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INSIDE

Prosthetic Valve Thrombosis — Urgent Surgery or Thrombolysis?

ABSTRACT & COMMENTARY

By Andrew J. Boyle, MBBS, PhD

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

This article originally appeared in the March 2011 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Ethan Weiss, MD. Dr. Crawford is Professor of Medicine, Chief of Cardiology, University of California, San Francisco, and Dr. Weiss is Assistant Professor of Medicine, Division of Cardiology and CVRI, University of California, San Francisco. Dr. Crawford is a speaker for Astra-Zenica, and Dr. Weiss reports no financial relationships relevant to this field of study.*

Source: Keulerrs S, et al. Comparison of thrombolysis versus surgery as a first line therapy for prosthetic heart valve thrombosis. *Am J Cardiol*. 2011;107:275-279.

THROMBOSIS OF PROSTHETIC HEART VALVES IS ONE OF THE MOST FEARED complications of heart-valve replacement. Thrombolysis and emergency surgery are two therapeutic options for prosthetic valve thrombosis (PVT), each receiving a class II recommendation in the AHA/ACC guidelines. However, there are little data comparing these two options. Accordingly, Keuleers and colleagues retrospectively evaluated their center's experience of patients presenting with PVT over 20 years.

They identified 31 patients with PVT causing valvular obstruction. In 30 patients, this involved a mechanical valve; in the other patient, it was a bioprosthesis. The treating physician made the choice for thrombolysis vs. surgery. Success of thrombolysis was defined as complete, partial, or failure, depending on the degree of clinical improvement and the resolution of the valve leaflet obstruction. The majority of cases involved the mitral valve (n = 17), eight involved the aortic valve, and six involved the tricuspid valve.

Most patients (90%) presented with dyspnea, 42% had NYHA class IV symptoms, 33% had hemodynamic compromise on admission, and 13% presented with systemic embolization. In the major-

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ity of patients (61%), symptoms started more than 1 week prior to presentation. Importantly, sub-therapeutic international normalized ratio (INR) was present in 15 of 31 patients (48%); in nine patients, a temporary cessation of anticoagulation within 2 months had preceded the event.

Results: Thirteen patients were treated with thrombolysis; all received rtPA with unfractionated heparin. There was immediate clinical improvement in 92%; 62% showed complete resolution and 31% showed partial resolution of echocardiographic changes. The one patient who failed thrombolysis was referred for urgent surgery. However, complications were relatively common. Recurrent PVT was seen in four patients (31%) over the following 18 months. Furthermore, stroke occurred in one patient (8%), TIA in 8%, major hemorrhage requiring surgery in 8%, and peripheral emboli in 15%.

Eighteen patients underwent immediate surgery, with two peri-operative deaths (11%) and two recurrences of PVT (11%) over a median follow-up of 76 months. Surgical patients also experienced significant complications, including acquired ventricular septal defect (n = 1), sepsis and sternitis with ICU stay > 1 month (n = 2), the need for a permanent pacemaker (n = 1), and the need for repeat surgery (n = 1). The authors conclude that thrombolysis is an attractive first-line therapy for patients with PVT, with clinical outcomes comparing favorably with the standard surgical approach.

■ COMMENTARY

The morbidity and mortality from PVT are high, and clinicians must have a high index of suspicion for this condition. It is interesting to note that the majority of patients had symptoms for over 1 week prior to presentation, and many of these had documented sub-therapeutic INR values or interruption of anti-coagulant therapy. Patients with a prosthetic valve presenting with dyspnea, especially if anticoagulation has been sub-optimal, should be carefully evaluated for PVT.

Whereas surgery has been the traditional treatment for this condition, several series have now demonstrated that thrombolysis may be an effective alternative. However, it is important to note the high rate of complications with either option. This study is limited by its small sample size and retrospective observational nature; however, the results are congruent with other series. In the absence of randomized, controlled trial evidence to support one treatment over the other, the best option, when confronted with PVT, appears to be a careful evaluation of the individual patient, with consideration of the risks of thrombolysis or surgery in that patient. ■

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Should ICU Patients Be Bathed Daily with Chlorhexidine?

ABSTRACT & COMMENTARY

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

This article originally appeared in the March 2011 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.*

Synopsis: *This observational study found a large reduction in central line-associated bloodstream infections compared to historical controls for surgical ICU patients bathed daily with chlorhexidine gluconate-impregnated cloths.*

Source: Dixon JM, Carver RL. Daily chlorhexidine gluconate bathing with impregnated cloths results in statistically significant reduction in central line-associated bloodstream infections. *Am J Infect Control*. 2010;38:817-821.

