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INSIDE

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Antiretrovirals for Acute HIV Infection — Not Ready for Prime Time

ABSTRACTS & COMMENTARY

By Dean L. Winslow, MD, FACP

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This article originally appeared in the November 2006 issue of Infectious Disease Alert. It was edited by Stan Deresinski, MD, FACP, and peer reviewed by Connie Price, MD. Dr. Deresinski is Clinical Professor of Medicine, Stanford University; Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center, and Dr. Price is Assistant Professor, University of Colorado School of Medicine. Dr. Deresinski serves on the speaker's bureau for Merck, Pharmacia, GlaxoSmithKline, Pfizer, Bayer, and Wyeth, and does research for Merck. Dr. Price reports no financial relationships relevant to this field of study.

Synopsis: *A multicenter, observational study retrospectively compared 59 individuals with acute or early HIV infection who elected to receive antiretroviral (ARV) therapy for 12 weeks to 337 patients who declined treatment. Initiation of ARV treatment within 2 weeks of presumed infection appeared to result in a trend toward higher CD4 counts and lower HIV RNA levels at 24 weeks. In contrast, a prospective trial of 20 patients with acute HIV infection who were randomized to antiretroviral therapy for 24 weeks vs no treatment showed no differences in either CD4 count or HIV RNA between treated and untreated patients 6 months after ARV was stopped.*

Sources: Hecht FM, et al. A multicenter observational study of the potential benefits of initiating combination antiretroviral therapy during acute HIV infection. *J Infect Dis*. 2006;194:725-733; Streeck H, et al. Immunological and virological impact of highly active antiretroviral therapy initiated during acute HIV-1 infection. *J Infect Dis*. 2006;194:734-739.

THE OPTIMAL TIME TO INITIATE ANTIRETROVIRAL THERAPY (ARV) in chronically-infected asymptomatic patients is now

felt to be when the CD4+ lymphocyte count falls to approximately 350 cells/uL,[1] based on the probability of developing an AIDS-defining illness within a relatively short period of time, as shown in a meta-analysis of cohort studies.[2] While evidence clearly supports treatment of chronic infection using these parameters, it remains unknown whether treatment during acute (within 2 weeks of infection) or early (2 weeks- 6 months after infection) HIV infection confers clinical benefit. It has been postulated that ARV therapy, instituted during acute or early infection, can reduce T-cell loss by limiting viral replication prior to activation of significant numbers of T-cells and, possibly, lower the viral set point even after ARVs have been discontinued. While this possible benefit has been widely discussed, only anecdotal, retrospective, cohort studies have suggested that such a benefit of early ARV treatment occurs.

The first study, by Hecht and colleagues, evaluated patients followed in the Acute Infection and Early Disease Research Program cohort who self-selected acute (n = 13) or early (n = 45) ARV treatment for 12 weeks (then stopped), and used the 337 patients who declined treatment as the control group. In the acute treatment group, there was an apparent trend toward higher CD4 counts and lower HIV RNA levels at 72 weeks, only in adjusted analyses. However, looking at the actual scatter plots, the trend is not at all impressive, and relies on some interesting (and creative) statistical methods to draw the lines supporting this conclusion. The unadjusted analyses show no significant benefit of therapy of acute infection. ARV therapy, initiated greater than 2 weeks following infection, was associated with modest, but diminishing CD4 benefit at 72 weeks and no evidence of viral load benefit at the same time point, using adjusted analyses. For all the measures examined, the confidence intervals overlapped considerably. The weak suggestion of benefit of ARV treatment of acute HIV infection is largely negated by the nonrandomized design of the trial, the small number of patients who received treatment, and the fact that very creative statistical methods needed to be used to parse out any suggestion of benefit.

