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INSIDE

Acetaminophen Toxicity

SPECIAL FEATURE

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Dr. Akhtar reports no financial relationship to this field of study.

This article originally appeared in the December issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD. Dr. Pierson is Professor, Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle, and Dr. Thompson is Associate Professor of Medicine, University of Washington. Drs. Pierson and Thompson report no financial relationships relevant to this field of study.*

ACETAMINOPHEN (KNOWN AS PARACETAMOL OUTSIDE THE UNITED STATES) is the most commonly used analgesic in the world, usually considered to be safe and benign. In 2008, however, according to the American Association of Poison Control Centers, acetaminophen overdose occurred in 27,790 cases, resulting in 13,650 hospitalizations and 43 deaths.[1] Acetaminophen overdose may lead to hepatotoxicity, acute tubular necrosis and, less likely, pancreatitis.[2] It is the most common cause of acute liver failure in many Western countries, accounting for 40%-50% of cases in the United States.[3,4] (Interestingly, of those cases with acute liver failure from acetaminophen, half or more are unintentional overdoses.) Fortunately, with current treatment, more than 90% of patients with acetaminophen toxicity recover completely. Of those who develop acute liver failure, 70% survive and recover fully with supportive care. Histologically, normal liver architecture is restored within about 3 months from initial ingestion/overdose.[2]

Factors that may slightly increase susceptibility to acetaminophen-related hepatotoxicity include age > 40 years, tobacco use, malnutrition or starvation, and anything else that may impact the way acetaminophen is metabolized in the liver: presence of certain polymorphisms of cytochrome isoenzymes, chronic alcohol ingestion, or chronic use of medications that induce P450 isoenzymes such as some anticonvulsants and isoniazid. Chronic liver disease is not associated with increased risk. Age < 5 years and acute alcohol ingestion seem to decrease susceptibility to acetaminophen toxicity.[2,5]

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PATHOPHYSIOLOGY

Acetaminophen is quickly absorbed from the GI tract and reaches peak serum levels in 1-4 hours. Normally, at recommended therapeutic doses (≤ 4 g in adults or 80 mg/kg in children, daily), more than 90% of ingested acetaminophen is converted in the liver by sulfation or glucuronidation to inactive metabolites, which are then excreted in the urine or bile. About 2% of acetaminophen is directly excreted in the urine; the remaining 5%-8% is metabolized in the liver by cytochrome P450 isoenzymes to the extremely toxic substance N-acetyl-p-benzoquinoneimine (NAPQI). Usually, glutathione inactivates NAPQI, ultimately forming mercapturic acid and cysteine conjugates, which are nontoxic and cleared in the urine.

When excess amounts of acetaminophen are ingested, however, the usual glucuronide and sulfate pathways are saturated and more drug passes through the P450 system; once glutathione stores are consumed, NAPQI accumulates and leads to direct injury of hepatocytes and to centrilobular necrosis. As previously noted, factors that deplete glutathione (such as starvation) or stimulate P450 isoenzymes (like chronic use of certain anticonvulsants) predispose patients to hepatic injury in the setting of acetaminophen ingestion.[2,5]

N-acetylcysteine (NAC) has been used as an antidote for acetaminophen toxicity since the mid-1970s. It works primarily by restoring glutathione, thus averting NAPQI buildup and hepatic injury. (Methionine and cysteamine have similar effects and were the first agents utilized for acetaminophen toxicity; they fell out of use because of significant side effects including severe flushing and vomiting.) NAC also stimulates sulfation and appears to have some anti-inflammatory, anti-oxidant, and vasodilating effects.[5,6]

CLINICAL PRESENTATION

The clinical presentation of acute acetaminophen toxicity is fairly predictable and can be divided into four stages, based on time from ingestion. During stage 1 (0-24 hours), patients experience anorexia, nausea, vomiting, abdominal pain, and general malaise. Laboratory studies (liver function tests, chemistries) may be normal or only minimally abnormal. In stage 2 (24-72 hours), hepatic injury becomes apparent; symptoms improve transiently but patients develop transaminitis, elevated bilirubin, and rising prothrombin time. Right upper quadrant pain and jaundice begin to appear late in this stage.

