way,” by the patient’s decision about what is in his or her best interest.

This current example illustrates what all of us who wear the physician’s mantle know: many choices in medicine are not easy. Should patients be required to undergo a treatment that will maim them in order to gain a few more years of life? Should patients have to bear pain because physicians fear the side effects of pain relief? Should a woman be compelled to carry a pregnancy to term if doing so will vastly increase her risk of premature death? Should patients be forced to receive food and fluids to prolong their lives? Decisions about what is best should be made among reasonable alternatives by individual patients, in collaboration with their loved ones, as guided by their physicians. Experience has taught us that everyone makes these decisions on the basis of his or her own values, desires, and beliefs; legislation has no place in this process.


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Vasopressin in Asystolic Cardiac Arrest

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Cardiac arrest remains a major health problem in the United States and other Western nations. Of the approximately 1000 sudden deaths that occur each day in the United States, it is estimated that as many as 20 to 40 percent result from asystolic cardiac arrest.1-3 In this issue of the Journal, Wenzel et al.4 demonstrate the success of vasopressin alone and vasopressin followed by epinephrine in refractory asystolic cardiac arrest — an important breakthrough in the science of resuscitation. These advances should be translated into a new standard of care without delay. Medical policymakers should do whatever is necessary to facilitate the orderly implementation of new guidelines based on this new information.

The most common and most treatable rhythm found in patients with cardiac arrest is ventricular fibrillation; in contrast, asystole has been the most refractory to resuscitation attempts. Precise figures for the incidence of the various rhythms associated with cardiac arrest are not available, since the incidence may vary in different study populations. It is likely that ventricular fibrillation is the cause of 60 to 80 percent of cardiac arrests, and asystole the cause of 20 to 40 percent.1,2 In at least one series, asystole was reported as the cause of cardiac arrest in more than 40 percent of cases, and its prevalence has been increasing since 1980.3,5 Pulseless electrical activity may be found in up to 10 percent of patients with cardiac arrest.

A number of theories have been proposed to explain the apparent refractoriness of asystole to resuscitation attempts, including impairment of the automaticity of the sinus node, the malfunction of related conduction pathways secondary to ischemia, the failure of neurogenic innervation of the heart, and the failure of reflex sympathetic performance, among other factors. Although one or another of these mechanisms may or may not be in play in asystole, it is clear that progressive ischemia and acidosis are always present. Epinephrine has been used routinely as the vasoactive drug of choice in asystolic cardiac arrest because of its potency as a vasopressor and because successful resuscitation has been shown to depend on coronary perfusion pressure during resuscitation.6 However, epinephrine and other catecholamines lose much of their effectiveness as vasopressors in a hypoxic, acidic milieu, and this fact, in addition to the notable rate of failure of epinephrine therapy, has stimulated efforts to identify an effective alternative to epinephrine for use in cardiac arrest.7

In the early 1990s, endogenous vasopressin levels were found to be higher in survivors of cardiac arrest than in patients who died, suggesting that vasopressin could be beneficial in cardiac arrest.8 Subsequent laboratory and clinical studies of the effects of vasopressin in cardiac arrest showed, as Wenzel et al. note, that this agent increased blood flow and oxygen delivery to the heart and the brain, increased the chances of successful resuscitation, and improved neurologic outcomes. In the light of these promising observations, Wenzel et al. undertook a large, multicenter trial to evaluate the effects of vasopressin and epinephrine on survival after out-of-hospital cardiac arrest in adults with ventricular fibrillation, pulseless electrical activity, or asystole.
The study was conducted in 33 communities with 44 physician-staffed emergency medical service units in Austria, Germany, and Switzerland. Patients were randomly assigned to receive either vasopressin (589 patients) or epinephrine (597 patients); they were given the first dose intravenously, and if spontaneous circulation was not reestablished within three minutes after the first dose, a second dose of the same drug at the same dose was injected. If spontaneous circulation was not reestablished even then, doses of epinephrine could be administered to patients in either treatment group at the discretion of the physician.

Surprisingly, among patients with asystole, the rates of restoration of spontaneous circulation and survival to hospital admission were significantly higher after vasopressin therapy than after epinephrine therapy (76 of 262 patients, or 29.0 percent, survived, vs. 54 of 266 patients, or 20.3 percent; P=0.02), and the rate of survival to hospital discharge was significantly higher as well (12 of 257 patients, or 4.7 percent, vs. 4 of 262 patients, or 1.5 percent; P=0.04). This rate of survival after asystolic cardiac arrest may be among the highest yet reported in a major resuscitation trial. It is also notable, although the numbers are small, that the rate of survival to hospital discharge was three times as high in the vasopressin group as in the epinephrine group.

Another unexpected result emerged among patients in whom spontaneous circulation could not be restored by the first two doses of either vasopressin or epinephrine. It had been agreed that additional doses of epinephrine could be given at the discretion of the managing physician if spontaneous circulation was not restored by the study drug. There were 732 patients in this category (62 percent of the 1186 study patients), and they were fairly evenly divided between the vasopressin group (373 patients) and the epinephrine group (359 patients). The rates of restoration of spontaneous circulation and survival to hospital admission after additional therapy with epinephrine were significantly higher among patients who were initially treated with vasopressin than among those who were initially treated with epinephrine (96 of 373 patients, or 25.7 percent, survived, vs. 59 of 359 patients, or 16.4 percent; P=0.002), as was the rate of survival to hospital discharge (23 of 369 patients, or 6.2 percent, vs. 6 of 355 patients, or 1.7 percent; P=0.002). This is a remarkable outcome, given that patients in this subgroup could have been deemed to be beyond hope of resuscitation and further resuscitative efforts could have been abandoned at the discretion of the physician.