The second study by Streeck and colleagues prospectively assessed 20 patients with acute HIV infection, 12 of whom initiated ARV treatment for 24 weeks then terminated therapy and 8 who did not receive therapy. In the treated group, suppression of viremia, increased CD4 counts, enhanced differentiation of HIV-1-specific CD+ T cells from memory to effector phenotype at week 24, and higher virus-specific interferon-gamma+ CD8+ T cell responses after viral rebound at week 48 were observed. However, no differences in HIV viremia or CD4 counts were found 6 months after discontinuation of ARV's compared to the untreated patients.

While it remains important to diagnose acute HIV infection to prevent the high rate of secondary transmission to sexual contacts of acutely infected individuals, benefits of early institution of antiretroviral therapy in this population appears to have negligible clinical benefits. It would appear that a study large enough and powered adequately to clearly demonstrate any long lasting clinical benefit of ARV therapy in this population would be prohibitively expensive and require years to conduct. My personal opinion is that these resources could be much better applied to providing additional antiretroviral drugs to patients in the developing world. ■

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Volume May (Or May Not) Impact Mortality in ICU Patients

ABSTRACTS & COMMENTARY

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

This article originally appeared in the November 2006 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, and Dr. Thompson is Staff Pulmonologist, VA Medical Center; Associate Professor of Medicine, University of Washington,. Dr. Pierson and Dr. Thompson report no financial relationships relevant to this field of study.

Synopsis: *In 2 studies, mechanical ventilation in a hospital with a high case volume was associated with reduced mortality for nonsurgical patients, either regardless of severity of illness (Kahn et al) or only in high-risk patients (Glance et al).*

Sources: Kahn JM, et al. Hospital volume and the outcomes of mechanical ventilation. *N Engl J Med*. 2006;355:41-50; Glance LG, et al. Impact of patient volume on the mortality rate of adult intensive care unit patients. *Crit Care Med*. 2006;34:1925-1934.

Associations between the number of patients managed (hospital volume) and improved patient survival have been extensively documented in the surgical literature—such as cardiac surgery, ruptured aortic aneurysm, and several types of cancer surgery—and suggested for selected medical conditions, such as acute myocardial infarction and the acquired immunodeficiency syndrome. Two recent studies attempted to determine whether high hospital volume was associated with reduced mortality following mechanical ventilation (MV).

Kahn et al examined data from 20,241 patients admitted to 37 ICUs in the Acute Physiology and Chronic Health Evaluation (APACHE) clinical information system who underwent MV from 2002 through 2003. The sample excluded surgical patients (as determined by admitting diagnosis code) and also admissions to eight "outlier" hospitals with very low (< 50 patients/year; n = 7) or very high (> 1000 patients/year; n = 1) volumes of patients receiving mechanical ventilation. The analysis controlled for severity of illness (APACHE III score), admission diagnosis, preadmission location, academic status of the hospital, type of ICU, geographic region, and presence of intensivists. The primary outcome variables were ICU and hospital mortality. An increase in hospital volume was associated with improved survival in the ICU and in the hospital. Admission to a hospital with the highest quartile volume (> 400 ventilated patients/year) was associated with a 37% reduction in odds of death in the ICU as compared with admission to a hospital in the lowest quartile (£ 150 ventilated patients/year) ($P < .001$). The absolute risk of death in a low-volume hospital was 34.2% vs 25.5% in a high-volume hospital.

Glance et al examined data from 70,757 patients admitted to 92 ICUs in the Project IMPACT (Society of Critical Care Medicine) database from 2001 to 2003. After controlling for patient risk factors and ICU characteristics, patients admitted to high-volume ICUs had improved outcomes ($P = .025$). However, the mortality benefit was only seen in high-risk patients managed in ICUs treating high volumes of high-risk patients, defined as a Simplified Acute Physiology Score (SAPS II) > 41. There was no association between ICU volume and outcomes when the volume calculation was based on all ICU admissions.

