Enormous advances have been made in the overall treatment of acute myocardial infarction in the last three decades. Undoubtedly, the impact on mortality and morbidity has been substantial. The introduction of closed-chest DC cardioversion in the early 1960s promptly led to the development of the concept of acute coronary care, with the main focus on controlling arrhythmias. The concept found immediate validity when continuous ECG monitoring demonstrated arrhythmias in about 90% of patients with acute myocardial infarction. The fact that acute coronary occlusion in experimental animals and in humans leads to frequent and complex premature ventricular contractions (PVCs), often culminating in ventricular tachycardia (VT) and ventricular fibrillation (VF), was recognized early. Attempts at their prophylactic suppression by antiarrhythmic therapy became the cornerstone of therapy in the coronary care unit (CCU) aimed at reducing the early mortality. Lidocaine emerged as the logical choice of agent because of its efficacy, short elimination half-life, predictable side effects, and the ease of administration by intravenous infusion with little cardiovascular or hemodynamic toxicity. The drug appeared to be ideal for preventing primary VF by ameliorating transient episodes of electrical instability in acute infarction in hearts otherwise "too good to die." It became accepted that the drug did prevent VF, although Pantridge found it ineffective in the very early stages of acute infarction in contrast to intravenous β-blockade with practolol. The beneficial effect of lidocaine on acute mortality, however, has always been less certain, and the long-term prognosis of infarct patients defibrillated for VF in the CCU did not appear to be affected. Nevertheless, the practice of routine lidocaine therapy in acute myocardial infarction after two decades of its inception remains deeply entrenched in numerous CCUs in the United States and possibly abroad.

During this period, there have been developments in the management of acute infarction in the CCU, the results of which have increasingly questioned whether this practice is now warranted or justified. There is evidence that although agents that fundamentally act by blocking sodium channels (class I actions) are effective in abolishing or eliminating PVCs or even VT and VF, they may actually increase mortality in many subsets of patients with ischemic heart disease. The issue has been highlighted by the results of the Cardiac Arrhythmia Suppression Trial. Class I agents exhibit a variable spectrum of activity for PVC suppression, but meta-analyses of randomized controlled trials have indicated that either these drugs have no influence on mortality in infarct survivors or they may increase it. Many years ago, it was demonstrated that, electrophysiologically, lidocaine was in fact a potent class I agent. In the setting of acute infarct, it too appears to produce a slight excess in mortality, as does its oral congener, mexiletine, during long-term prophylactic administration in the survivors of acute infarction.

The overall data on sodium-channel blockers, including lidocaine, indicate that the effects of these drugs on the manifestations of an abnormal substrate might seemingly be beneficial for arrhythmia suppression, but mortality might be increased from further derangement of electrical instability that might induce death by asystole, bradycardia, or an unpredictable proarrhythmic reaction. Clearly, if this were so, the focus should be on augmenting electrical stability of the myocardial substrate rather than continuing with lines of therapy designed merely to suppress the manifestations of a deranged substrate and leaving the possibility open for increasing mortality by associated proarrhythmic reactions. Indeed, much progress has been made in this direction. Perhaps the most striking is the timely use of thrombolytic agents to reduce early mortality and increase ventricular ejection fraction. Presumably, by reducing ischemia, they improve myocardial conduction and reduce electrical instability, as suggested by a lower incidence of late ventricular potentials recorded on the signal-averaged ECG. The effects of early anti-ischemic therapy, particularly in the case of β-blockers, might be qualitatively similar and additive to thrombolytic therapy. The net effect is a reduced incidence of primary VF in acute infarction.
For these reasons, the report by Antman and Berlin\textsuperscript{17} in the present issue of \textit{Circulation} on the declining incidence of VF is not only timely but of major practical importance. The most striking observation is the steep decline in the incidence of primary VF between 1970 and 1990. In the early days of the CCU, the overall incidence was considered to be about 10%.\textsuperscript{7} From a critical meta-analysis of the available data from randomized controlled clinical trials spanning two decades, Antman and Berlin\textsuperscript{17} estimated that the primary VF rate was 4.51% in the control group in 1970 and fell to 0.35% in 1990; the corresponding figures for the lidocaine-treated groups were 4.32% in 1970 and 0.11% in 1990. They calculated that currently about 400 patients would need to be treated prophylactically with lidocaine to prevent a single episode of VF complicating acute infarction. Based on these data and those from previously reported excess mortality in the meta-analyses of randomized trials of lidocaine,\textsuperscript{2,11,12} the authors question the wisdom of routine lidocaine prophylaxis in acute infarction. They conclude that rarely is prophylactic lidocaine use now justified in acute infarction.

Their findings, when interpreted in light of the emerging data on the potential of sodium channel blockers as a class to increase rather than decrease mortality in different subsets of patients with heart disease, are compelling enough to suggest that routine lidocaine prophylaxis in the CCU as a standard practice should be abandoned.

