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INSIDE

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Missed Opportunities to Improve the Quality of End-of-Life Care

ABSTRACT & COMMENTARY

By Leslie A. Hoffman RN, PhD

Department of Acute/Tertiary Care School of Nursing, University of Pittsburgh

Ms. Hoffman reports no financial relationships related to this field of study.

Synopsis: *When communicating about end-of-life care, the most common missed opportunities involved responding to family concerns, acknowledging and addressing family emotions, and sharing key principles of medical ethics.*

Source: Curtis JR, et al. Missed Opportunities during Family Conferences About End-of-Life Care in the Intensive Care Unit. *Am J Respir Crit Care Med*. 2005;171:844-849.

THE MAJORITY OF DEATHS IN AMERICAN ICUS INVOLVE WITHholding or withdrawing life-sustaining therapy. When such decisions are considered, patients are typically unable to communicate for themselves and, therefore, family members may become the decision-makers. Few guidelines exist to direct the structure of family conferences in these circumstances, despite their importance.

Curtis and colleagues identified 51 family conferences when the attending physician anticipated discussion of withdrawing life-sustaining therapy or delivering bad news. The conferences were audiotaped and their content analyzed using qualitative methods. The study was conducted in 4 hospitals, including a county hospital, a university hospital, and 2 community hospitals. Participants included 20 attending physicians, 15 residents or fellows, 50 nurses, 25 social workers, 12 clergy members, and 227 family members. The number of clinicians present ranged from 1 to 12 (mean, 4.3). Most (86%) conferences involved discussions of withdrawing or withholding treatment, and the remainder dealt with relaying news regarding a worsening prognosis or worsening clinical status.

"Missed opportunities" were defined as passages when all clinicians present failed to provide information or emotional support to the family. These passages, identified in 29% of the conferences, fell into 3 categories:

- missed opportunities to answer family questions or follow-up on important statements, the most common category. For example, when asked whether brain damage had occurred, the response focused on how brain function is tested without relating this information to patient status;
- missed opportunities to acknowledge emotions, support family grief, or attempt to alleviate family guilt. For example, when family members expressed sadness or guilt, the conversation was changed to an unrelated topic; and
- missed opportunities to explain key tenets of medical ethics and palliative care, including exploration of patient treatment preferences, explanation of surrogate decision-making, or affirmation that the patient would not be abandoned. For example, clinicians failed to explicitly state that the patient would not be abandoned when transitioning to palliative care or to explore beliefs influencing choices in surrogate decision-making.

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EDITORIAL GROUP HEAD: Lee Landenberger.

MANAGING EDITOR: Robert Kimball.

ASSOCIATE MANAGING EDITOR: Leslie Hamlin.

MARKETING PRODUCT MANAGER: Gerard Gernazian.

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The study also assessed family satisfaction with these conversations, and found significantly lower satisfaction ratings for conferences with missed opportunities.

COMMENTARY

Although recognized as extremely important, communication about withdrawing and withholding life-sustaining treatment is commonly assessed as less than optimal by family members. There is no simple way to teach "improved communication;" and studies testing interventions to improve communication are often sketchy in regard to the details of the communication intervention. Curtis et al did not provide demographic information about the participating clinicians, with the exception of physicians leading the conferences, who were predominately male (66%) attending physicians (57%) with a specialty in internal medicine (74%), neurology (14%), surgery (7%), or anesthesiology (3%) who had been practicing for 12.4 ± 9.7 years. Given the experience of these attending physicians, it is likely that they, as others attending the conferences, viewed their communication to be appropriate. Of significance, the large majority (71%) of audiotaped conferences were judged to meet family needs.

The contribution of this study is the specific examples cited in the text illustrating missed opportunities. These circumstances, coded into 3 categories, included missed opportunities to actively listen and directly respond to family questions, to acknowledge and support the emotional distress experienced, to provide insight regarding the ethical basis for surrogate decision-making, and to affirm that the patient will not be abandoned in the process of withdrawing or withholding treatment.