Stage 3 (72-96 hours or longer) represents the peak of hepatotoxicity and it is during this stage that frank acute liver failure may manifest. Gastrointestinal (GI) symptoms return or worsen and jaundice, general malaise, and hepatic encephalopathy (confusion, somnolence, or coma, sometimes with cerebral edema) occur. Liver function tests reach their maximum levels.[2,5] Coagulopathy may be severe, so bleeding risk is high. Acute renal failure (due to acute tubular necrosis and dehydration) will occur in 25% of patients with severe hepatotoxicity and in more than 50% of those with acute liver failure.[7] Lactic acidosis, hypoglycemia, and hypophosphatemia are also commonly noted. Finally, recovery occurs in stage 4 (96 hours to 14 days), with resolution of symptoms and gradual normalization of liver function studies.[2,5,6]

DIAGNOSIS

Diagnosis of acute acetaminophen overdose relies on a detailed history and high suspicion in patients presenting with GI symptoms without another clear etiology, altered mental status, drug ingestion, or suicide attempt. It is important to remember that acetaminophen is present in many combination medications (analgesics, antipyretics, allergy and sinus medications, etc). The history should elicit information about all available drugs, dosage, route, and time of ingestion. A single ingestion of ≥ 150 mg/kg or ≥ 10-15 g of acetaminophen will result in hepatotoxicity. Chronic daily ingestions at lower doses (4-10 g) may also lead to hepatotoxicity.[2,5]

Serum acetaminophen level should be measured at 4 and 24 hours after ingestion or at presentation if > 4 hours have passed since ingestion. (A false-positive acetaminophen level may be found in the setting of severe hyperbilirubinemia, > 10 μg/mL, from another cause.) In the case of a single ingestion at a known time, serum acetaminophen level at 4-24 hours post-ingestion can be used to predict the risk of hepatotoxicity using the Rumack-Matthew nomogram.[5]

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The diagnosis of acetaminophen toxicity in the setting of chronic ingestion is more difficult. A detailed drug history is essential. An acetaminophen level simply confirms ongoing ingestion but is not useful for prediction risk of hepatotoxicity.[2]

Measurement of the NAPQI-protein adducts released following hepatocellular injury has been evaluated as a more reliable way to identify acetaminophen toxicity in acute or chronic ingestions. This test is not widely available or part of standard clinical practice at this time.[5]

MANAGEMENT

Treatment of acute acetaminophen toxicity begins with gastric lavage and administration of activated charcoal within 1-4 hours of ingestion, in the setting of a protected airway (in order to avoid aspiration).[2]

Early initiation of NAC is the "gold standard" for those patients at risk of hepatotoxicity. Again, for single ingestions with clear timing, this risk is measured and predicted by the Rumack-Matthew nomogram. Most experts and poison control centers also recommend giving NAC for patients with acetaminophen level > 10-20 μg/mL and undeterminable time of significant (> 150 mg/kg or > 10 g) ingestion, history of significant ingestion with laboratory evidence of hepatotoxicity, or history of repeated supratherapeutic ingestions with elevated liver function studies or associated GI symptoms (abdominal tenderness, jaundice, malaise).[5]

When indicated, NAC should be started as soon as possible, ideally within 8-10 hours of ingestion; serious hepatotoxicity is rare if NAC is started in this interval. Although some benefit has been documented even if NAC is started up to 24-48 hours after ingestion, the effect is decremental. In the largest prospective study of NAC for acetaminophen toxicity including more than 11,000 subjects with suspected acetaminophen overdose and about 2500 that met criteria for NAC, severe hepatotoxicity occurred in 2.9% of patients treated within 8 hours, 6.1% treated within 10 hours, and in 26.4% of patients treated at 10-24 hours.[9]

NAC may be dosed orally (140 mg/kg x 1, best tolerated as a 5% solution in cola or juice, followed by 70 mg/kg every 4 hours for 17 doses) or intravenously (150 mg/kg followed by 50 mg/kg over 4 hours and then 100 mg/kg over 16 hours), with equivalent response. The duration of therapy should be extended if patients still have measurable acetaminophen levels, elevated transaminases, or coagulopathy (INR > 1.5-2.0) at the end of the usual course of treatment.[5]

Common side effects of oral NAC include nausea, vomiting, diarrhea, and rash. IV NAC is generally well-tolerated but 10%-20% of patients may have anaphylactoid reactions; after usual supportive treatments (diphenhydramine, corticosteroids, and bronchodilators) and transient (1-2 hours) cessation of the infusion, the remaining course of NAC can generally be completed without difficulty at a slower infusion rate.[2,6]

Although outpatient management with self-administration of NAC has been suggested for selected patients with acetaminophen toxicity and no symptoms or laboratory abnormalities, most patients will require hospital admission.

