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 ± 33.4% compared with 25.6 ± 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 ≥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-

come reporting was noted in some of these trials. This report supports registration of clinical trials to ensure that the outcome of the research is fully understood.

Back pain during war: An analysis of factors affecting outcome. Arch Intern Med 2009; 169: 1916–23

Nonbattle-related injuries are the leading basis for soldier attrition; specifically, spine pain and other musculoskeletal conditions are associated with the lowest return-to-unit rate among service members medically evacuated out of Operations Iraqi and Enduring Freedom. Similar to the civilian sector, nonantomical factors (*e.g.*, psychopathalogic and psychosocial stressors) are major determinants of disability. This prospective study was conducted to identify which variables are associated with return to unit in soldiers with back pain.

Data were prospectively collected at the Deployed Warrior Medical Management Center in Germany on 1,410 consecutive soldiers between 2004 and 2007. These soldiers were all medically evacuated out of combat for a primary diagnosis related to back pain.

Of the 1,410 soldiers, 92% were men, 54% had a history of low-back pain, and 28% had a coexisting psychiatric disease. The mechanism of injury was unknown in 66% of cases, attributed to lifting objects (18%) or from falls (11%). Only 5% were sustained during combat.

The overall return-to-unit rate was only 13%. Women were 57% more likely to return to duty after injury as were patients with a history of lower back pain (50%). Additional factors associated with a positive outcome included deployment to Afghanistan and being an officer. Trends toward not returning to duty were found for navy and marine service members, coexisting psychiatric morbidity, and not being seen in a pain clinic.

Interpretation

Return-to-unit rate of soldiers with back pain was low. Future studies will determine whether treatment can improve the low return-to-unit rate of soldiers deployed for combat.