tional, investigative, and service needs of anesthesiology intensivists. Over the ensuing 12 yr, ASCCA has continued to grow and expand its educational activities, including an annual meeting, biannual refresher course, resident education manual[1] (currently undergoing revision for a second edition), review textbook,[2] electronic communication program (http://gasnet.med.yale.edu/ascca/), and fellowship directory to supplement the American Medical Association "green" book.[3] Recently, ASCCA has developed an evolving relationship with the Foundation for Anesthesia Education and Research to sponsor research awards and promote acquisition of new knowledge in critical care. ASCCA members include academic and private practice subspecialists and generalists with evolving acute and critical care, perioperative medicine, and "hospitalist" practices.

The formal affiliation of ASCCA with ANESTHESIOLOGY is the culmination of the efforts of many individuals, particularly, Dr. Michael Todd, editor-in-chief of ANESTHESIOLOGY, Mr. Gary Hoormann, executive secretary of ASCCA, and Mr. Craig Percy of Lippincott-Raven, publishers of the Journal. The relationship between ASCCA and ANESTHESIOLOGY will be a mutually beneficial liaison, allowing ASCCA access to superb editorial evaluation and the broadest readership of any journal in our parent specialty. The ASCCA anticipates a productive editorial interaction with the journal board, advocates submission of high-quality scientific and clinical critical care manuscripts to the journal, and continues to promote excellence in critical care within the ASA and the greater medical community.

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β-adrenergic–Blocking Drugs

Incredibly Useful, Incredibly Underutilized

β-ADRENOCEPTOR antagonists are composed of a large number of drugs that possess a host of pharmacologic properties, some of which are attributable to activity at the β receptor, whereas others are not. These features include cardioselectivity for β_1-adrenergic receptors, intrinsic sympathomimetic activity (partial agonist-type properties), membrane-stabilizing effects, pharmacokinetic advantages (*e.g.*, inability to cross the blood–brain barrier or ability to be rapidly metabolized), or inclusion of additional properties (*e.g.*, α-adrenergic receptor antagonism or vasodilator actions) that make each agent of particular advantage for a patient. These drugs were initially developed for the management of cardiac arrhythmias, hypertension, and angina pectoris. Other significant potential benefits of β blockers are now recognized and include protection against reinfarction and reduction of long-term mortality after myocardial infarction.

In this issue of ANESTHESIOLOGY, Wallace *et al.*[1] have

This Editorial View accompanies the following article: Wallace A, Layug B, Tateo I, Li J, Hollenberg M, Browner W, Miller D, Mangano DT, for the McSPI Research Group: Prophylactic atenolol reduces postoperative myocardial ischemia. ANESTHESIOLOGY 1998; 88:7–17.

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demonstrated in a randomized, placebo-controlled, double-blind study that relatively brief treatment with the β-adrenergic antagonist, atenolol, of patients at risk for coronary artery disease undergoing noncardiac surgery decreases the incidence of perioperative myocardial ischemia. This reduction in perioperative ischemic events may ultimately translate into a decrease in cardiac morbidity and mortality rates as shown by the same group of investigators in a long-term follow-up evaluation of these patients.[2] The evidence is overwhelming that patients at risk for coronary artery disease will dramatically benefit from administration of these drugs. Unfortunately, the β blockers are underused[3-7] for reasons that are not clear.

The mechanism of action of β blockers in myocardial ischemia is most certainly multifactorial. These agents improve myocardial oxygen supply-demand balance. β-adrenergic-blocking agents decrease myocardial oxygen consumption by reducing major determinants of oxygen demand. A decrease in heart rate and inotropic state result in less "stress" placed on potentially ischemic myocardium. The drugs prevent the deleterious actions of an increase in sympathetic nervous system tone by attenuating the actions of endogenous catecholamines on β-adrenergic receptors. Some of these agents may also act within the central nervous system to reduce overall sympathetic outflow. In general, β blockers have no direct vasodilator activity, but these agents increase oxygen supply to ischemic zones through a redistribution of myocardial blood flow from normal regions. This is evident whether the origin of perfusion is *via* coronary collaterals in the presence of a total coronary artery occlusion or *via* decreased antegrade flow in the presence of a critical coronary stenosis. Increased perfusion of ischemic myocardium, especially in subendocardial areas most susceptible to infarction, occurs as a result of a decrease in heart rate and is also accompanied by a decrease in myocardial oxygen consumption. As a result, the intensity of ischemia is decreased, and even the extent of myocardial infarction can be demonstrated to be decreased. This is a basic principal well established in a variety of experimental models of coronary artery disease. Further, the antiischemic properties of β-blockers in ambulatory patients have been documented in small and large multicenter clinical investigations. If so, why are β-adrenergic antagonists relatively underused?

