

Black and Hispanics had a higher odds of being uninsured compared with white patients (3.29 *vs.* 4.36) as did male patients compared with female patients. Using in-hospital death as the dependent variable, unadjusted results revealed a significantly higher mortality for uninsured patients (odds ratio [OR], 1.39;  $P < 0.001$ ); this remained true when sex, race, age, Injury Severity Score, Revised Trauma Score, and injury mechanism were controlled (OR, 1.80;  $P < 0.001$ ). In a subgroup analysis of young patients unlikely to have comorbidities, uninsured patients had a significantly higher mortality (OR, 1.89;  $P < 0.001$ ), as did patients with head injuries (OR, 1.65;  $P < 0.001$ ) and patients with one or more comorbidities (OR, 1.52;  $P < 0.001$ ).

### Interpretation

Uninsured patients who suffered penetrating or blunt trauma had a higher risk-adjusted mortality rate compared with patients who were insured. Possible reasons for this disparity include treatment delay and differing care.

### Impact of left ventricular assist device bridging on posttransplant outcomes. *Ann Thorac Surg* 2009; 88:1457–61

Demand for donor hearts is higher than the supply, and therefore, bridging options such as left ventricular assist device (LVAD) and intravenous inotropes may be used in patients who are not effectively stabilized with conservative measures. However, there are conflicting data regarding the short- and long-term efficacy of LVAD therapy.

A retrospective review was performed to evaluate outcomes in United Network of Organ Sharing status 1 heart transplant recipients who were bridged to transplant with an implantable LVAD ( $n = 86$ ) or with intravenous inotropes only ( $n = 173$ ) from 1994 to 2007.

Although patients had similar baseline characteristics and pretransplant hemodynamics, patients in the LVAD group had a significantly higher incidence of mechanical ventilation at the time of transplant (6.7% *vs.* 4.6%;  $P < 0.02$ ). Hemodynamics, as measured by cardiac index, pulmonary vascular resistance, central venous pressure, and pulmonary capillary wedge pressure, significantly improved in the LVAD group.

	LVAD ( $n = 86$ )	Intravenous Inotropes ( $n = 173$ )	<i>P</i>
Survival, %			
30 d	96.7	98.3	—
1 yr	84.9	88.1	—
3 yr	79.1	77.1	—
5 yr	72.7	76.1	—
Length of stay, mean days $\pm$ SEM			
Total	21 $\pm$ 16	14 $\pm$ 14	0.15
Intensive care unit	5 $\pm$ 3	6 $\pm$ 6	0.41

The incidence of posttransplant infectious complications and rejection episodes during the first year was similar. However, the incidence of posttransplant renal dysfunction was higher in patients bridged with inotrope.

### Interpretation

In patients with end-stage heart failure, intravenous inotropes or LVADs can be used as a bridge before heart transplantation. In the past, mortality was high in patients receiving LVAD implantation. However, using newer generation LVAD devices, both short-term and long-term survival and morbidity after transplantation were similar to patients who received only inotropic infusions.

### Critical Care Medicine

Jean Mantz, M.D., Ph.D., Editor

### IV drug administration during out-of-hospital cardiac arrest: A randomized trial. *JAMA* 2009; 302:2222–9

Epinephrine is widely used as an integral part of advanced cardiac life support (ACLS) despite a paucity of clinical data supporting its use with cardiopulmonary resuscitation. Recent studies have demonstrated a potential association with epinephrine and poor outcomes.

To determine whether removing intravenous drug administration from an ACLS protocol would improve survival to hospital discharge after out-of-hospital cardiac arrest, a prospective, randomized controlled trial was conducted. Consecutive adult patients ( $n = 418$  ACLS with intravenous drug administration and  $n = 433$  ACLS without intravenous drugs) with out-of-hospital nontraumatic cardiac arrest treated within the emergency medical service system were included.

Short-term survival was significantly longer in patients who received intravenous drugs and ACLS compared with ACLS alone ( $P = 0.004$ ). However, the rates of survival to hospital discharge (10.5% *vs.* 9.2%;  $P = 0.61$ ), survival with favorable neurologic outcome (9.8% *vs.* 8.1%;  $P = 0.45$ ), and survival at 1 yr (10% *vs.* 8%;  $P = 0.53$ ) were similar between the two groups. No difference in the quality of cardiopulmonary resuscitation was observed. After adjustment for ventricular fibrillation, response interval, witnessed arrest, or arrest in a public location, there was no significant difference in survival to hospital discharge for the ACLS plus intravenous drug administration group *versus* the ACLS-alone group.