There is increasing evidence that attention to family communication matters. Symptoms consistent with a moderate-to-major risk of post-traumatic stress disorder (PTSD) have been reported by 33% of family members 90 days after ICU discharge or death.[1] Higher rates of PTSD were noted among family members who felt information was incomplete (48%), whose relative died in the ICU (50%), and who shared in end-of-life decision-making (82%). These findings support the need to sharpen listening skills, to continuously evaluate success in communicating in difficult circumstances, to identify deficiencies, and to work toward improving these things. By taking full advantage of opportunities to provide information to families, clinicians can address the specific needs of each family, improve shared decision-making, and help to decrease family stress. ■

Reference

1. Azoulay E, et al. Risk of post-traumatic stress symptoms in family members of intensive care unit patients. *Am J Respir Crit Care Med*. 2005:171:987-994.

Another Reason to Avoid Unnecessary Transfusions

ABSTRACT & COMMENTARY

By Saadia R. Akhtar, MD, MSc

Professor, Pulmonary and Critical Care Medicine, Yale University School of Medicine

Dr. Akhtar does research for Eli Lilly.

Synopsis: *This secondary analysis of a multicenter, prospective, observational study of ICU transfusion practices reveals that packed red blood cell transfusions are associated with an increased risk of blood stream infections.*

Source: Shorr AF, et al. Transfusion practice and blood stream infections in critically ill patients. *Chest*. 2005; 127:1722-1728.

A GROWING BODY OF LITERATURE DESCRIBES AN association between packed red blood cell (pRBC) transfusions and nosocomial infections.[1,2] Shorr and colleagues set out to add to this by investigating the relationship between pRBC transfusions and bloodstream infections (BSI) in a large heterogeneous population of ICU patients. They performed a secondary analysis of a multicenter, prospective, observational cohort study (the CRIT trial)[3] to compare pRBC transfusion rates in patients who acquired a BSI in the ICU to those who did not.

The presence of BSI was defined by positive blood culture. The original study was conducted from August 2000 to April 2001 at 284 US ICUs. Adult patients with anticipated ICU length of stay > 48 hours were eligible. Patients admitted to pediatric, cardiac, cardiothoracic and neurology ICUs were excluded. Patients were also excluded for renal failure on dialysis or if they were prohibited from receiving transfusions. For this secondary analysis, patients with BSI at or within 48 hours of admission to the ICU were excluded. Usual demographics, diagnoses, severity of illness scores, antibiotics given, presence of central line or parenteral nutrition and number of pRBC transfusions were recorded. Patients were followed for 30 days or until death or hospital discharge (if within 30 days). Standard statistical analyses were used.

Of the 4892 patients in the CRIT trial, 3502 patients were enrolled in the current study. (The remainder were excluded for early death or early ICU discharge, not otherwise defined, or early BSI as defined above.) Of 3502 enrolled patients, 117 (3.3%) developed BSI after a median of 11 days in the ICU. Univariate analysis revealed that patients who developed BSI were slightly younger. The presence of a central line and the use of cephalosporins were associated with BSI but receiving parenteral nutrition was not. Seventy six percent (76%) of patients with BSI received pRBC transfusions compared to 48.7% of those without BSI. Multivariate analysis identified use of cephalosporins, severity of illness on day 3-4, and pRBC transfusion as being independently associated with BSI. The odds ratio for BSI with pRBC transfusion was 2.23 (95% CI, 1.43-3.52), with a clear dose-response relationship.

COMMENTARY

Shorr et al's report reinforces our increasing appreciation of the fact that pRBC transfusions are not benign. There are apparent immunomodulatory and immunosuppressive effects of transfusions that may lead to significant infectious complications such as BSI. These finding are consistent with prior data.[1,2]

The study is limited in ways that most secondary analyses are limited: it is retrospective, and it may include biases and confounders not accounted for in the adjusted analyses. Shorr et al did not have information on the patients' transfusion history prior to ICU admission, or on the transfusion of products other than pRBC. They also excluded about 25% of the original cohort for early death or early discharge from the ICU. BSI and/or transfusion in a portion of these latter patients could have markedly altered the results. Despite these problems, it is reassuring to note that the magnitude of the associations noted by Shorr et al correlate well with those reported in other studies. The presence of a dose-dependent response (that is, increased risk of BSI with increased numbers of pRBC transfusions) provides further support for the validity of their findings.

