanent pacemaker, once implanted, is typically not sensed by the patient and acts to replace the natural electrophysiology of an intact cardiac conduction system.

For those individuals who make such a distinction, deactivating an ICD may be considered a form of passive euthanasia that removes a barrier to a natural death. Indeed, this concept is similar to withholding external cardiopulmonary resuscitation. Deactivating a permanent pacemaker may more properly be considered a form of active euthanasia because it removes a noninvasive (in the sense that it is not felt by the patient), automatic, and completely internalized surrogate for a natural process. Moreover, in many end-of-life situations, the diagnosis responsible for the patient’s deteriorating condition has no relationship to the heart block that is being treated with the permanent pacemaker. By deactivating the permanent pacemaker of a pacemaker-dependent patient, the physician may be viewed as actively killing the patient as opposed to allowing the natural dying process to unfold.

For some patients in some situations, deactivation of the ICD or the permanent pacemaker may be suitable. To consider the actions similar and the ethical principles surrounding them to be shared, however, is inappropriate.

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Potential Financial Conflicts of Interest: None disclosed.

Reference
1. Berger JT. The ethics of deactivating implanted cardioverter defibrillators. Ann Intern Med. 2005;142:631-4. [PMID: 15838070]

TO THE EDITOR: The review by Berger (1) highlights the complex end-of-life issues posed by the presence of ICDs. This dilemma is particularly difficult for those physicians treating patients who have advanced heart failure, a group that is receiving implantable devices at an increasing rate and whose prognosis is ambiguous. The American College of Cardiology/American Heart Association practice guidelines for chronic heart failure offer the consensus view that such devices are of little benefit in those patients with New York Heart Association class IV symptoms typical of end-stage disease (2).

We agree with Berger that formal guidelines do not exist to address these issues and to date, most discussion has centered on illustrative cases (3). The recent paper by Goldstein and colleagues (4) in this journal emphasized the importance of communication in this process. Their research showed that for 100 unselected patients who were dying with an ICD in situ, 81 of whom had heart failure, discussion on device inactivation took place in only 27 cases. This discussion was confined to the last few days of life, and 21 patients opted for withdrawal of this therapy. Fragmentation of the care plan was evident; 27 of these 100 patients received a shock in the month before death—in the last few minutes of life for 8 of these patients. This action contributed to the discomfort of dying and was distressing for those around them.

Improvement of the dying process for patients with ICDs demands open and objective discussion with patients and their families (or surrogates) regarding the usefulness of these technologies as the underlying disease progresses. Uncertainties specific to prognostication in heart failure should be acknowledged. Opportunities for such interaction may occur at the time of ICD implantation, when preferences for resuscitation are explored in the setting of advanced disease or impending death, after withdrawal of antiarrhythmic therapy, or on recovery from a crisis typical of the heart failure disease trajectory. We have recently incorporated ICD deactivation as a formal element of the Liverpool Care Pathway for the care of those dying of heart failure in the hospital (5), and we will soon pilot this protocol in a multicenter study in England.

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Potential Financial Conflicts of Interest: None disclosed.

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The need to discontinue use of an ICD is not an occasional consideration; it is a predictable part of the course of dying for any patient with an ICD who will die a natural death. With demographic analysis now showing that more than 80% of Americans die while covered by Medicare (elderly or disabled) and 90% live with serious chronic illnesses for many months before dying, recipients of ICDs will routinely be better served if they avoid the discomfort and disruption of having shocks while dying.

One obvious ethical response is that patients should be aware at the time of implantation that this device should ordinarily be stopped when life is getting to be short and life’s continuation is tenuous because of conditions other than arrhythmia, or when dying with an arrhythmia becomes a better course than what otherwise awaits. Because ICDs otherwise are generally “lifelong therapy,” planning for eventual death should be a standard part of the consent process and the ongoing management for anyone accepting such a device.