Although not specifically discussed by Antman and Berlin,\textsuperscript{17} there are broader implications of their meta-analytic findings. In the case of certain antiarrhythmic agents or classes of agents, their data suggest that suppressant effects on disorders of rhythm may be divergent from those on mortality. This was evident in the case of flecainide and encainide in the CAST study\textsuperscript{10} and possibly in the case of quinidine in atrial fibrillation in meta-analysis of randomized controlled clinical trials.\textsuperscript{18} If this were so with lidocaine, clearly there should be concern about the continued use of lidocaine or other class I agents in the control of arrhythmias in other clinical settings in which lidocaine is often used prophylactically. This might be so during the induction of anesthesia and during intraoperative, perioperative, and postoperative periods in patients undergoing cardiac or noncardiac surgery. Here too, arrhythmia might be suppressed at the expense of an increase in overall mortality. To what extent this may also be applicable to patients admitted with manifest VT or VF outside the setting of acute infarction is uncertain, as no controlled observations have been made. The question whether lidocaine should remain the first-line approach in these settings or whether alternative regimens that might be equally effective but would not have the potential for a deleterious impact on mortality should now merit serious consideration.

Antman and Berlin\textsuperscript{17} suggested that the widespread use of \(\beta\)-blockers in coronary artery disease and hypertension and in those admitted to the CCU might have contributed to the declining incidence of primary VF between 1970 and 1990. They did not raise the possibility, however, that in situations in which lidocaine might still be justifiable (these appear to be very few), one might now consider the use of intravenous or oral \(\beta\)-blockade in place of lidocaine unless specific contraindications exist. There appears to be a reasonably compelling base of experimental and clinical data that favor such an approach. \(\beta\)-Blockers do not exhibit significant proarrhythmic effects, nor do they interfere adversely with myocardial conduction. As a class, they have an aggregation of pharmacological properties that is of great relevance to patients with ischemic heart disease. These drugs increase VF threshold and limit infarct size.\textsuperscript{19} The slowing of heart rate not only reduces oxygen consumption but also increases coronary blood flow by augmenting diastolic perfusion.\textsuperscript{20} In the ischemic myocardium, bradycardia decreases the extent of dispersion of refractory period.\textsuperscript{21} Such an array of pharmacological properties is likely to be conducive to the electrical stability of the ischemic myocardium. Therefore, it is not entirely surprising that rate-lowering \(\beta\)-blockers reduce sudden death incidence in the survivors of acute infarction\textsuperscript{19}; they increase survival in the long QT interval syndrome,\textsuperscript{22} and they may reduce recurrences in the case of aborted sudden death.\textsuperscript{23} Therefore, in the context of the CCU, \(\beta\)-blockers assume particular importance. When given intravenously to patients admitted with infarction, they lower the 10-day mortality by 10%\textsuperscript{24}; they reduce the incidence of VF when given during the early stages of acute infarction in humans.\textsuperscript{25,26} For example, Norris et al\textsuperscript{26} showed that propranolol, given about the time of presumed coronary occlusion and subsequently continued, significantly reduced the incidence of VF in the hospital compared with the effects of a matching placebo. In the metoprolol study,\textsuperscript{26} there were 17 cases of VF in the placebo group of 697 patients, but only six episodes in the \(\beta\)-blocker group of 698 patients (\(p<0.05\)). Thus, unlike lidocaine, which also reduces the incidence of VF in the setting of acute myocardial infarction but may produce an excess of mortality, \(\beta\)-blockers reduce VF while prolonging survival. The remarkable confluence of data on the beneficial effect of \(\beta\)-blockers on mortality in different cardiac disorders, including acute myocardial infarction, emphasizes their increasing role for the prevention of VF. Their observed beneficial effects appear to be mediated through a multiplicity of pharmacological effects impinging on and ameliorating the electrical instability of the ischemic myocardial substrate.\textsuperscript{19} In contrast, lidocaine and related agents prevent VF in the setting of acute infarction by reversing transient electrical instability as their sole action but leave open the possibility of a deleterious effect on the substrate in terms of further delay in conduction in certain patients. This may produce a net adverse impact on total mortality. The data are consistent with the effects of all or nearly all class I agents, which produce an excess mortality in different subsets of patients with ischemic heart disease.\textsuperscript{9,10} Therefore, it would appear that in those patients with acute infarction in whom prophylactic therapy to prevent the development of VF might still be considered clinically necessary, and these appear to be relatively few, \(\beta\)-blockade would be preferable if there are no specific contraindications. Conversely, in the setting of an extremely low incidence of primary VF, which applies to all but a few patients, as the Antman and Berlin meta-analysis data indicate,\textsuperscript{17} the conclusion is inescapable that routine prophylactic lidocaine therapy in acute myocardial infarction is an idea whose time is all but gone.
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Key Words: lidocaine • myocardial infarction, acute • Editorial Comments
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Circulation. 1992;86:1033-1035
doi: 10.1161/01.CIR.86.3.1033

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/86/3/1033.citation

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