As we await prospective trials of transfusion practices designed to evaluate infection risk, I suggest that this preliminary but growing body of data combined with the evidence on safety of lower transfusion thresholds[4] is enough for all of us to continue to work to change our practices and limit use of pRBC transfusions. ■

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fusion and albumin administration are independent risk factors for the development of postoperative infections after colorectal surgery. *Can J Surg*. 2000;43: 212-216.
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Does a Negative CT Scan Rule Out Pulmonary Embolism?

ABSTRACT & COMMENTARY

By David J. Pierson, MD, Editor

Professor of Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington

Synopsis: *Meta-analysis of studies reporting follow-up of patients who were not anticoagulated after a negative CT angiogram showed that this test excludes pulmonary embolism as effectively as does conventional pulmonary angiography.*

Source: Quiroz R, et al. Clinical validity of a negative computed tomography scan in patients with suspected pulmonary embolism: a systematic review. *JAMA*. 2005;293:2012-2017.

In this meta-analysis, Quiroz and colleagues attempted to identify all English-language reports published since 1990 that included at least 3 months of follow-up in patients clinically suspected of having pulmonary thromboembolism (PTE), whose CT angiograms were negative and who did not receive anticoagulant therapy. The purpose was to determine the incidence of subsequent episodes of PTE and thus the negative likelihood ratio (NLR) and negative predictive value (NPV) of a negative CT scan in such patients.

Of 22 studies identified through PubMed, MEDLINE, EMBASE, the Cochrane Database, and other sources, 15 studies (3500 patients) met Quiroz et al's criteria for inclusion in the meta-analysis. Twelve of these studies used single-slice CT, 2 used multidetector-row CT, and 1 used electron-beam CT. Among the 3500 patients in the included studies, there were 36 episodes of PTE and 6 additional instances of deep venous thrombosis during the 3 to 12 months of follow-up. Fifteen deaths were attributed to PTE.

The overall NLR of VTE after a negative CT angiogram was 0.07 (95% confidence interval [CI], 0.05-0.11), and the NPV was 99.1% (95% CI, 98.7-99.5%). There was no difference between single-slice CT (NLR, 0.08; 95% CI, 0.05-0.13) and multidetector-row CT (NLR, 0.15; 95% CI, 0.05-0.43) with respect to ruling out PTE in the included studies. Quiroz et al conclude that the clinical validity of using CT to rule out PTE is similar to that of conventional pulmonary angiography.

COMMENTARY

The results of this study suggest that clinical outcome is not adversely affected if anticoagulant therapy is withheld based on a negative CT scan. The overall NPV for this test compares favorably with the NPVs previously reported for conventional pulmonary angiography, and is superior to those reported for negative- or low-probability ventilation-perfusion scans.

The principal limitation of CT scanning, which has delayed acceptance of this test as a gold standard for excluding PTE, is its questionable ability to detect isolated peripheral emboli. The clinical importance of this limitation is uncertain, however, particularly in the evaluation of patients who are ill enough to be admitted to the ICU. In the absence of severe co-morbidities such as obstructive lung disease or advanced congestive heart failure, it is doubtful whether sub-segmental PTE in the absence of more central clots would explain acute life-threatening illness. Although the present study found no difference in the performance of single-slice vs multiple-detector CT scanners, it is likely that the latest machines are better able to detect small peripheral emboli than their predecessors of 10 or 15 years ago.

I think we can now regard CT scanning as a second (and more readily available) gold standard in ruling out all but the tiniest pulmonary emboli—provided that equipment of relatively recent manufacture has been used, and the study is judged technically adequate by the interpreting radiologist. For patients in the ICU, there remains a role for ventilation-perfusion scanning in those few patients suspected of having PTE who cannot be given intravenous contrast material and who do not have serious concomitant cardiopulmonary disease. However, in most instances, a CT angiogram is the procedure of choice. If it is negative, pulmonary embolism

can be excluded confidently enough to obviate the need for anticoagulation. ■

Special Feature

Managing Bronchopleural Fistula During Mechanical Ventilation

By David J. Pierson MD, Editor

DEVELOPMENT OF A BRONCHOPLEURAL FISTULA (BPF) in a patient receiving mechanical ventilation is a serious complication that causes concern on the part of caregivers and often prompts a variety of changes in management. This essay explains what is meant by a BPF in this context, summarizes the possible ways it may occur in the ventilated patient, discusses the potential implications for the patient, and presents an approach to management based on both logic and the available evidence.[1,2]

What is a BPF?