COMMENTARY

Several expert task forces sponsored by the National Institutes of Health, the Society of Critical Care Medicine, and the American College of Chest Physicians have proposed that critical care medicine be regionalized, with the goal of providing improved patient outcomes at lower cost. The premises behind these recommendations are that patients who require mechanical ventilation need complex care that is best provided by a team of highly experienced clinicians, and such teams are more likely to be found in high-volume institutions. Accordingly, the findings of these two studies have important health policy implications.

Study results suggest a volume-outcome association, but do not clarify whether this association is restricted to high-risk patients managed in ICUs that admit large numbers of such patients, or applies to all nonsurgical patients admitted to a high-volume institution, regardless of their risk status. Several differences in methodology likely explain these somewhat divergent findings. First, the databases used to identify subjects differed, with one study using the APACHE III database (which collects data from hospitals in the United States), and the second the Project IMPACT database (which includes hospitals in the United States, as well as Australia, Brazil, Puerto Rico, and Canada). The types of patients enrolled also differed, with one study restricting entry to nonsurgical patients, based on the rationale that a volume-outcome relationship had already been established for many surgical procedures, and the second including surgical patients. The scoring systems used to assess severity of illness (APACHE III, SAPS II) were different, and one study focused on hospital volume whereas the second focused on ICU volume. In addition,

the methods used for statistical analysis differed in regard to the techniques used for model development and variables introduced to control for potential confounders.

There are many potential causes for improved survival in patients who require mechanical ventilation. These include differences in organizational structure, access to an intensivist, nurse-to-patient ratio, and patient management. The last of these would include differences with respect to evidence-based care, the use of protocols for such things as sedation, mechanical ventilation and glycemic control, and other aspects of care. Clinicians in high-volume hospitals are likely to have more experience in the care of critically ill patients, which should translate into improved outcomes. However, high-volume hospitals are also likely to be challenged by the numbers of patients seen, frequent rotation of coverage, inconsistency in attending and nurse staffing, and organizational directives that at times seem adverse to optimal care practices.

Findings of these studies suggest that hospital volume may be an important determinant of outcome among critically ill patients who require mechanical ventilation, especially if they are high risk and managed in an ICU that admits large number of such patients. ■

Clinician Estimates of Ideal Body Weight Are Inaccurate

ABSTRACT & COMMENTARY

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Dr. Pierson reports no financial relationship relevant to this field of study.

This article originally appeared in the November 2006 issue of Critical Care Alert. It was peer reviewed by William Thompson, MD. Dr. Thompson is Staff Pulmonologist, VA Medical Center; Associate Professor of Medicine, University of Washington. He reports no financial relationship relevant to this field of study.

Synopsis: *When ICU clinicians estimated rather than calculated ideal body weight in mechanically ventilated patients in order to set tidal volume, the majority of such estimations were sufficiently inaccurate that the resulting tidal volume was outside the unit's target range.*

Source: Diacon AH, et al. Challenges in the estimation of tidal volume settings in critical care units. *Intensive Care Med.* 2006;32:1670-1671.

Over a 3-month period, all patients who required mechanical ventilation in the ICU of Tygerberg Academic Hospital in Cape Town, South Africa, were enrolled in this study. To test the authors' hypothesis that the ideal body weight (IBW) estimated by experienced clinicians would be significantly different from calculated IBW, the former was recorded for each patient in a concealed fashion by 21 ICU nurse practitioners, 2 ICU technologists, 9 registrars (residents), and 4 senior intensivists. These estimated IBWs were then compared to the value calculated for the patient using gender-specific formulas similar to those used in the ARDS Net low-tidal-volume study.[1] The authors then classified the resulting tidal volume (VT) settings as appropriate (6-8 mL/kg), too low (< 6 mL/kg), or too high (> 8 mL/kg).