Patients with frank acute liver failure will need supportive care in an ICU setting. Common complications are encephalopathy with inability to protect airway; thus, intubation and mechanical ventilatory support may be needed. Cerebral edema may occur and consideration must be given to ICP monitoring in selected patients. Severe coagulopathy will be present, but, in general, transfusion of fresh frozen plasma should be avoided unless necessary (for bleeding complications or procedures) as the INR may be one of the most useful indicators for tracking recovery of hepatic function.[3] Dialysis support for acute renal failure may be necessary. IV NAC is indicated in patients with acetaminophen overdose and acute liver failure; IV NAC appears to decrease the risk of disease progression, cerebral edema, and mortality in this population.[10] Furthermore, consideration should be given to transferring such patients to liver transplantation centers early in the course of their acute liver failure. Poor prognosis without rapid liver transplantation is seen in patients with persistent arterial pH < 7.30 after resuscitation or prothrombin time > 100 seconds, serum creatinine > 3.4 mg/dL, and advanced grade (III or IV) encephalopathy (King's College criteria).[5]

CONCLUSION

Acetaminophen is a commonly used and generally safe analgesic, but overdose has high morbidity and is potentially lethal. It is important to maintain a high suspicion for acetaminophen toxicity in the right clinical setting because prompt identification and early treatment with NAC can avert hepatotoxicity, prevent death, and result in essentially full recovery for the majority of affected patients. For those with acute hepatic failure due to acetaminophen overdose, aggressive supportive care and management at a liver transplantation center should be considered. ■

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Can We Diagnose *C. difficile* Diarrhea with One Sample and One Test?

ABSTRACT & COMMENTARY

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Synopsis: *Clinicians who send samples to the 95% of U.S. laboratories that test for* Clostridium difficile *infection using an enzyme-immunoassay (EIA) for toxins A and B are often frustrated by a negative laboratory result that doesn't fit their clinical impression or their olfactory suspicions. A recent spate of publications has shown that the EIA tests are shamefully insensitive vs. the new gold standard, recovery of the organism on anaerobic culture and subsequent detection of toxin production by the* C. difficile *isolate recovered using a cell-culture cytotoxin neutralization method. A new study shows that if a reliable test is used, in this case nucleic acid amplification of the toxin B gene sequence by PCR, an initial negative result for toxigenic* C. difficile *can be trusted, and a repeat test is useful only for a subset of patients with new onset of symptoms ≥ 7 days later.*

Source: Luo RF, Banaei N. Is repeat PCR needed for diagnosis of *Clostridium difficile* infection? *J Clin Microbiol.* 2010;48:3738.

The authors tested samples sent to Stanford Hospital microbiology laboratory for diagnosis of *C. difficile* infection (CDI). That laboratory had been using the cell culture cytotoxin neutralization test as a first assay, followed by a bioMerieux Vidas™ EIA method for toxins A and B if the cell culture exhibited non-specific toxicity. Although the laboratory had decreed no repeat testing within 7 days of a positive test, there were no rules for negative test results. Apparently, physicians were sending multiple stool samples, as shown by the data presented in the publication.

Toxin tests are now known to lack sensitivity for diagnosis of CDI.[1,2,3] Even use of a glutamate dehydrogenase initial test (thought to be highly sensitive but known to be non-specific) required either a molecular or cell culture-based confirmatory test to yield reliable results, which took more than a day to complete.[1,4] A straight-talking paper by Peterson and Robicsek explained, with an example, how the predictive value of a positive result fell rapidly with repeated tests on the same patient when the sensitivity of the test was 73%, specificity was 97%, and prevalence was 10%.[5] And based on numerous studies, we now know that the sensitivity of EIA tests is more akin to 50%.[1,2,3] A previous publication from Mayo Clinic also found that repeat testing (using another method) was not clinically helpful.[6]

The authors' laboratory-developed PCR assay had a sensitivity of 87.2% and a specificity of 98.6%, compared with toxigenic culture, the gold standard. After implementation of the new PCR test, previous ordering patterns continued. The samples were received over 6 months in 2009, during which time both toxigenic cultures and PCR were performed on all samples. A total of 1,287 patients were initially evaluated, mostly adults. Almost one-fourth of all patients (293) had at least one repeat specimen sent for testing. There were a total of 405 repeat samples received, or an average of 1.5 samples per patient tested for CDI. Only 10 samples yielded a new positive result after an initial negative result, one of which was considered to be a false-positive. Among the new positive results, seven occurred at 7 or more days later. Chart reviews of those patients showed medical reasons, relapse, or new onset

of diarrhea in most cases. For all negative test results that had another sample submitted for the same test within the first 7 days, only 1% yielded a different (positive) result. In fact, overall, 97.5% of all tests remained negative on repeat(s). There may be a small subset of patients who exhibit new disease symptoms after 7 days for whom another molecular test for CDI could be valuable.