With very few exceptions, detection of a pneumothorax in a mechanically ventilated patient should be followed promptly by insertion of a chest tube and the application of external suction. Evacuation of air from the pleural space is shown by bubbling through the water seal of the chest drainage device. If there is no direct communication between the airways and the pleural space, this bubbling ceases within an hour or two once the lung is fully reinflated. When the bubbling continues for 24 hours or more, a BPF may be said to be present. Most such leaks consist of only a few bubbles escaping through the water seal during the ventilator's inspiratory phase; although in a few cases the leak persists through both inspiration and expiration, and its volume may reach several hundred milliliters per breath.

Persistent bronchopleural air leak would be a more descriptive term, and would avoid confusion from the common implications of inflammation and suppuration associated with the word fistula in surgery and other settings. However, the term BPF has come to denote any air leak during mechanical ventilation, and its use has become so widespread that change is unlikely.

Bronchopleural fistula is a relatively uncommon complication, even in institutions managing large numbers of patients with the acute respiratory distress syndrome (ARDS) and other forms of severe acute respiratory failure. Of 1700 patients ventilated during one 4-year period at a major trauma center in the early 1980s, 39 (2%) developed a bronchopleural air leak that persisted at least 24 hours after chest tube insertion.[3] Tidal volumes and minute ventilations were considerably larger when that series was collected than those that are recommended today, but, as noted subsequently, whether this has reduced the incidence of BPF among ventilated patients, remains to be seen.

What are the Possible Causes of a BPF in the Ventilated Patient?

There are 3 main mechanisms that can result in a BPF. The first is airway disruption or alveolar rupture prior to the initiation of ventilatory support. Chest trauma is a common example, in which the airway injury can be either direct, as with laceration of the lung by fractured ribs or a penetrating object, or as a result of blunt injury with transient alveolar overdistension and rupture. Partial or complete rupture of a central airway is an uncommon but serious form of blunt deceleration injury, usually in patients with other major thoracic trauma such as great vessel injury or fractures of the first rib or scapula; the air leak in such cases is usually (but not always) massive, typically with persistent lung collapse despite pleural suction. Alveolar rupture can also occur during over-zealous mouth-to-mouth resuscitation or manual ventilation. The airway may be lacerated during attempted intubation, or the visceral pleura may be punctured during central line placement, thoracentesis, or tube thoracostomy.

The second potential mechanism leading to a BPF is direct laceration of visceral pleura or airway while the patient is receiving mechanical ventilation. Most commonly this occurs during attempted central line placement, but it can also complicate thoracentesis, tube thoracostomy, transbronchial biopsy or brushing, or other airway procedures.

Finally, BPF in the ventilated patient may follow *spontaneous* alveolar rupture, the latter either as a manifestation of the primary disease process (as in necrotizing pneumonia) or from inadvertent alveolar overdistension. A classic scenario is accidental intubation of the right mainstem bronchus, with atelectasis of the left lung and overdistension of the right lung leading to pneumothorax and subsequent BPF. Even without right bronchial intubation, overzealous manual ventilation or the use of high levels of positive end-expiratory pressure (PEEP) may distend alveolar regions to the point of