THE AUTHORS SET OUT TO DETERMINE WHETHER DAILY BATHING of patients with 2% chlorhexidine gluconate (CHG)-impregnated cloths could reduce central line-associated blood-

stream infection (CLABSI) rate by at least 30% in a surgical ICU where CLABSI rates were above National Healthcare Safety Network averages. The study took place at a single, nine-bed surgical ICU in the United States; usual interventions for reduction of CLABSI (maximal sterile barrier precautions, appropriate protocols for dressing and tubing changes, daily review for necessity of lines, etc.) were already in place.

All patients admitted to this ICU during the study period and without a known sensitivity to CHG were included. A well-defined protocol was used by nursing staff for CHG bathing and the CHG-impregnated cloths were used after incontinence clean-up as well. The authors performed an initial 3-month observational study to determine effectiveness of their intervention and then extended the observational period and data-gathering for another 14 months. Historical control data (from the 17 months preceding the start of this study) were used for comparison. Any adverse reaction to CHG (such as rash) was recorded and data were collected on CLABSI rates (number of CLABSIs per number of central line days × 1000). Usual statistical methods were employed.

During the initial 3-month observational period, 144 patients were included and the CLABSI rate was found to be 3.17 compared to a historical control of 12.07 per 1000 central line days. (This historical control rate may have been derived from the 3 months immediately preceding the study, but this is not clear from the article.) Based on this statistically and clinically significant reduction, CHG bathing was continued with data collection and observation for another 14 months. For the entire 17-month study period, CLABSI rate was 2.1 compared to 8.6 per 1000 central line days for the 17 months immediately preceding the study, a statistically significant reduction of 76%. Inclusion and compliance were 100% and there were no adverse events.

■ COMMENTARY

Prevention of CLABSIs remains a key goal and initiative in most ICUs. The recommendation to consider bathing patients daily with CHG in areas with unacceptably high CLABSI rates, despite use of other preventive strategies, has been a part of recent national guidelines for prevention of hospital-acquired infections. Daily bathing with CHG is not yet advised as a first-line measure; the current study adds some credence to the idea that perhaps it should be in the future.

Bathing with CHG has been investigated as a means of reducing colonization with resistant organisms, postoperative/surgical wound infections, and other hospital-acquired infections. Available studies are, like the current one, usually small, single-center and often with design limitations such as absence of concurrent controls, though they generally have shown promising results. A 1-year long crossover trial of daily bathing with CHG with concurrent controls in two medical ICUs at a single hospital in 2007 found an approximately 60% reduction in bloodstream infections.[1] A more recent 6-month cohort study using historical controls in a trauma ICU found a 75% reduction in CLABSI and a large decrease in rates of colonization with methacillin-resistant *Staphylococcus aureus* (MRSA) or *Acinetobacter* species.[2] Other studies of bathing patients with CHG also suggest reduced colonization with MRSA and vancomycin-resistant enterococcus (VRE) in surgical and medical ICUs and perioperative settings and lower rates of CLABSIs in patients at long-term acute care hospitals.

As the authors of this investigation discuss, daily bathing of patients with CHG is a simple, benign, and likely cost-effective strategy. It is easily incorporated into current nursing care practices (perhaps even reducing bathing time since a rinse is not indicated). Even if "real-life" reduction of bloodstream infections is lower than that seen in the study, the cost-savings and potential decreases in morbidity and mortality could be considerable.

Thus, I agree with the authors' recommendation to consider implementation of daily bathing of ICU patients with CHG as an addition to other usual measures for placement and management of central lines such as: use of appropriate central line kits and checklists for insertion and care, maximal sterile barrier precautions for insertion, avoiding femoral site whenever possible, dressing and tubing changes, and cleaning/access of the ports and line per usual national guidelines, daily assessment of the need for the line and routine monitoring/audits of compliance, infection rates, and local resistance patterns. ■

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Early Aggressive Therapy for Myasthenia Gravis

ABSTRACT & COMMENTARY

By Michael Rubin, MD

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

This article originally appeared in the March 2011 issue of Neurology Alert. *It was edited by Matthew E. Fink, MD, and peer reviewed by M. Flint Beal, MD. Dr. Fink is Interim Chair and Neurologist in Chief, Department of Neurology and Neuroscience, Weill Cornell Medical College, New York Presbyterian Hospital, and Dr. Beal is Anne Parrish Titzel Professor, Department of Neurology and Neuroscience, Weill Cornell Medical College. Drs. Fink and Beal report no financial relationships relevant to this field of study.*

Synopsis: *Early plasmapheresis and high-dose intravenous corticosteroids may be as effective as conventional oral corticosteroid therapy in the treatment of myasthenia gravis.*

Source: Nagane Y, Suzuki S, Suzuki N, Utsugisawa K. Early aggressive treatment strategy against myasthenia gravis. *Europ Neurol* 2011;65:16–22 DOI: 10.1159/000322497.