The clinicians generated 545 estimates of IBW from the 18 men and 22 women who required mechanical ventilation during the study period. Mean estimated and calculated IBW values were 68.3 ± 19.1 and 57.2 ± 11.2 kg, respectively—a difference that averaged 19% too high. ICU nurses' estimated IBW values were significantly higher than those of the other clinicians (69.7 ± 20.1 vs 65.9 ± 16.9 kg; $P = 0.02$). The median range of IBW for each patient among the 36 staff members was 31 kg. Only 44% of the estimated IBW values (240/545) resulted in VTs in the target range, with 25.5% of estimates too low and 30.5% too high. More men than women had estimations that led to too-small VT (101 vs 38; $P < 0.01$), and more women than men had estimations that led to VT settings that were too large (> 8 mL/kg; 143 vs 23; $P < 0.01$).

The authors conclude that the practice of estimating IBW informally at the bedside results in markedly inaccurate weights and thus VT settings that are outside the intended range in the majority of patients. They recommend that patient height be measured routinely when patients are placed on mechanical ventilation, and that VT be based on calculated rather than estimated IBW.

■ COMMENTARY

Lung-protective ventilation, with low VT based on IBW and maintenance of end-inspiratory static pressures less than about 30 cm H_2O, has become the standard of care for patients with acute lung injury (ALI) or the acute respiratory distress syndrome (ARDS). The ARDS Network demonstrated that ventilating ALI-ARDS patients with VT of 6 mL/kg IBW or less, as opposed to 12 mL/kg IBW, saved 1 life for every 11 patients enrolled.[1] As a result of that study and several others, clinicians

everywhere are using lower VT than they used to use—not only for patients with ALI-ARDS but also in other patients as well.

Although it has been shown convincingly in animals with initially normal lungs that large-volume ventilation can induce an ALI-ARDS-like condition, and although there is some evidence suggesting that critically ill patients without ALI-ARDS are more likely to get it if large tidal volumes are used, the benefit of low-VT ventilation has not been directly demonstrated in such patients. There is also some evidence suggesting that the trend toward using lower VT in routine ventilator management in recent years has been accompanied by an increase in the incidence of atelectasis.[2] Thus, while low-VT ventilation is evidence-based in ALI-ARDS and has rightly become the standard of care, it remains to be seen whether this is the best approach for patients without either ALI-ARDS or severe obstructive lung disease.

In the present study, we are not told whether any of the patients had ALI-ARDS. The study thus demonstrates that clinicians are poor at estimating IBW at the bedside, but it is not entirely certain that the target VTs used were optimal. I still recommend VT 10-12 mL/kg for the average ventilated patient without ALI or obstructive lung disease, keeping plateau pressure < 30 cm H_2O. This places me in an ever-dwindling minority, however, and I have to admit that the evidence for harm from low-VT ventilation in patients without ALI-ARDS is weak. An initial VT of 8 mL/kg has become the standard for virtually all ventilated patients at my institution. Fortunately, calculation of IBW has also become part of the routine ICU admission procedure for ventilated patients. As shown by this study, actually calculating IBW rather than estimating it at the bedside is the only way to be sure that an appropriate VT will be employed, whatever the target value may be. ■

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Risk Stratification in Acute Coronary Syndromes

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

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Dr. Crawford is on the speaker's bureau for Pfizer.

This article originally appeared in the November 2006 issue of Clinical Cardiology Alert. It was peer reviewed by Rakesh Mishra, MD, FACC. Dr. Mishra is Assistant Professor of Medicine, Weill Medical College, Cornell University; Assistant Attending Physician, NewYork-Presbyterian Hospital. Dr. Mishra reports no financial relationship relevant to this field of study.

Synopsis: *ECG ST depression was strikingly predictive of outcomes in ACS patients, compared to new biomarkers.*

Source: Westerhout CM, et al. Short- and long-term risk stratification in acute coronary syndromes: The added value of quantitative ST-segment depression and multiple biomarkers. *J Am Coll Cardiol*. 2006:48:939-947.