Table

Bronchopleural Fistula in the Ventilated Patient: 10 Principles of Management

1. Base ventilator management primarily on the patient's overall condition, rather than specifically on the BPF, since the latter will nearly always resolve as the former improves
2. Use the lowest number of mechanical breaths that permits acceptable alveolar ventilation
   - a Reduce both mean airway pressure and number of high-pressure breaths per minute
   - b Discontinue ventilatory support completely if possible, even if patient must remain intubated
   - c Consider pressure support or other form of partial (as opposed to full) ventilatory support
   - d Avoid respiratory alkalosis (PaCO2 < 40 mm Hg), in order to minimize minute ventilation
   - e Unless contraindicated (eg, by intracranial hypertension, ongoing cardiac ischemia, or serious arrhythmias), consider reducing minute ventilation even further, with permissive hypercapnia
3. Use low tidal volumes (eg, 6 mL/kg returned volume)
4. Minimize inspiratory time
   - a Keep inspiration:expiration ratio low (eg, 1:2)
   - b Use high inspiratory flow (eg, >70 L/min)
   - c Avoid end-inspiratory pause and inverse-ratio ventilation
   - d Use low-compressible-volume, non-disposable ventilator circuit, to reduce the tidal volume the ventilator must generate to produce target (corrected) tidal volume
5. Minimize total PEEP (both set PEEP and auto-PEEP)
6. Use the least amount of chest tube suction that maintains lung inflation
7. Explore positional differences, and avoid placing patient in positions that exacerbate the leak
8. Treat bronchospasm and other causes of expiratory airflow obstruction
9. Consider specific or unconventional measures only if the patient remains unstable, develops clinically harmful, uncorrectable respiratory acidosis despite above measures, or if the lung fails to completely re-expand
   - a Independent lung ventilation
   - b Surgical closure (not usually technically feasible)
   - c Endobronchial measures (see text)
10. Treat underlying cause of respiratory failure, maintaining nutritional and other support, with goal of discontinuing mechanical ventilation as soon as possible

Adapted from references 1 and 2

rupture, with subsequent BPF.

Does ventilation with lower tidal volumes reduce the incidence of BPF? Although the evidence is compelling that lung-protective, low-tidal-volume ventilation improves survival and other outcomes in patients with acute lung injury and ARDS, evidence that this approach leads to fewer instances of barotrauma, including BPF, is lacking. Boussarsar and colleagues[4] reviewed the findings of 11 studies (2270 patients) reporting the incidence of barotrauma in patients with ARDS. These studies varied with respect to patient population and ventilator management, and reported incidences of barotrauma that varied from zero to 76 percent. However, the authors found that end-inspiratory plateau pressure was the only ventilator management-related variable that correlated statistically with the occurrence of barotrauma. There were no significant correlations with tidal volume (either absolute or expressed in mL/kg), PEEP, or peak inspiratory pressure.

In an international study of 5183 mechanically ventilated adult patients with a wide variety of diagnoses, Anzueto et al[5] found no correlation between any ventilator setting or pressure measurement and the development of barotrauma. Despite the substantial and increasing number of other studies on ventilator management in ARDS, none to date has directly shown a relationship between how the ventilator is set and the subsequent development of barotrauma, including BPF.

In What Ways is a BPF Harmful?

The presence of a bronchopleural air leak following insertion of a chest tube could potentially create several important clinical problems. If the lung fails to completely re-expand, atelectasis and ventilation-perfusion mismatching may worsen hypoxemia; this is especially a problem with very large leaks (eg, several hundred mL per breath), or underlying pulmonary fibrosis or other condition causing increased elastic lung recoil. Loss of a large proportion of each delivered tidal volume via the BPF may impair expansion and ventilation of other lung areas, thus also contributing to ventilation-perfusion mismatching. Hypoxemia may also be worsened if a large air leak prevents the effective application of PEEP in patients with acute lung injury.

While it is logical to assume that a large BPF would compromise alveolar ventilation and impair CO_2 removal, this turns out not to be the case, at least in

ARDS. During its passage through the lung, the leaked volume actively participates in gas exchange-and in fact, may contain more CO_2 than the gas exiting through the endotracheal tube.[6] Thus, except in the case of a large proximal airway disruption, hypercapnia in the presence of a BPF is more a reflection of general gas exchange derangement than of the air leak per se.

Depending on the mode employed and how the ventilator is set, a large air leak can interfere with effective ventilatory support. In the assist-control mode, high pleural suction pressures can be transmitted to the central airways and cause factitious triggering. On the other hand, depending on the ventilator brand and the inspiratory flow cut-off threshold used in the pressure support mode, a large bronchopleural air leak may prevent the inspiratory phase from terminating.