The case presented by Berger (1) reflects the failure to plan ahead, thereby putting the patient in a position of substantial and unwarranted risk to well-being. This error, just like other errors, should necessitate a response by the current responsible physicians to notify the previous care providers of the need to attend to this part of a complete protocol for consent to ICD implantation. Otherwise, those who provide care “downstream” to patients who bear the brunt of such errors just endure the harms with patients and families, and those “upstream” never realize the problems that they cause.

Recently, a hospice patient with cancer endured more than 50 shocks in the last day of life, anguishind between shocks as to whether stopping the now-hated device amounted to mortal sin. Although that is a challenging question, surely it would be better contemplated back at the time of implantation (or even a few weeks before dying) rather than having patient, family, and caregivers caught up in such torment. Surely, the practitioner responsible should know of the harms caused by failing to consider this outcome. And just as surely, standard practice should require decent notice of such a possibility and the opportunity to avert it.

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Reference
1. Berger JT. The ethics of deactivating implanted cardioverter defibrillators. Ann Intern Med. 2005;142:631-4. [PMID: 15838070]

IN RESPONSE: Ms. Ross argues that disabling a permanent pacemaker is active euthanasia because a pacemaker replaces natural cardiac physiology, because it is automatic and implanted, and because its action is not felt by the patient. These distinctions are not medically or ethically relevant to decisions regarding the appropriate continued use of pacemakers or to distinguishing active from passive euthanasia. Many treatments simply replace normal physiology (for example, insulin pumps, left ventricular assist devices, ventilators, renal replacement therapy through hemodialysis) and are automatic (ventilators, balloon pumps) or internalized (insulin pumps). Furthermore, for many neurologically impaired patients, life-sustaining treatments are “not felt by the patient,” yet, contrary to Ms. Ross’s criterion, these interventions are not typically considered to be “non-invasive.” Continued use of pacemakers should not be accepted because they are already implanted and in use; rather, pacemakers are simply another medical intervention that can sustain life, the use of which should be based on whether the patient determines that its net effects are valuable.

I support Dr. Beattie, Mr. Ellershaw, and Dr. Lynn in their call for greater attention to advance care planning with regard to ICDs, in addition to other life-sustaining technologies. Advance directives can assist families and physicians in implementing appropriate treatment plans and can remove legal obstacles to appropriate care. Unfortunately, several concerns remain with advance health planning, including widespread public reluctance to engage in this activity, culturally based discordance with advance directives, and other barriers that limit its influence in treatment (1–3). These challenges should not dissuade professionals from discussing treatment preferences with their patients. Rather, the health and legal systems should better integrate advance planning as well as family decision-making processes for patients who choose not to plan. Barriers to dialogue between physicians and patients should also be further examined (4, 5).

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Potential Financial Conflicts of Interest: None disclosed.

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Acupuncture for Low Back Pain

TO THE EDITORS: I believe Manheimer and colleagues (1) may have overestimated the principal findings of their study, the short-term effects on pain for acupuncture compared with sham. First, in their Figure 1, Manheimer and colleagues reported a larger effect size than was originally reported by Leibing and associates (2). Second, they included a study by von Mencke and colleagues (3) that had several included a study by von Mencke and colleagues (3) that had several
30 patients randomly assigned to receive sham acupuncture because 63% of the sham group ended up receiving real acupuncture and therefore could not be included in the sham-versus-acupuncture comparison. Third, none of the 4 studies included in the sham pooled result tested the credibility of their sham, which is usually accomplished by asking patients to guess if they received real or sham acupuncture. Without an assessment of the credibility of the sham, we cannot conclude that the study was effectively “blinded,” and the possibility of expectation bias cannot be excluded. Exclusion of the von Mencke study and use of the effect-size estimate of 0.27 that was reported in the Leibing study yielded a pooled effect size for the remaining 3 studies of 0.425 (95% CI, 0.19 to 0.66). This effect size translates into a change in pain intensity of 10.6 mm on a 100-mm visual analogue pain scale, which is at the threshold of what is considered clinically significant. This result probably represents the upper boundary of the estimated efficacy of acupuncture in these studies because the possibility of expectation bias cannot be excluded. On the basis of these data, I believe it is premature to conclude that “acupuncture effectively relieves chronic low back pain.” Before such a conclusion can be reached, we need better-quality, randomized, controlled trials that report statistically and clinically significant benefits for acupuncture compared with a demonstrably credible sham therapy.