### Interpretation

These results indicate an apparent lack of long-term benefit of epinephrine and other intravenous medications in the management of out-of-hospital cardiac arrest. The results should be interpreted with caution because the study overes-

timated survival rates in the nondrug group. Nevertheless, these data suggest that factors other than intravenous drug administration contribute to long-term outcome after out-of-hospital cardiac arrest.

### Prolonged mechanical ventilation after cardiac surgery: Outcome and predictors. J Thorac Cardiovasc Surg 2009; 138:948–53

Prolonged mechanical ventilation after cardiac surgery is associated with in-hospital mortality rates as high as 40% and is also a serious economic burden on the healthcare system. Furthermore, it is difficult to predict which patients will require prolonged mechanical ventilation. This prospective observational study consecutively enrolled patients mechanically ventilated 3 days after surgery, and preoperative, intraoperative, and postoperative data were recorded.

Among 2,620 patients who underwent cardiac surgery on day 3, 163 patients were still receiving ventilatory assistance. By day 10, 50 (31%) patients had been successfully weaned, 78 (48%) were still receiving mechanical ventilation and 35 (21%) died. Factors associated with successful weaning on day 3 included urine output more than or equal to 500 ml/24 h, Glasgow Coma Score of 15, arterial bicarbonates more than or equal to 20 mM, platelet count more than or equal to 100 g/l, patients without inotropic support with epinephrine/norepinephrine, and absence of lung injury. Data from this study were used to develop a scoring system. This scoring may help identify patients who can be rapidly weaned from ventilator support and reduce the need for interventions in patients likely to be extubated.

#### Interpretation

These data may be helpful in preventing invasive procedures, such as tracheostomy, in patients with high probability of successful weaning after cardiac surgery. Prospective validation of the scoring system proposed in other intensive care units (ICUs) dedicated to cardiac surgery is necessary to assess the external validity of the proposed score.

### International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009; 302:2323–9

Infection is a major cause of morbidity and mortality in ICUs worldwide, and cases of infection-related deaths are increasing. Relatively little information is available about the global epidemiology of such infections.

To examine the extent and patterns of ICU infections worldwide, the Extended Prevalence of Infection in Intensive Care II study, a 1-day, prospective, point prevalence study with follow-up was conducted including 14,414 patients.

Fifty-one percent of patients were infected on the study day, and the majority of these infections were respiratory (64%). Patients who had longer ICU stays before the study day had higher rates of infection, especially infections from

resistant staphylococci, *Acinetobacter*, *Pseudomonas* species, and *Candida* species:

	Infected Patients (n = 6,659)	Noninfected Patients (n = 6,352)	P Value
ICU mortality rate, %	25.3	10.7	<0.001
Hospital mortality rate, %	33.1	14.8	<0.001
Length of stay, d			
ICU	16	4	
Hospital	29	13	<0.001

Central and South America had the highest infection rate (60%), and Africa had the lowest rate (46%). Gram-negative infections were more common in all regions, except North America (49.9 *vs.* 55.1, for Gram-negative *vs.* Gram-positive). Countries with lower healthcare expenditures reported higher infection rates.

#### Interpretation

This large international epidemiologic study from 1,265 ICUs in 75 countries is a comprehensive, current picture of infections in ICUs. Infection remains a major concern with direct effect on mortality and morbidity. Major international differences were detected in the prevalence and types of infections, as well as mortality rates, suggesting differences in approaches to improve infection prophylaxis, and management should be identified and perhaps adopted.

### Hospitalized patients with 2009 H1N1 influenza in the United States, April–June 2009. N Engl J Med 2009; 361:1935–44

In 2009, a pandemic influenza A (H1N1) virus emerged and spread globally, infecting patients in 191 countries and territories by September. Risk factors for severity and additional clinical characteristics are still being described. In this article, the authors describe the clinical characteristics of patients who were hospitalized with 2009 H1N1 influenza in the United States from April 2009 to mid-June 2009.

Data were collected from 272 patients in 24 states (25% of all cases reported to the Centers for Disease Control and Prevention during this time period) who were hospitalized for at least 24 h for influenza-like illness and who tested positive for the 2009 H1N1 virus. Forty-five percent of the patients were children younger than 18 yr, and 5% were 65 yr of age or older. Seventy-three percent of the patients had at least one underlying medical condition (*e.g.*, asthma; diabetes; heart, lung, neurologic diseases, and pregnancy), including 60% of children, 83% of adults, and 100% of patients 65 yr or older of age. Of the 249 patients who underwent chest radiography at admission, 40% had findings consistent with pneumonia. Of the 268 patients for whom data were avail-

able regarding the use of antiviral drugs, such therapy was initiated in 200 patients (75%) at a median of 3 days after the onset of illness.

