inotropic agents (such as the catecholamines, calcium ions, and digitalis), and paired electrical stimulation. Entropy also increases during congestive heart failure, which may be thought of as an expression of a defect in the utilization of energy, a partial chemomechanical uncoupling.

The entropy of the myocardial cell tends to be reduced by negative inotropic agents, such as the β-adrenergic blocking drugs, as well as by antidysrhythmic drugs. It is also reduced by direct-current conversion of dysrhythmias, during hibernation (either natural or induced), during hypothermic or chemical cardiac arrest, by cardiopulmonary bypass, or during the use of mechanical cardiac assistance.

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Nitrous Oxide Administration and Hemodynamics

Nitrous oxide is the oldest and most widely used drug for inhalation-induced analgesia. Nitrous oxide produces surgical anesthesia only at pressures greater than 800 mm Hg; but at lower pressures, corresponding to concentrations between 25 and 80 percent, it produces varying degrees of analgesia, amnesia, and alteration of consciousness which may elicit excitement, movement, laughter, and nausea. The rapid and reversible qualities of this analgesic are now being used in some places to relieve the pain of coronary ischemia. Unfortunately, it is not widely appreciated that there are direct cardiac and peripheral vascular actions of nitrous oxide. These effects are manifest in a moderate decrease in myocardial contractility, an increase in peripheral vascular resistance with reduced peripheral blood flow, and a rise in central venous pressure. These changes have been documented in awake humans, among both healthy volunteers1 and patients with coronary arterial disease.2 Certainly the central effects and probably the cardiovascular effects of nitrous oxide are dependent on dosage.

An article in this issue (see page 316) entitled “Administration of Nitrous Oxide in Normal Subjects: Evaluation of Systems of Gas Delivery for Their Clinical Use and Hemodynamic Effects,” written by Lichtenthal et al, describes several systems of delivery for administering nitrous oxide (30 to 50 percent) with simultaneous noninvasive hemodynamic measurements in healthy volunteers. Lichtenthal et al conclude that an airlines mask is superior to nasal prongs or to standard plastic rebreathing masks in terms of attaining nitrous oxide equilibration, expressed as the ratio of expiratory concentration to inspiratory concentration.

Among 22 subjects in this study by Lichtenthal et al, 30 percent nitrous oxide produced significant decreases in mean arterial blood pressure (89.9 to 75.6 mm Hg) and heart rate (78.8 to 64.1 beats per minute). In eight subjects ranging in age from 19 to 28 years, studies of left ventricular function, including end-systolic volume index, cardiac index, ejection fraction, echocardiographic ventricular wall velocity, ejection time, and pre-ejection period/ejection time, indicated no changes during 30 minutes of inhaling 30 percent nitrous oxide. From this, Lichtenthal et al concluded that 30 percent nitrous oxide does not affect left ventricular function, and they speculate that the fall in blood pressure indicates a greater effect (reduction) on aortic impedance than on peripheral vascular resistance. If this were the case, then the pre-ejection period should have been shortened, rather than unchanged, since a fall in afterload should decrease the time of isovolumetric contraction. It is equally plausible to reason that a prolonged pre-ejection period was obscured by the reduced afterload.

In this study the calculated cardiac index was unchanged, while both the measured heart rate and mean blood pressure fell, which indicates a substantial increase in stroke volume. If contractility is unaltered, then an increase in stroke volume should increase the ejection time, yet the reported ejection time was unchanged. Conclusions regarding ventricular function based on noninvasive measurements must be interpreted with caution, since noninvasive cardiac data are strongly influenced by preload, afterload, and heart rate.4

The use of nitrous oxide for analgesia for angina and infarctional pain is not new, nor is such usage necessarily safe. In areas where this use of nitrous oxide has been reported, there is no convincing evidence of its effectiveness as an analgesic alone,
nor are the complications associated with its use fully discussed. The human response to nitrous oxide in terms of analgesia is quite variable and often 30 percent nitrous oxide has little or no effect, whereas in some individuals, 30 percent nitrous oxide produces excitement which can only be harmful to cardiac patients. For analgesia, nitrous oxide is most effective when combined with a narcotic that can effectively suppress the undesirable aspects of nitrous oxide, ie, excitement and peripheral veno-constriction; however, this combination becomes a general anesthetic when the concentration and dose are increased. Studies have shown that this combination depresses cardiac function more than administration of either nitrous oxide or the narcotic alone. Therefore, it is a potentially dangerous technique for achieving analgesia in the cardiac-damaged patient. It makes more sense to use only a reversible narcotic, since it produces a desirable fall in peripheral vascular resistance and does not usually depress the myocardium, at clinical levels of dosage.

It is apparent that we need to collect more data on the hemodynamic effects of nitrous oxide alone in the damaged patient. It is encouraging that Lichtenthal et al have found an efficient and comfortable apparatus for more accurately delivering a gas without intubation. In regard to the use of nitrous oxide in the coronary care unit, I believe that there are very real additional risks that must be understood when using nitrous oxide; these include a wide variability in response by patients, unpredictable interactions of drugs, and potential technical problems in management of the airway, any of which could invalidate any and all benefits of analgesia. There should be an awareness and acceptance of these risks if further evaluations of analgesia with nitrous oxide for angina are to be undertaken.

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