Another way in which a BPF can potentially be harmful to the patient is by permitting airway organisms to reach the normally sterile pleural space, leading to clinical infection and further impeding closure of the leak. Although this is an obvious threat in patients with bacterial pneumonia, airway colonization without overt lung infection could also give pathogenic organisms access to the pleural space. As with other aspects of this topic, there is little or no experimental evidence to support or refute these statements.

How Should a BPF Be Managed?

In this era of evidence-based medicine, there is essentially no high-quality evidence in which specific interventions to reduce the volume of gas leaked through a BPF lead to better patient outcomes. Most of the literature consists of descriptions of techniques and anecdotal descriptions of immediate and short-term physiological changes. Common to much of this literature is a lack of convincing evidence that "conventional" ventilator management had been inadequate before the experimental intervention was used. The subjects of most published reports have been desperately ill patients who died in spite of the short-term physiologic improvements associated with the touted intervention.

Several reports have described the use of independent lung ventilation via a double-lumen endotracheal tube and two ventilators.[2] As with the use of this ventilatory technique in other settings, improved gas exchange has generally been achieved. The total reported experience is with only about a dozen patients. Placement and maintenance of a double-lumen endotracheal tube in a critically ill patient require considerable expertise, and the small lumens of these tubes make bronchial hygiene difficult in patients with lots of airway secretions.

Bronchopleural fistula is one of the primary clinical settings in which high-frequency jet ventilation has been used, although enthusiasm has waned and there have been few new reports of the use of this technique in the last 20 years.[2] Clinical experience with jet ventilation in patients without underlying lung disease, as in traumatic bronchial disruption or during tracheobronchial surgery, has generally been positive; however, both short-term and outcome results have been discouraging when BPF occurs in ARDS or other diffuse disease. High-frequency oscillatory ventilation has also been tried in BPF, but whether this technique offers any advantage over adjustments in conventional ventilation remains to be seen.

Several approaches have been reported for decreasing the size of the air leak through manipulation of the pleural drainage system, although again in very few patients.[2] Their application becomes progressively more difficult as the number of chest tubes increases in a given patient, and incomplete lung expansion on the side of the leak is a common problem. Plugging or otherwise sealing BPFs using the flexible or rigid bronchoscope (with laser therapy, cauterization, mechanical plugs, Gelfoam, tissue glue, and other things) has been reported in numerous case reports and small series.[2] However, only about 10% of the patients in these reports have had BPFs in the setting of ventilator-associated barotrauma; most of the reported experience is with BPFs following lung resection.

Although it is tempting to think that the ultimate therapy for a BPF would be direct surgical closure, this is seldom possible for technical reasons in settings other than acute traumatic tracheobronchial disruption. If the fistula is localized and associated with a necrotizing pneumonia, resection of the affected lobe may be feasible. A BPF after open lung biopsy or other procedure may be amenable to surgical repair. In most instances of barotrauma, however, the air leak is a manifestation of the severity of the underlying pulmonary disease, and direct suture or cautery of the leak or leaks is simply not technically feasible.

For most patients, ventilatory management in the presence of a BPF is the same as if the air leak were not there, provided that a functioning chest tube and pleural drainage system are in place. In the majority of instances, a BPF can be thought of as an indicator or manifestation of the severity of a patient's illness rather than as a condition requiring specific treatment. Sound general management is more important than any specific measure directed at the leak itself. The accompanying table provides a guide to management, based on patho-

physiology, the author's experience, and the available literature, that incorporates both general measures and an approach to specific manipulations for controlling the leak.[1,2] ■

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CME Questions

20. The most common category of missed opportunities in conversations involving end-of-life decision making involved which of the following?
a. Not answering family questions or following up on important statements
b. Not explaining the meaning of brain death
c. Not discussing opportunities for organ donation
d. Not defining palliative care
e. Identifying a pivotal family decision maker

21. Moderate-to-major risk for post-traumatic stress disorder has been shown to be present in what percentage of family members of critically ill patients 90 days after discharge or death?
a. 10%
b. 21%
c. 33%
d. 51%
e. 76%