CAN EARLY AGGRESSIVE THERAPY (EAT) IMPROVE THE LONG-TERM outcome of newly diagnosed myasthenia gravis (MG)? EAT was defined as a single plasma exchange, followed by 1 g intravenous methylprednisolone, immediately, and on the two subsequent mornings, followed by low-dose oral corticosteroids to maintain clinical improvement. To assess the efficacy of EAT, a retrospective analysis of patients with new-onset, generalized MG, was undertaken, and patients treated with the EAT protocol were compared to new-onset MG patients treated with high-dose oral prednisone alone, administered in a conventional fashion (10-20 mg per day and slowly increasing the dose on a weekly basis by 5-10 mg per day, to a maximum of 1 mg/kg per day). Patients were maintained on this dose until maximum improvement was appreciated. Prednisone then was tapered, on a monthly basis, by 20% of the previous daily dose. Pyridostigmine bromide was given as needed. Inclusion criteria required having received treatment for at least 1 year with continued follow-up, and availability of complete medical records, including clinical severity scores, comprising the quantitative MG (QMG) score or the quantified MG strength (QMGS) score. Exclusion criteria for EAT included having received plasma exchange, intravenous immunoglobulin, or high-dose methylprednisolone in the absence of myasthenic crisis; not having received maximum prednisone dosage due to side effects; or having received oral prednisone for uncontrolled symptoms. Statistical analysis was provided using the Mann-Whitney U test for continuous variables, the X^2 test for categorical variables, and the Wilcoxon signed-ranks test, with $P < 0.05$ considered statistically significant.

Among 410 new-onset MG patients seen at Hanamaki General Hospital and Keio University Hospital in Tokyo, Japan, between April 1995 and November 2009, 281 were diagnosed with generalized MG, of which 76 received EAT and 81 received high-dose oral prednisolone therapy. Of these, 49 EAT patients and 22 high-dose oral prednisolone patients satisfied entry criteria and served as the basis for this retrospective study. EAT patients demonstrated marked early improvement with lower subsequent oral prednisone dosage requirements compared to the high-dose prednisolone group, and minimal manifestations of disease were seen in the EAT group at 1 year and at final observation at 4.1 years. Both new-onset diabetes and moon facies were less frequent in the EAT group but additional short-term hospitalizations were required in this group for additional EAT to maintain remission. EAT may have some advantages over high-dose oral prednisone but these may be outweighed by the disadvantages of requiring repeated hospitalizations. As a retrospective study, the above findings need to be replicated in a prospective, randomized treatment trial comparing the two regimens.

■ COMMENTARY

Patients with generalized myasthenia also benefit from thymectomy, regardless of whether a hyperplastic or atrophic thymus is present.[1] Among 175 myasthenia patients who underwent trans-sternal thymectomy between 1990 and 2004, 128 had hyperplastic and 47 had atrophic thymus glands. Median time to remission was similar in both groups (4.8 vs. 4.9 years) but median time to clinical improvement was 1 year longer ($P = 0.005$) in the atrophic thymus group, which also demonstrated more ectopic thymus in the anterior mediastinum. Both hyperplastic and atrophic thymus tissue exhibited increased B-cell activating factor receptor, CD19, and CD21. Thymectomy is warranted for MG patients even in the presence of an atrophic thymus. ■

Reference

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And the Bands Played On

ABSTRACT & COMMENTARY

By Stan Deresinski, MD, FACP
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This article originally appeared in the December 2010 issue of Infectious Disease Alert. *It was peer reviewed by Timothy Jenkins, MD. Dr. Jenkins is Assistant Professor of Medicine, University of Colorado, Denver Health Medical Center. Dr. Deresinski does research for the National Institute of Health, and is an advisory board member and consultant for Merck, and Dr. Jenkins reports no financial relationships relevant to this field of study.*

Synopsis: *Physicians may not be able to rely upon their clinical laboratory to accurately report the neutrophil "band count."*

Source: Geissal ED, Coffey T, Gilbert DN. Clinical importance of the failure to detect immature neutrophils by an automated hematology analyzer. *Infect Dis Clin Pract*. 2010;18:374-378.

Knowledge of the presence of an increased proportion of band neutrophils (neutrophils with non-segmented nuclei) is believed by many clinicians to assist them in the diagnosis and management of some patients with suspected or known infection. Automated hematology analyzers, however, are not capable of providing a "band count." The identification of band neutrophils instead depends upon manual review of a blood smear. The need for such a review may be indicated as a result of the machine having detected a predetermined degree of abnormality, such as in the cell volume, cell number, or light scatter. This may be followed by a rapid visual scan of the smear and, then, if abnormalities are suggested by that review, by a more extensive examination with reporting, among other things, of the proportion of white blood cells (WBC) made up of bands and other earlier immature forms. Greissal and colleagues determined the overall sensitivity of this process in the detection of "bandemia" by comparing the proportion of smears with an increased proportion of band forms when processed with this screening procedure, or by routine visual examination of smears of all blood samples (i.e., the degree of sensitivity of flagging a possible abnormality by the automated analyzer).