Finally, a very recent paper evaluating results of a seven-site study using a commercially available real-time PCR assay compared with various other test methods showed that the performance of EIA and GDH assays varied widely depending on the ribotype of *C. difficile* tested.[7] For the 027 epidemic strain, known to produce higher toxin levels and many more spores, the sensitivity of several EIA assays was relatively higher, but not to the level of toxigenic culture or PCR.[7] But even GDH no longer appears to be equally robust for all strains of *C. difficile*, with sensitivity dropping to 72% overall for stools containing non-027 strains vs. 91% for stools from patients harboring 027 strains.[3,7] This startling new fact may help explain published differences in sensitivity and specificity of the same test method in different settings. Fortunately for patients and physicians, the new molecular tests, similar to the old toxigenic culture test methods, seem to perform well regardless of the strain type of the pathogen. This is comforting to those whose laboratories have made the switch to molecular diagnostics, as recommended by several authorities.[5,8] ■

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Public Reporting of Central-line Infections Called into Question

ABSTRACT & COMMENTARY

By Joseph F. John, MD, FACP, FIDSA, FSHEA

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Dr. John reports no financial relationships relevant to this field of study.

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Source: Lin MY, et al. Quality of traditional surveillance for public reporting of nosocomial bloodstream infection rates. *JAMA*. 2010;304:2035-2041.

Central line-associated infections, particularly bloodstream infections (BSI), remain a huge issue in our technological age. Four academic medical centers were used to accumulate 165,963 central-line days associated with 241,518 patient days. Using the electronic medical record, an algorithm was used to determine if a BSI occurred. These results were compared to the determination by an infection preventionist who used routine infection-control activity to determine if a central line-associated BSI occurred. The median rates, as determined by both methods, differed significantly ($p < 0.001$), with the preventionists' finding 3.3 infections per 1,000 central-line days and the algorithm finding 9.0 infections. The so-called goodness-of-fit represented how closely the observations clustered around the regression line; the fit varied widely. For example, for an algorithm rate of 9 per 1,000 central-line days, the infection-preventionist observations would vary, depending on the hospital, from 1.1 to 4.9. Ironically, the hospital named hospital C, had the lowest infection-preventionist rate (2.4) and the highest corresponding algorithm rate (12.6). The authors were surprised by the degree of vari-

ability between the two methods of determining central-line BSIs.

■ **COMMENTARY**

These differences between the computer-generated rates for central line-related BSI and algorithm-generated rates are unnerving, to say the least, particularly when the infection-preventionist rates would be the ones sent out for public review. The authors, who were, in general, associated with the surveillance programs in their respective hospitals, postulate several reasons for the discrepancies. The reasons include the quality of the infection-preventionist reviews, the type of chart review performed, the variation in local practices in culturing, and the rigor of medical record documentation.

Whatever the reason, these rates can vary greatly, and there is no true gold standard. The computer algorithm is simply another way to look at the rate but, if more valid than the infection-preventionists observations, we need to find more consistent ways to determine if a central-line BSI has occurred (see Woeltje KF, et al. *Infect Control Hosp Epidemiol*. 2008;29:842-846).

Coagulase-negative staphylococci can cause true confusion in studies like these. The definition for organisms like *S. epidermidis* as the cause of infection included having two positive cultures with the same species, the same species within 2 hospital days, or a single positive culture with vancomycin having been administered within the 2 subsequent days. We are not told if the staphylococci were indeed speciated or if all isolates were considered *S. epidermidis*. We need to have better technology in the future to resolve this type of issue regarding skin commensals.