New biomarkers are pushing for a place in our risk stratification of acute coronary syndromes. Their role, as compared to clinical characteristics of the patients and the venerable ECG, is unclear. Hence, Westerhout and colleagues evaluated the GUSTO-IV database to assess the role of ECG ST changes, troponin, C-reactive protein (CRP), and N-terminal pro-brain natriuretic peptide (NT-proBNP) in 7800 patients with non-ST elevation acute coronary syndrome (ACS) in predicting outcomes. Patients were eligible for GUSTO-IV if, within 24 hours of ischemic chest pain, they had an elevated troponin or new ST-segment depression (≥ 0.5 mm). Although the trial was designed to compare abciximab to placebo, since abciximab did not change outcomes, all the patients were considered for this analysis. Coronary angiography was withheld until 12 hours after the study infusion, and additional therapy was at the managing physician's discretion.

The primary end points were 30-day death or myocardial infarction (MI) and one-year mortality. The 30-day death rate was 4%, and 4.5% more died by one year. The 30-day death or MI rate was 8%. The baseline biomarkers, the magnitude of ST depression and heart rate, were all higher in those with events in 30 days or 1 year. Although 13 factors contributed to the 30-day mortality risk, ECG ST depression contributed most to the predic-

tive model; next were creatinine clearance and troponin. Other factors including NT-proBNP were less predictive. However, NT-proBNP was a powerful predictor of one-year death, but was not more predictive than the ECG. CRP was only predictive of one-year death. Westerhout et al concluded that the magnitude of ECG ST depression was strikingly predictive of outcomes in ACS patients, compared to new biomarkers and old measures such as creatinine clearance.

COMMENTARY

This study illustrates that for the critical 30-day death or MI prediction, the initial ECG is king, especially if it is quantitated, followed closely by troponin. These findings probably explain the utility of the TIMI score, which includes both these factors. Among the newer or non-traditional markers, creatinine clearance was most useful and NT-proBNP was of some value, but CRP did not contribute. Thus, markers of the extent of ischemic injury (ECG and troponin) were the most important for predicting 30-day death or MI, and should be strongly weighted in clinical decisions involving ACS patients.

One-year mortality was also best predicted by initial ECG changes; almost as well was creatinine clearance, closely followed by troponin and NT-proBNP. CRP added to the prediction, but was only 3% of the model as compared to 10% by NT-proBNP. Patients with ECG changes could be sicker, but these results held up when adjusted for baseline characteristics. Creatinine clearance emerged as a powerful predictor, number 3 for 30-day outcomes and second for one-year death, despite the fact that those with severe renal dysfunction were excluded from the study. NT-proBNP correlated best with death at any time point. Surprisingly, CRP performed least well, adding nothing to the prediction of 30-day events and a small amount to one-year mortality.

Westerhout et al developed their own score based upon 7 factors: age, body weight, heart rate, creatinine clearance, ST depression, troponin, and NT-proBNP. However, it is not a simple 7-point score like the TIMI score because each factor is divided into 3 quantitative levels, with different weighted points for each, such that the maximum score is 39-51 depending on the outcome being predicted. Clearly, this is too complicated to ever catch on clinically, but the list of factors is different from others; only 3 are also in the TIMI score. Body weight, heart rate, creatinine clearance, and NT-proBNP are new factors. Thus, creatinine and NT-proBNP should be added to the evaluation of ACS patients.