The answer to this question lies in the misperception of the risk-to-benefit ratio for a patient. Blockade of β-adrenergic receptors can result in conduction disturbances, left ventricular dysfunction as a result of a reduction in inotropic state in patients dependent on sympathetic nervous system activity, and other actions that are not related to the cardiovascular system, such as exacerbation of reactive airway disease. Such risks probably represent the motivating factor for many physicians to avoid use of β-adrenergic antagonists. This may be especially true in the intraoperative period wherein patients are also exposed to other negative inotropic agents such as volatile anesthetics. Unfortunately, for the patient, avoidance of such risks at the expense of not receiving β-adrenergic antagonists is detrimental[3,6] and for the most part unnecessary. For example, in the presence of left ventricular dysfunction, β-adrenergic blockers may actually improve filling dynamics and provide beneficial systemic hemodynamic effects.[5]

Wallace *et al.*[1] and Mangano *et al.*[2] have demonstrated that β blockers administered perioperatively not only decreased the number of ischemic events in treated patients acutely but also resulted in a reduction in mortality and cardiovascular complications for as long as 2 yr after the surgical procedure. Moreover, this was accomplished *without any detectable increase in the frequency of side effects*, despite many of their patients having coexisting cardiac and pulmonary disease. Their work supports and extends several major multicenter studies, including ISIS-1, MIAMI, MAPHY, and ASYST studies of β-adrenergic blockade in ambulatory patients with coronary artery disease. The present investigation strongly suggests that the majority of patients with risk factors for coronary artery disease should be treated with at least some type of β blocker perioperatively. Long-term medical management of untreated patients identified at the time of surgery might also best be accomplished with the chronic oral administration of β-blocking agents, although whether such would result in a greater clinical benefit needs to be further tested. The mechanism for a reduction in mortality 2 yr after perioperative administration of atenolol is unclear, but the evidence from this and other studies indicates the short-term and long-term benefits of β blockers are remarkable.

β-adrenergic antagonists are especially underused in elderly and female patients and in those patients with a history of heart failure or bronchospastic disease. Unfortunately, the assumption that adverse drug effects will occur has caused these agents to be avoided in a variety of clinical situations despite evidence in multiple investigations that β blockers are well tolerated. The intraoperative period represents a special example in which the tolerance to this class of drugs can be examined acutely and rapidly reversed if required. Intravenous administration of a short-acting, quickly metabolized β blocker allows rapid assessment of efficacy, and if adverse effects are not observed, prolonged oral administration may be indicated. Patients with relative contraindications to β blockers undergoing thrombolytic therapy for acute myocardial infarction have been treated with esmolol relatively successfully, and it has been suggested that esmolol may be a good predictor of subsequent outcome with oral β-adrenergic-blocking therapy in these patients.[8]

Previous investigations[9-12] have demonstrated the utility of β-adrenergic blockade perioperatively. These studies have certain limitations, including few patients or a lack of follow-up evaluation of long-term mortality. Wallace *et al.* are convincing in their argument that patients with risk factors for coronary artery disease undergoing general anesthesia should be treated with a β-adrenergic- blocking agent. Further, the investigators demonstrate excellent tolerance to these drugs. Whether ancillary properties such as cardioselectivity, lipophilicity, intrinsic sympathomimetic activity, and so on would be of special benefit to specific patients remains controversial[13] and requires further study. Whether patients that continue to have perioperative ischemia despite adequate treatment with β-adrenergic antagonists have an especially poor prognosis also deserves investigation. Nevertheless, if adequate blockade of β-adrenergic receptors can be achieved, it is highly likely that the benefit to the patient would be reflected in a decrease of perioperative ischemia, cardiac morbidity, and long-term mortality.

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ADDENDUM

Two recently published papers describing assessment and management of perioperative risk from coronary artery disease in patients undergoing noncardiac surgery were published by Paida and Detsky of the American College of Physicians.[14,15] These are important "position papers" describing clinical guidelines for this patient population. Based on the findings of Mangano *et al.*,[16] the American College of Physicians recommends the perioperative use of atenolol in patients with coronary artery disease or risk factors for coronary artery disease as originally defined by Mangano *et al.*,[16] unless significant contraindications to the use of β blockers are present. — DCW

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Anesthetic Drug Interactions

An Insight into General Anesthesia — Its Mechanism and Dosing Strategies

IN this issue of ANESTHESIOLOGY, Katoh and Ikeda[1] present a study describing the interaction of sevoflurane and fentanyl to achieve loss of consciousness and ablation of somatic responses to skin incision. This is one of a few articles investigating the concentration response of the interaction between opiates and volatile anesthetics[2] or propofol.[3,4] What can we learn from these drug interaction studies?

The interaction between fentanyl, sufentanil, alfentanil, and remifentanil (analgesics) with either isoflurane, desflurane, sevoflurane, or propofol (hypnotics) for the prevention of purposeful movement at skin incision is remarkably similar. There is an initial steep decrease (40–50%) in the MAC/Cp_{50} with low (analgesic concentrations) of an opiate. Thereafter, the decrease in MAC/Cp_{50} with increasing opiate concentrations tends to flatten until a ceiling effect is observed. The interaction for loss of consciousness is different to that for skin incision, with only a 10–20% decrease in the MAC/Cp_{50} awake value when combined with an analgesic concentration of an opiate. The different interaction for these two endpoints is strong evidence that loss of consciousness and response to skin incision are not a single continuum of increasing "anesthetic depth" but

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Key words: Alfentanil; fentanyl; isoflurane; mechanisms of volatile anesthetics; opiates; remifentanil; sevoflurane; sufentanil.