22. What percentage of ICU patients in the study by Shorr et al of the relationship of transfusion to bloodstream infection developed bloodstream infections?
a. 1.6%
b. 3.3%
c. 6%
d. 13.3%
e. 25%

23. The odds ratio for bloodstream infection in a patient who received a packed red blood cell transfusion was
a. 0.5
b. 1.0
c. 2.2
d. 3.7
e. Not determined in this study

24. Which of the following is the implication of a negative CT angiogram in a patient clinically suspected of having pulmonary embolism?
a. The patient should have a conventional pulmonary angiogram.
b. The patient should be anticoagulated and re-evaluated in 24-48 hours.
c. The likelihood of pulmonary embolism over the next 3 months, if the patient is not anticoagulated, is at least 10%.
d. All of the above.
e. None of the above

25. Which of the following statements is true regarding a negative CT angiogram in a patient suspected of having acute pulmonary thromboembolism (PTE)?
a. The negative predictive value is as good as that for conventional pulmonary angiography.
b. It is not as specific for excluding PTE as a normal ventilation-perfusion scan.
c. The patient still has a 10% chance of having PTE if the scan was performed on a single-slice CT scanner.
d. The likelihood of a serious or fatal PTE during the next 3 months is at least 10% if the patient does not receive anticoagulant therapy.
e. None of the above.

Answers: 20 a; 21 c; 22 b; 23 c; 24 e; 25 a

CME / CE Objectives

After reading each issue of *Critical Care Alert*, readers will be able to do the following:

- Identify the particular clinical, legal, or scientific issues related to critical care.
- Describe how those issues affect nurses, health care workers, hospitals, or the health care industry in general.
- Cite solutions to the problems associated with those issues.

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Supplement to Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.

Antibiotic Treatment of Acute Lower Respiratory Infection

Acute lower respiratory tract infection (bronchitis) is the most common complaint bringing patients to the doctor in England, where it is estimated that 75% of these patients receive an antibiotic at the first visit. A new study from England defines acute lower respiratory tract infection as an uncomplicated acute illness, with cough as the primary symptom and at least one symptom or sign localized to the lower respiratory tract including sputum, chest pain, dyspnea, or wheeze.

In a recently published study, 807 patients were randomized to an information leaflet, no leaflet, immediate antibiotics, delayed antibiotics, or no antibiotics. Patients with chronic lung disease and those with suspected pneumonia were excluded. A total of 562 patients subsequently returned diaries regarding duration and severity of symptoms. Cough lasted a mean of 11.7 days after the initial visit. Antibiotics, either delayed or immediate, had no effect on cough duration (delayed, 0.75 days; 95% CI, -0.37 to 1.88; immediate, 0.11 days; 95% CI, -1.01 to 1.24). The information leaflet also had no effect on the main outcomes. There were slightly more return visits for patients who were not prescribed antibiotics and also for patients who received information leaflets. Patients with colored sputum were no better with antibiotics, and elderly patients were actually less likely to benefit from antibiotics than younger patients. The authors conclude that withholding or delaying antibiotics has no effect on the course uncomplicated lower respiratory tract infections and is an acceptable alternative to immediate antibiotic treatment. They also found that most patients are agreeable to this strategy as long as it is explained to them (Little P, et al. *JAMA*. 2005;293:3029-3035). An accompanying editorial reviews the data in the United States that suggests that most patients with presenting complaint of cough and diagnosis of acute bronchitis received an antibiotic in 2002. The editorial suggests that these antibiotics are generally of no value, and that patients will have 3 weeks of cough with or without antibiotic treatment. The editorial states ". . . physicians have no duty to fill patients' expectations for inappropriate care, such as prescribing antibiotics when they are not indicated. . ." and urges physicians to hold off on antibiotics for acute uncomplicated lower respiratory tract infections (Ebell MH. *JAMA*. 2005;293:3062-3064).