IN RESPONSE: We thank Dr. Shkelle for the opportunity to further clarify our methods, data, and conclusions. First, we calculated standardized mean differences using post-treatment mean values and SDs for each group. For the study by Leibing and colleagues (1) only, we used baseline SDs because post-treatment SDs were not reported. We prereferred a comparison of post-treatment scores, which may have been superior to comparisons of between-group changes among trials in which SDs for differences in changes were incompletely reported (2). We recognize that between-group change scores and post-treatment scores may result in different standardized mean differences when there are baseline differences between the groups (as occurred in the Liebing study). To address the possibility that between-group changes and final value analysis methods might result in different effect sizes, we used between-group changes to recalculate our effect sizes for comparisons between sham acupuncture and acupuncture. The trial by Molsberger and colleagues (3) did not report SDs of between-group changes or any statistics that would allow us to calculate these. For the 4-week data from this trial, we assumed a within-subject pretest–post-test correlation of 0.5. For the trial by Mendelson and colleagues (4), the authors appear to have reported 2 different t values in the abstract (t = 0.52) and in a footnote to Table 4 (t = 0.34). Because of our uncertainty over which, if either, of these t values was correct, we have performed 3 different meta-analyses of between-group changes. We used t = 0.34 for the first and t = 0.52 for the second; for the third, we assumed a conservative pretest–post-test correlation of 0.5. Recalculation with our estimated scores of between-group changes resulted in slightly smaller effect sizes (between 0.51 and 0.57) and wider confidence intervals that were still statistically significant.

Second, for the trial by von Mencke and colleagues (5), we used the outcome data from immediately after the end of the first treatment period (that is, a point less than 6 weeks and closest to 3 weeks following the end of treatment). There were no dropouts or crossovers at this measurement point; data shown in Table 12 of the trial report suggested that all 65 patients were available for analysis at this time point. We have used a second independent German translation to confirm the accuracy and appropriateness of the data we used.

Third, we also considered whether trials evaluated credibility of the sham by using a modified Jadad scale, which substituted the credibility testing item for a randomization-stated (yes or no) item. This substitution had the effect of reducing all trial scores by 1 point on the 5-point quality scale. Although we evaluated the credibility testing item and penalized the quality scores of all trials in our sample by doing so, we believe that the validity of this item is unclear and warrants further study.

Last, we believe that our original analyses based on post-treatment mean values and our subsequent analyses based on between-group changes support our conclusion: Current preliminary data suggest that acupuncture may be more effective than inactive controls for providing short-term relief of chronic low back pain.
The Future of Generalism in Medicine

TO THE EDITOR: I was gratified to read the candid and incisive editorial by Larson and colleagues (1) regarding the future of generalism in medicine. With clarity rarely encountered in medical journals, the authors boldly validated what every practicing general internist already knows: Economic pressures pose the greatest threat to generalist medicine in the United States, and a permanent fix of the flawed reimbursement system is imperative to revitalize general internal medicine. With limited numbers of graduating medical students electing to pursue training programs in primary care fields, fewer graduating medical residents pursuing primary care careers, and increasing numbers of hospitalists, the ranks of general internists are being ever depleted. A recent study indicates that only 27% of third-year internal medicine residents intended to pursue general internal medicine in 2003, down from 54% in 1998 (2). The same report states that merely 19% of trainees in their first postgraduate year were planning general medicine careers.

One statement in the editorial deserves special mention because it is symbolic of much of why general internal medicine finds itself in its present predicament. The authors observe that “To date, no advocacy group has emerged to advocate for primary care.” This comment is startling. It seems painfully obvious that the American College of Physicians, our professional society, should be leading the charge for economic reform.