The authors are to be commended for tackling this issue and for such a massive study. They have uncovered a potential trend in variable reporting of central line-associated BSI, important due to the public reporting of such data. If, as the authors imply, at the outset, public reporting is to be promoted as improving patient safety, the public deserves the very best data that our systems can deliver. ■

Intravenous Peramivir for Seasonal Influenza

ABSTRACT & COMMENTARY

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This article originally appeared in the December 2010 issue of Infectious Disease Alert. *It was edited by Stan Deresinski, MD, FACP, and peer reviewed by Timothy Jenkins, MD.*

Synopsis: *Outpatients with uncomplicated seasonal influenza were treated with single doses of IV peramivir 300 mg/kg, 600 mg/kg, or placebo. Peramivir significantly reduced the time to alleviation of symptoms at both doses compared with placebo. Peramivir was well-tolerated, and side effects were comparable to placebo.*

Source: Kohno S, et al. Efficacy and safety of intravenous peramivir for treatment of seasonal influenza virus infection. *Antimicrob Agents Chemother*. 2010;54:4568-4574.

In this study, 296 previously healthy eligible adults ages 20-64 with onset of influenza-like symptoms within the previous 48 hours and a positive rapid antigen test were enrolled in a double-blind, placebo-controlled trial conducted at Nagasaki University. Patients were randomly assigned to receive a single dose of IV peramivir 300 mg/kg (n = 99), 600 mg/kg (n = 97), or matching placebo (n = 100). Influenza symptoms and body temperature were self-assessed for 14 days. Nasal and pharyngeal specimens were obtained, and influenza virus titers were determined. Peramivir at both doses was shown to significantly reduce ($p = 0.0092$) the median time to alleviation of symptoms compared with placebo (59.1 hours for 300 mg, 59.9 hours for 600 mg, and 81.8 hours for placebo). Efficacy was demonstrated against both A/H1 and A/H3 influenza virus subtypes. Virus titers in respiratory samples were significantly lower in both active treatment arms than in the placebo arm on both day 2 and day 3 of treatment. Adverse events observed with both doses of peramivir were similar to those reported in the placebo group.

■ **COMMENTARY:**

Peramivir is an investigational sialic-acid analogue-neuraminidase inhibitor with potent in-vitro activity against influenza A and B viruses, and is available in an intravenous formulation. It has a strong affinity for influenza virus neuraminidase and a low off-rate, suggesting that infrequent dosing would be feasible. During the 2009-2010 season, a novel H1N1 strain became pandemic and displayed high mortality rates in both young and old patients. In critically ill patients, oral absorption of oseltamivir due to ileus or other factors and unreliable delivery to pulmonary tissue by inhalation route of zanamivir exist as major concerns to treating clinicians. Due to the lack of FDA-approved parenteral formulations of other neuraminidase inhibitors (oseltamivir and zanamavir), IV peramivir was released under a compassionate-use protocol for use in critically ill patients with confirmed pan-

demic H1N1 influenza. Formal analysis of the total experience of compassionate use of IV peramivir has yet to be published in the peer-reviewed literature, but smaller case series suggest that it showed significant efficacy and safety in many of these critically ill patients.

The impressive efficacy of single-dose IV peramivir in outpatients with uncomplicated influenza, and the clinical evidence for efficacy and safety in critically ill patients, support the effectiveness of this agent, as well as the need for additional randomized, controlled trials in larger numbers of patients and special populations (including children and immunocompromised patients).

One common misconception, which needs to be addressed, is the false belief that antiviral agents are not effective in patients who have duration of influenza symptoms of greater than 48 hours. It should be pointed out that while most antiviral agents studied over the last 40 years (amantadine, rimantadine, oseltamivir, zanamivir, and peramivir) seem to demonstrate greater relative efficacy vs. placebo when studied in clinical trials with duration of symptoms < 48 hours, as opposed to longer duration of symptoms, this result is, in part, due to the inclusion criteria of the trials themselves. Certainly, critically ill patients with influenza, especially those requiring mechanical ventilation or extra-corporeal membrane oxygenation, should not be denied antiviral therapy despite duration of symptoms > 48 hours. ■

QI Process Promotes Early Mobilization of ICU Patients

ABSTRACT & COMMENTARY

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Dr. Hoffman reports no financial relationship to this field of study.

This article originally appeared in the December issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD.*

Synopsis: *Using a quality improvement (QI) process, ICU delirium, physical rehabilitation, and functional mobility were significantly improved and associated with a decreased length of stay.*

Source: Needham DM, et al. Early physical medicine and rehabilitation for patients with acute respiratory failure: A quality improvement project. *Arch Phys Med Rehabil.* 2010;91:536-542.