Similarly, the use of antibiotics in children with infective conjunctivitis may be unnecessary in the majority of cases. In a study also from England, 326 children aged 6 months to 12 years with the clinical diagnosis of conjunctivitis were randomized to chloramphenicol eye drops or placebo eye drops. The primary outcome was clinical cure at

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. Questions and comments, call: (404) 262-5416. E-mail: leslie.hamlin@thomson.com.

day 7. All children were followed for 6 weeks to identify relapse. Clinical cure by day 7 occurred in 83% of children in the placebo group, compared with 86% of children in the chloramphenicol group (risk difference 3.8%; 95% CI, -4.1% to 11.8%). Four percent of children in the chloramphenicol group and 3% of children in the placebo group had further conjunctivitis episodes within 6 weeks. Adverse reactions were rare and evenly distributed between the groups. The authors suggest that acute infective conjunctivitis in children does not require treatment with an antibiotic (Rose PW, et al. *Lancet*. 2005;366:37-43).

What to do with the Cox-2s

A Canadian advisory panel has opened the door for rofecoxib (Vioxx) to be reintroduced to the Canadian market. An expert panel met at the request of the Canadian government to review all Cox-2 inhibitors including celecoxib (Celebrex) which has remained on the market, rofecoxib (Vioxx), which was voluntarily withdrawn from the market in September of 2004, and valdecoxib (Bextra), which was withdrawn from both the Canadian and US markets in April 2005. The panel reviewed cardiovascular data from the 3 drugs and recommended that Celebrex stay on the market and Vioxx be allowed back on the market with appropriate labeling and patient warnings. They also voted to keep Bextra off the market because of lack of data on the drug's safety and efficacy. Bextra has also been associated with severe skin disorders, as well as cardiovascular disease. Cox-2 inhibitors, especially Vioxx, have been associated with increased cardiovascular mortality in several studies. The Canadian panel felt, however, that with appropriate patient selection, that the drug may be safely offered as an alternative for pain relief.

Can Mucomyst Prevent CIN?

The practice of using N-acetylcysteine (Mucomyst) to prevent contrast-induced nephropathy (CIN) in patients undergoing cardiac catheterization may be of no value according to new study from Brazil. Patients who were at low-to-moderate risk of CIN were randomized to N-acetylcysteine 600 mg orally twice a day for 2 days or placebo prior to coronary angiography or percutaneous coronary intervention. Only low osmolality ionic contrast medium was used in the procedures. Of the 156 patients enrolled, 16 patients developed CIN within 48 hours; 8 of 77 patients in the N-acetylcysteine group and 8 of 79 patients in the placebo group (P = 1.00). The mean serum creatinine was similar in both groups, and no difference was observed in the change in creatinine clearance between the N-acetylcysteine and placebo. The authors conclude that N-acetylcysteine does not prevent contrast-induced nephropathy in patients at low to moderate risk who are undergoing cardiac catheterization with low osmolality contrast medium. The authors recommend appropriate hydration and a small volume of contrast medium in patients at risk (Gomes VO, et al. *Heart*. 2005;91:774-778).

Benzodiazepines and Medicare Coverage

Congress is debating a controversial aspect of the Medicare Part D prescription benefit plan that excludes benzodiazepines from coverage. Mental health experts are lobbying to add coverage for the drug class which includes diazepam (Valium), alprazolam (Xanax), lorazepam (Ativan), and clonazepam (Klonopin). A bipartisan bill has been introduced to reverse the exclusion which would affect approximately 1.7 million low income seniors currently taking the drugs. Initially excluded because benzodiazepines are thought to be generally inappropriate for elderly patients, Congress may need to rethink the policy. Sponsors of the bill to reverse the exclusion include the AMA, the American Psychiatric Association, and the National Alliance for the Mentally Ill.

FDA Actions

The FDA has approved sildenafil citrate for the treatment of early-stage pulmonary hypertension. The approval was based on a priority review of a randomized, double-blind trial in 277 patients that showed that sildenafil significantly increased exercise ability from baseline, compared with placebo. Pfizer, which also markets sildenafil for erectile dysfunction under the trade name Viagra, will market the drug for this indication of the trade name Revatio.

The FDA has approved insulin detemir injection, a new long-acting subcutaneous insulin preparation. The drug is approved for adults who require once or twice a day administration of a basal insulin to control hyperglycemia. Insulin detemir is active for up to 24 hours, but is generally active in a relatively flat action profile from 2 to 14 hours. Insulin detemir will be marketed by Novo Nordisk as Levemir.