Unfortunately, over the past 30 years, while doing an excellent job with educational services and practice guidelines for internists, the College has been ineffective at achieving an improved economic landscape for general internists (there are rare exceptions, such as payments for home-based services and care plan oversight). At the same time, however, the College has been a willful accomplice to the homogenization of primary care in the United States. This development has allowed the special expertise of general internists in diagnosing and managing adults with complex medical histories to be obscured by the title of “primary care provider,” which we now share with family practitioners, general practitioners, and nurse practitioners. The huge undersupply of general internists that looms in our future can be laid directly at the feet of the College because of its anemic advocacy to policymakers.

I fear the time has largely passed, but like Larson and his colleagues, I believe the only hope for replenishment and revitalization of general internal medicine is strong and durable economic reform. The College must, as its first priority, aggressively focus on convincing lawmakers and others who control the purse strings of the urgent need for rapid and sustained payment reform for primary care services. The arguments for a vital national cadre of primary care physicians are well-articulated in the articles in the Annals supplement.

Potential Financial Conflicts of Interest: None disclosed.

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CLINICAL OBSERVATIONS

Cimetidine and Acute Intermittent Porphyria

TO THE EDITOR: Background: Management of acute porphyric crisis involves withdrawal of offending drugs, treatment of symptoms with appropriate medications, and attempts to reverse factors that increase aminolevulinic acid synthetase activity. Hematin, the standard therapy for porphyria, is not always immediately available. Cimetidine may have a role in the treatment of acute intermittent porphyria by inhibiting heme oxidase activity, decreasing heme consumption, and inhibiting aminolevulinic acid synthetase through a negative feedback mechanism (1–4). We successfully treated 4 patients with acute intermittent porphyria with cimetidine; the drug also appeared to be effective for secondary prevention of subsequent episodes.

Objective: To determine whether cimetidine is an acceptable alternative to hematin for treatment of acute intermittent porphyria.

Case Reports: Patient 1 was a 25-year-old woman who arrived at the hospital with intense abdominal pain, generalized tonic–clonic convulsive crisis, and a serum sodium level of 108 mmol/L. Results of electromyography suggested segmentary motor demyelinating neuropathy. Her urinary porphobilinogen (PBG) level was 221 μmol/d (normal range, 0 to 9 μmol/d). We began therapy with intravenous cimetidine, 300 mg/6 h; 36 hours later, the patient’s pain subsided and hyponatremia was corrected without neurologic sequelae. Four days later, urinary PBG level was 13 μmol/d. During 4-year follow-up with cimetidine, the patient has experienced only 2 clinical episodes of moderate abdominal pain. Her urinary PBG levels have fluctuated from 75 to 137 μmol/d.

Patient 2 was a 29-year-old woman with a history of 4 exploratory laparotomies who was hospitalized for acute flaccid quadriparesis, intense abdominal pain, and a serum sodium level of 119 mmol/L. In addition, the patient showed an embryonic pregnancy. Results of electromyography demonstrated peripheral neuropathy with mixed polyneuropathic pattern. Her urinary PBG level was 172 μmol/d. We initiated therapy with intravenous cimetidine, 300 mg/6 h, and her symptoms improved within 48 hours. The patient underwent uterine dilation and curettage. On discharge from the hospital, urinary PBG level was 23 μmol/d. After 1 year of follow-up, the patient showed complete neurologic improvement and has experienced only 2 episodes of slight abdominal pain. The patient’s latest urinary PBG level was 9 μmol/d.

Patient 3 was a 38-year-old woman who was hospitalized because of flaccid quadriparesis and moderate high blood pressure. Results of electromyography showed segmentary demyelinating neuropathy. Her urinary PBG level was 75 μmol/d. We initiated therapy with intravenous cimetidine, 300 mg/8 h; we observed clinical improvement after 72 hours. The patient later underwent cholecystectomy; cimetidine therapy was continued postoperatively without complications. The patient’s condition has remained stable for 5 years.