Following a chart review that indicated few (24%) medical ICU (MICU) patients received consultation for physical therapy (PT) or occupational therapy (OT) — a percentage almost 50% lower than at two other academic medical centers in the same city — as well as a higher prevalence of deep sedation, the authors elected to initiate a QI project designed to reduce the use of deep sedation and improve patients' functional ability. The project, based on the "4Es" (Engage, Educate, Execute, Evaluate), involved the following steps:

- MICU admission orders were modified to change the default activity level from "bed rest" to "as tolerated";
- Clinicians were encouraged to order benzodiazepines and narcotics "as needed" rather than by continuous infusion;
- Guidelines were disseminated to encourage PT and OT consultation;
- New safety-related guidelines were developed to identify eligible patients;
- Staffing was changed to include a full-time PT and OT; and,
- Consultations to a neurologist were encouraged for patients with severe muscle weakness.

Compared to before the QI project was initiated, the proportion of days on which patients received benzodiazepines decreased (from 50% to 25%; $p = 0.002$), with lower median daily sedative doses (47 mg vs. 15 mg midazolam equivalents [$p = 0.09$]; 71 mg vs. 24 mg morphine equivalents [$p = 0.01$]). Patients had more days when they were alert (30% vs. 67%; $p < 0.001$) and not delirious (21% vs. 53%; $p = 0.003$). There were a greater number of rehabilitation treatments per patient ($p < 0.001$) with a higher level of functional mobility (56% vs. 78%; $p = 0.03$). Patients had similar (low) pain ratings prior to and following the QI project (0.6 vs. 0.6; $p = 0.79$) based on nursing assessments using a 0-10 scale. Comparison with historical controls indicated a decrease in ICU and hospital lengths of stay by 2.1 days (95% confidence interval [CI], 0.4-3.8) and 3.1 days (95% CI, 0.3-5.9), respectively. The only adverse events were four instances in which a rectal or feeding tube was dislodged.

■ COMMENTARY

Historically, early mobilization of ICU patients was promoted by eminent clinicians such as Thomas Petty and Louise Nett, who observed that "when we first started our unit in 1964, patients who required mechanical ventilation were awake and alert and often sitting in a chair."[1] However, early mobilization was uncommon until recently when clinicians, prompted by concerns about complications faced by ICU survivors and evidence regarding the benefits of less sedation, began to test the ability to safely provide mobility interventions.

Following an initial survey that identified the need to change practice, Needham and colleagues implemented a QI project that involved many meetings aimed at presenting the problem, identifying barriers and solutions, and developing the structure of the project. A unique component of this process involved having patients who participated in early mobilization activities return to the MICU to share feedback about their experiences and subsequent recovery. These patient visits provided compelling evidence of potential benefits and lack of adverse consequences (videos of patient interviews are available at www.hopkinsmedicine.org/oacis).

The subsequent QI project achieved significant changes in routine clinical practice in a relatively short period of time (4 months). Notably, since implementation of the project, the hospital funded a program that allowed the multidisciplinary team used for the project to be sustained, solidify gains, and design new projects to implement and evaluate additional approaches to promote early mobility, such as cycle ergometry and neuromuscular electrical stimulation therapy. ■

Reference

1. Petty TL. Suspended life or extending death? *Chest.* 1998;114:360-361.

CME Questions

13. In the report by Needham et al, the implementation of a quality-improvement project designed to improve ICU delirium, increase physical rehabilitation, and functional mobility, led to which of the following patient outcomes?

a. No substantial changes in outcomes following implementation of the protocol.

b. More days of patients receiving a benzodiazepine.

c. More days without pain.

d. A higher level of functional mobility.

14. According to the study by Kohno et al, a single dose of intravenous peramavir in adult patients with early-onset influenza-like symptoms led to:

a. reduced duration of symptoms from influenza A virus.

b. improved outcomes compared to oseltamavir.

c. reduced 30-day mortality

d. increased risk of viral pneumonia.

15. Based on the recent report by Lin et al, comparing two methods of determining central line-associated infections at four academic hospitals, all of the following observations were made except:

a. the infection rates reported by computer algorithm were significantly lower than the rates reported by an infection-control practitioner.

b. the infection rates did not differ significantly between the two methods.

c. the infection rates reported by computer algorithm were significantly higher than the rates reported by an infection-control practitioner.

d. public reporting of nosocomial central-line infections is not warranted.

Answers: 13. (d); 14. (a); 15. (c)

CME / Objectives

Upon completion of this educational activity, participants should be able to:

- discuss pertinent safety, infection control and quality improvement practices;
- explain diagnosis and treatment of acute illness in the hospital setting; and
- discuss current data on diagnostic and therapeutic modalities for common inpatient problems. ■