There are limitations to this study. The ECG and troponin are criteria for admitting the patients to the trial, so there is some bias toward these measures that may not be totally correctable. Reduced renal function may elevate some of the biomarkers confounding these factors. Blood pressure was not evaluated, yet older studies show it has predictive value, especially for death. The study may not be applicable to the general ACS population, as the GUSTO-IV population all underwent cardiac catheterization on their initial admission. Thus, the population is likely higher risk than a more general ACS population. On the other hand, the ECG and troponin will be of value in triaging less sick patients, and useful information can be gained from creatinine and BNP. So, I would use this approach on all potential ACS patients. ■

The Effect of Maternal Oxygen Administration on Fetal Pulse Oximetry During Labor in Fetuses with Nonreassuring Fetal Heart Rate Patterns

ABSTRACT & COMMENTARY

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Dr. Hobbins reports no financial relationship relevant to this field of study. This article originally appeared in the November 2006 issue of OB/GYN Clinical Alert. It was edited by Leon Speroff, MD, and peer reviewed by Catherine LeClair, MD. Dr. Speroff is Professor of Obstetrics and Gynecology, Oregon Health and Science University, Portland, and Dr. LeClair is Assistant Professor, Department of OB/GYN, Oregon Health and Science University. Dr. Speroff is a consultant for Barr Laboratories, and does research for Wyeth. Dr. LeClair reports no financial relationship relevant to this field of study.

Synopsis: *The administration of supplemental oxygen to laboring patients with nonreassuring fetal heart rate patterns increases fetal oxygen saturation substantially and significantly. Fetuses with the lowest initial oxygen saturations appear to increase the most.*

Source: Haydon ML, et al. The effect of maternal oxygen administration on fetal pulse oximetry during labor in fetuses with nonreassuring fetal heart rate patterns. *Am J Obstet Gynecol*. 2006;195:735-738.

For years clinicians have been administering oxygen by mask to patients with worrisome fetal heart rate patterns. Yet, a Cochrane database review has questioned this practice because of the lack of solid date to demonstrate its benefit.[1]

A group from University of California-Irvine set out to see if oxygen by mask could boost the fetal oxygen saturation in those fetuses that might actually need extra oxygen—those with nonreassuring fetal heart rate patterns in labor. Twenty-four women in labor were recruited to participate in the study. Each had fetuses who demonstrated combinations of decreased beat-to-beat variability with tachycardia and/or late decelerations. After baseline values at room air were obtained, the patients were given 40% by simple face mask and later (after a washout time of 30 minutes), 100% fraction of inspired oxygen (FIO_2) by nonrebreathing mask. The fetal oxygen saturation was determined continuously by a pulse oximeter applied to the fetal cheek.

The study resulted in the following findings:

- In those with normal O_2 saturation (>50%), there was little change after maternal oxygen administration.
- In those fetuses with low values initially there was, on average, a 5% increase in baseline O_2 saturation with 40% FIO_2 and a 6.5% rise with 100% FIO_2.
- The nine fetuses with the lowest baseline O_2 saturation (< 40%) had the largest rise, 7.0% with 40% administered FIO_2 and 12.6% after 100% FIO_2.

COMMENTARY

This study only concentrated on the population of fetuses who might need O_2 the most—those with evidence of non-reassuring fetal heart rate tracings, many of whom had low O_2 saturation. To me, here was a clear demonstration that O_2 by mask can work in raising the O_2 saturation in fetuses showing evidence of "fetal distress"—now a term that is no longer politically correct. However, we need to be very selective in using O_2 by mask. First, it is confusing and downright annoying for a patient that wants to, and needs to, move around and even ambulate. Second, it is anxiety provoking in many already fearful patients by indirectly indicating their fetuses may be in trouble.

Unfortunately, while we continue to interdict patients from having food or drink in labor, we liberally hand out O2 masks to anyone in labor who looks at us cross-eyed. Also, O_2 saturation monitoring investigation has shown that patients whose fetuses demonstrate moderate to severe variable decelerations, a very common occurrence that triggers O_2 by mask in virtually every hospital in the country, will have no drop in their O_2 saturation during these episodes.

O_2 saturation monitors have fallen out of favor because studies involving large numbers have not demonstrated an improved benefit in outcome when it is used. However, here is an example of how investigation that would not be otherwise possible has demonstrated something that many have wondered about for years: Does maternal O_2 delivery by mask really improve O_2 saturation in the fetus? This study says "yes" but only in those who might really need it.