Epinephrine consumes oxygen, whereas vasopressin increases coronary blood flow and the availability of oxygen to the myocardium. These dynamics may contribute to the success of vasopressin therapy in asystolic cardiac arrest and the lack of success of epinephrine therapy. Oxygen consumption in ventricular fibrillation may be further accelerated by the increased endogenous catecholamine levels that are characteristically present after cardiac arrest. Additional exogenous epinephrine could be expected to exacerbate hypoxemia and advancing acidosis, both of which would be expected to further impair the vasopressor effects of epinephrine as well. Thus, epinephrine might be not only ineffectual, but also potentially detrimental in early asystolic cardiac arrest, whereas vasopressin appears to be beneficial.

Usually, major changes in the guidelines for resuscitation are adopted at international conferences of experts on cardiopulmonary resuscitation and emergency cardiac care, but such conferences are generally held only at intervals of four to five years. Because of the size and power of the study by Wenzel et al., the dismal rate of resuscitation among patients with asystolic cardiac arrest, and the apparent absence of any added risk of injury to patients who may be treated according to the new therapeutic sequences, practitioners should perhaps be encouraged to incorporate the use of vasopressin into their resuscitation protocols immediately. The best approach to optimizing survival as soon as possible would be to have the appropriate committees of the American Heart Association and the American College of Cardiology convene in order to issue an interim guideline incorporating these important new therapeutic advances.

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**The Elusive Goal of Therapy for Usual Interstitial Pneumonia**

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Idiopathic pulmonary fibrosis, defined pathologically as usual interstitial pneumonia, is a fatal disease that occurs most commonly among persons who are 60 years of age or older and in otherwise good health. Usual interstitial pneumonia progressively impairs breathing, but because its onset is insidious, patients are frequently treated for other diseases for many months. By the time the diagnosis is established, pulmonary function has often substantially deteriorated.1

Several entities fall under the wide umbrella of chronic interstitial pneumonias,2 including usual interstitial pneumonia, nonspecific interstitial pneumonitis, desquamative interstitial pneumonia, acute interstitial pneumonia, respiratory bronchiolitis–associated interstitial lung disease, and cryptogenic organizing pneumonia.3 The prognosis and treatment may vary according to the type of pneumonia, which must therefore be established before treatment is initiated. The workup often includes open lung biopsy. For the clinician, there is a clear separation between usual interstitial pneumonia and all the other idiopathic interstitial pneumonias. Although the other types usually respond to corticosteroid therapy, there is no effective treatment for the majority of cases of usual interstitial pneumonia.

Patients present with tachypnea; a nonproductive cough; bilateral inspiratory crackles with a distinctive tone to them, which are often referred to as “cellophane” or “Velcro” rales; restrictive pulmonary dysfunction; and exercise-related hypoxemia. Clubbing is common, and pulmonary hypertension and cor pulmonale may ensue. Signs of airway disease are minimal. Chest radiographs reveal small lung volumes, bibasilar linear reticulations, and honeycombing. High-resolution computed tomography (CT) is excellent for distinguishing usual interstitial pneumonia from other fibrosing entities.4

The clinician must rule out multiorgan connective-tissue diseases in which the lung is one of several fibrotic organs. A thorough occupational history-taking is essential, since pulmonary asbestosis can have a similar clinical presentation.

It is vital to differentiate usual interstitial pneumonia from the other interstitial pneumonias, especially nonspecific interstitial pneumonitis, since the latter disease usually has a better prognosis and response to treatment.5 Fortunately, the diagnosis of usual interstitial pneumonia can generally be confirmed by findings of a heterogeneous distribution of patchy, peripheral reticular densities, broad bands of fibrosis, and honeycombing on high-resolution CT. Some ground-glass opacities may be present. In a patient with an appropriate history, findings on physical examination, and functional abnormalities, the typical pattern on high-resolution CT is diagnostic of usual interstitial pneumonia, and in this circumstance, many clinicians forgo a confirmatory lung biopsy.6 However, when uncertainty exists, lung biopsy is required. If granulomatous or neoplastic disease or infections remain to be ruled out, bronchoscopic biopsy and bronchoalveolar lavage may be diagnostic. However, the definitive diagnostic biopsy for usual interstitial pneumonia is open lung biopsy by means of video-assisted or standard thoracotomy.

Since the cause of usual interstitial pneumonia is unknown, nonspecific antinflammatory or immunosuppressive therapy has been considered appropriate. Common treatments include prednisone at an initial dose of 1 mg per kilogram of body weight.1 Colchicine, azathioprine, cyclophosphamide, pentamidine, and pirfenidone have been used alone or as corticosteroid-sparing drugs.7,8 No well-controlled, randomized, and blinded studies have shown any of these medications to be efficacious.

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