Overall, 25% of patients were admitted to an ICU and 7% died. The majority of deaths were in patients with underlying medical conditions (68%). All patients who died had received antiviral therapy; however, none of the patients had received therapy within 48 h after the onset of symptoms.

### Interpretation

This article is the first epidemiologic report on influenza H1N1 in 2009 in hospitalized patients in the United States. Comorbidities in hospitalized patients are reviewed, such as age less than 65 yr, pregnancy, and immunosuppression. In addition, other factors such as morbid obesity seem to influence severity of illness caused by H1N1. Antiviral therapy provided benefit to some patients when received within 48 h of symptom onset.

### Pain Medicine

*Timothy J. Brennan, Ph.D., M.D., Editor*

**Selective antagonism of opioid-induced ventilatory depression by an ampakine molecule in humans without loss of opioid analgesia.** *Clin Pharmacol Ther* 2010; 87:204–11

Ventilatory depression, a significant risk associated with the use of opioids, may occur in up to 17% of patients with potentially fatal outcomes. Agents that modulate neuronal pathways responsible for respiratory drive while maintaining opioid analgesia may provide significant clinical benefit. AMPA receptors are responsible for respiratory rhythmogenesis maintenance and the ampakine CX717 counteracted opioid-induced ventilator depression in preclinical studies.

A double-blind, placebo-controlled, crossover study assessed the effects of CX717 pretreatment on opioid-induced ventilatory depression in healthy volunteers (N = 16). Patients received a single oral dose of either 1,500 mg CX717 or placebo. Volunteers also received a 2-h intravenous infusion of alfentanil (target concentration, 100 ng/ml) for 100 min and 1.6 mg naloxone for 160 min after CX717 administration, respectively.

After CX717, alfentanil decreased the respiratory frequency by only  $2.9 \pm 33.4\%$  compared with  $25.6 \pm 27.9\%$  during placebo coadministration ( $P < 0.01$ ). Blood oxygenation and the ventilatory response to hypercapnic challenge also showed significantly smaller decreases with CX717 than with placebo. In contrast, CX717 did not affect alfentanil-induced analgesia in either electrical or heat-based experimental models of pain. Both ventilatory depression and analgesia were reversed with 1.6 mg of naloxone. CX717 was well tolerated, and no volunteers required interventions for

side effects. However, CX717 did produce a significant increase in tiredness during combination treatment with alfentanil ( $P = 0.03$ ).

### Interpretation

Opioid-induced respiratory depression is common in the perioperative period. To date, only opioid receptor blockade can be used to reverse opioid-induced respiratory depression; however, analgesia is compromised by opioid-receptor antagonism. This study shows a novel mechanism for reversal of respiratory depression by opioids without affecting analgesia.

**Outcome reporting in industry-sponsored trials of gabapentin for off-label use.** *N Engl J Med* 2009; 361:1963–71

There are documented reports of selective outcome reporting in published reports of randomized clinical trials. These may include modifications to primary endpoints after statistical testing has been completed and may constitute bias reporting.

To examine the reporting practices for trials of gabapentin funded by Pfizer and Parke-Davis for off-label indications (prophylaxis against migraine and treatment of bipolar disorders, neuropathic pain, and nociceptive pain), 20 internal company documents were matched and compared with 12 published reports. Many of the source documents were available as a result of recent litigation:

Variable, n (%)	Trials (N = 12)
Primary outcome in report differed from protocol	8 (67)
Primary outcome changed when statistically significant differences favoring gabapentin reported	5 (63)
New primary outcome introduced	6 (50)
Failure to distinguish primary and secondary outcomes	2 (17)
Relegation of primary outcomes to secondary outcomes	2 (17)
Failure to report $\geq 1$ protocol-defined primary outcomes	5 (42)

Of the 28 primary outcomes described in the published reports, 12 were newly introduced. Trials that presented findings that were not significant ( $P \geq 0.05$ ) for the protocol-defined primary outcome in the internal documents either were not reported in full or were reported with a changed primary outcome.

### Interpretation

For these industry-sponsored clinical trials for gabapentin that included trials of neuropathic pain, modification of out-