Now, whether this translates out into an improved outcome may have to await further study. However, let's narrow down its use to only those at highest risk for fetal compromise and leave the others alone. ■

Reference

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Fatal Plague in the US

UPDATE

By Carol A. Kemper, MD, FACP

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Dr. Kemper reports no financial relationship relevant to this field of study.

This article originally appeared in the November 2006 issue of Infectious Disease Alert. It was edited by Stan Deresinski, MD, FACP, and peer reviewed by Connie Price, MD.

Source: CDC. *MMWR Morb Mortal Wkly Rep*. 2006;55:940.

EACH YEAR IN THE UNITED STATES, A FEW ISOLATED cases of plague are reported. This year, possibly because of increased spring rains leading to an increase in the rodent population, an unprecedented 13 cases of plagues have occurred in 4 states (New Mexico, California, Colorado, and Texas). Importantly, 5 (38%) patients had primary septicemic plague and, therefore, lacked an obvious tell-tale buboe. The remaining 8 (62%) patients had bubonic plague, 2 of whom developed secondary pneumonia. Two patients (15%) died.

Most human infection is acquired through the handling of infected animals (eg, domestic cats, rabbit and hare carcasses, squirrels, chipmunks) and from the infected fleas of various rodents. Pneumonic plague is highly contagious, and any individual with suspected disease should be placed in respiratory isolation. Family members, close contacts, and exposed health care workers require post-exposure prophylaxis with doxycycline. Delays in recognition of infection lead to an increased risk of mortality, as occurred in this report. Septicemic and pneumonia plague is quickly fatal if not promptly treated, and bubonic plague is about 50% fatal if not recognized.

Possible sources of infection in the current *MMWR* report included rabbit carcasses from Lea County, New

Mexico and from Kern County in northern California, and infected fleas from various rodents on the victims' properties. Dogs owned by 3 of the victims had serologic evidence of past infection with *Y. pestis*. In one case, a 28-year-old woman living in Los Angeles came in contact with the raw meat from the Kern County bunny, presumably brought home for cooking. She developed painful right axillary swelling, fever, and septic shock. Because she had not traveled outside of Los Angeles and had none of the usual risk factors for plague, plague was not suspected.

As an aside, human plague in the developing world is much more common than in the United States. An outbreak of suspected pneumonic plague in the Congo this year has resulted in more than 100 deaths, promulgated by working conditions in crowded and poorly ventilated mines, leading to increased human transmission. ■

CME Questions

4. **In the study of risk stratification in acute coronary syndromes by Westerhout et al, mortality is most strongly predicted by:**
   a. C-reactive protein
   b. troponin
   c. ECG ST segment changes
   d. NT-proBNP
   e. LDL cholesterol

5. **According to the recent study by Diacon et al, when bedside clinicians estimated ideal body weight, instead of measuring it, to set tidal volume for mechanically ventilated patients:**
   a. the estimated ideal body weights were essentially identical to the measured ones.
   b. the estimated ideal body weights were always less than the measured ones.
   c. the estimated ideal body weights were always more than the measured ones.
   d. it led to tidal volume settings outside the intended range in the majority of patients.

6. **Which of the following statements regarding human plague is true?**
   a. Human plague is much more common in the developing world than in the United States.
   b. Human plague can present primarily as sepsis without obvious buboes.
   c. Most human infections are acquired through the handling of infected animals.
   d. Family members, close contacts, and exposed health-care workers require post-exposure prophylaxis with doxycycline.
   e. All of the above.

Answers: 4. (c); 5. (d); 6. (e)

CME Objectives

The objectives of *Hospital Medicine Alert* are to:

• review pertinent safety, infection control, and quality improvement practices;

• discuss diagnosis and treatment of acute illness in the hospital setting; and

• review current data on diagnostic and therapeutic modalities for common inpatient problems. ■