Patient 4 was a 35-year-old woman with a family history of acute intermittent porphyria who was hospitalized because of intense generalized abdominal pain. Her urinary PBG level was 115 μmol/d, and her serum sodium level was 108 mmol/L. We initiated intravenous cimetidine, 300 mg/8 h; symptoms completely resolved within 72 hours. Over the next 3 years, the patient experienced only 2 episodes of less intense abdominal pain. Subsequent urinary PBG determinations ranged from 13 to 27 μmol/d.

Discussion: Although the usefulness of cimetidine therapy for acute porphyric crisis has been demonstrated (2–4), to our knowledge this report is the first with long-term follow-up to show that cimetidine also appears to be effective prophylactic therapy that stabilizes and prolongs periods of remission. In all 4 patients, we administered 900 to 1200 mg of intravenous cimetidine daily during the crisis and observed clinical improvement after 48 to 72 hours of treatment. In addition, 3 of our patients had acute hyponatremia during the porphyric attack. Urinary porphyrin levels diminished in an average of 7 days (although not to normal ranges) and were associated with evident clinical improvement. In all 4 patients, we prescribed 400 to 800 mg of oral cimetidine daily for secondary prevention; in each case, periods of prolonged remission were observed. In 1 case, cimetidine was given prophylactically during the preoperative period, suggesting its usefulness in high-risk patients who are scheduled to undergo surgery (Table). No deaths or side effects were reported.

Conclusion: Cimetidine may be effective for treatment of acute porphyric crisis and for secondary prevention of future episodes. Cimetidine constitutes a therapeutic alternative when hematin is not available.

Table. Usefulness of Cimetidine for Treatment and Prevention of Acute Intermittent Porphyria*

| Patient | Medical History | Serum Sodium Level, mmol/L | Urinary PBG Level, μmol/d | Urinary PBG Level after Intravenous Cimetidine, μmol/d | Urinary PBG Level at Follow-up, μmol/d† |
|---------|----------------|-----------------------------|---------------------------|------------------------------------------------------|----------------------------------------|
| 25-year-old woman | Abdominal pain, convulsive crisis | 108 | 221 | 13 | 75–137 over 4 y |
| 29-year-old woman | Abdominal pain, flaccid quadriparesis | 119 | 172 | 23 | 9 at 1 y |
| 38-year-old woman‡ | Abdominal pain, flaccid quadriparesis | 135 | 75 | – | – |
| 35-year-old woman | Abdominal pain, family history of acute intermittent porphyria | 108 | 115 | – | 13–27 over 3 y |

* PBG = porphobilinogen.
† Patients receiving long-term therapy with oral cimetidine.
‡ Patient underwent cholecystectomy; oral cimetidine therapy was continued postoperatively, and patient’s condition has remained stable for 5 years.
immediately available; in addition, it is less expensive and has fewer side effects. Larger studies are required to confirm these encouraging results before routinely using cimetidine for acute intermittent porphyria.

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CORRECTIONS

Correction: Acupuncture for Low Back Pain
In the abstract of a meta-analysis on acupuncture for low back pain (1), the first sentence of the Conclusions section should have read, “Current preliminary data suggest that acupuncture may be more effective than inactive controls for providing short-term relief of chronic low back pain.” Also, the reference number cited for the von Mencke trial in Figure 1 should have been 50, not 56.

Reference
1. Manheimer E, White A, Berman B, Forys K, Ernst E. Meta-analysis: acupuncture for low back pain. Ann Intern Med. 2005;142:651-63. [PMID: 15838072]

Correction: Comparison of Rosiglitazone and Metformin for Treating HIV Lipodystrophy
An article that compared rosiglitazone with metformin for treatment of HIV lipodystrophy (1) contained an error. The metformin dosage given to trial participants was 2 g/d, not 2 mg/d as described in the abstract. The dosage is stated correctly in the article text.

Reference
1. van Wijk JP, de Koning EJ, Cabezas MC, Roodt J, Joven J, Rabelink TJ, et al. Comparison of rosiglitazone and metformin for treating HIV lipodystrophy: a randomized trial. Ann Intern Med. 2005;143:337-46. [PMID: 16144892]