In addition to other triggers, specimens were flagged if, in addition to other findings, the machine (Beckman Coulter LH 750) detected a total WBC < 3,000 cells/μL or > 30,000 cells/μL, or an absolute neutrophil count < 3,000 cells/μL or > 20,000 cells/μL. Blood from 101 consecutive patients with positive blood cultures was tested. The need for a quick visual examination of a smear was indicated for 87 of the patients, and complete visual examination confirmed bandemia in 42 of the 46 (91%) whose quick scan had indicated a need for full examination. The rapid exam was deemed to be negative and, therefore, not indicative of a need for a full examination in 41. Performance of a complete examination of these specimens found, however, that 20 had > 13% band forms on their peripheral blood smears. Thus, the rapid screen missed 20 of 41 (49%) patients with bandemia despite automated flagging. Complete smear examination of blood from the 14 patients whose specimens were not flagged found that 4 (29%) had > 13% band forms. Overall, using a conservative threshold for bandemia of > 13%, the standard process missed its detection in 24 of 101 (24%) of these selected patients.

The detection of bandemia is often of particular interest to the clinician evaluating patients who do not have leukocytosis, as was the case in 11 of these bacteremic patients with WBC 2,400-9,800 cells/ μL. Four of the 11 were not flagged, and three of these had elevated band counts. In the other seven, rapid scanning of the smear was felt to not indicate the need for a complete examination but, in fact, four had bandemia. Thus, the normal process failed to detect bandemia in seven of 11 bacteremic patients who did not have leukocytosis.

■ COMMENTARY

While pathologists seem to often disagree, clinicians commonly believe that measurement of the percentage of band neutrophils is often useful in patient management. While some published evidence suggests that knowledge of bandemia is not useful, others suggest that knowledge of this may provide useful clinical information. One setting in which this may be so is in emergency departments. A very recent evaluation of 289 bacteremic patients seen in an emergency department found that one-third had a normal temperature (36°C-38°C) and 52% had a normal WBC.[1] Of the 210 patients who had a "full differential" performed, 172 (82%) had > 5% bands. The band count was elevated by this criterion in 79% of those with a normal total WBC and 80% with a normal temperature. Fifty-two patients had both normal temperature and WBC; 28 of these had a "full differential" and 21 (75%) had bandemia. Thus, knowledge of bandemia may be helpful as a clue to the presence of sepsis in patients in whom other suggestive findings are absent.

Careful examination of blood smears in order to determine the proportion of neutrophil bands is, unfortunately, time consuming and, therefore, adds significantly to the labor costs of a laboratory procedure that is otherwise totally automated. It would be desirable if automated systems could accurately detect band neutrophils.

The machine used by Greissal et al, the Coulter LH 750, examines 8,000 leukocytes per sample and determines cell volume for each cell type by measurement of direct current impedance, the internal cell composition by measurement of conductivity by radio frequency opacity, and cytoplasmic granularity by measuring light scatter with a laser. Neutrophils of septic patients have increased mean volume, as well as a greater distribution of volumes and decreased light scatter. Measurement of mean neutrophil volume and neutrophil volume distribution width has been reported to be more sensitive and specific as indicators of the presence of sepsis than manual band count, total neutrophil count, and CRP.[2] That, however, cannot be true for the patients in whom bandemia is not detected.

Greissal et al have performed a careful analysis of the sensitivity of a standard laboratory algorithm, starting with an automated analyzer in the detection of bandemia and found it wanting in patients with bacteremia. This finding was perhaps of greatest importance to the clinician in patients without other common markers suggestive of sepsis, even with the use of a much higher threshold for bandemia (> 13%) than in the study by Seigel and colleagues (> 5%).

Thus, I believe that an accurate band count is of clinical value in the patient with suspected infection with a normal total WBC.[3] Another frequently encountered circumstance in which I, correctly or incorrectly, utilize the band count is in patients receiving corticosteroid therapy, which routinely

causes leukocytosis. The detection of bandemia may provide a mechanism for judging whether the elevated WBC observed in a patient receiving corticosteroids is due to the medication alone or whether it is a reflection, at least in part, of inflammation, including inflammation resulting from infection.[4] The leukocytosis associated with prednisone administration consists of mature neutrophils, and one investigation found that the presence of > 6% band forms is suggestive of the presence of infection.[4]

Thus, while our pathology colleagues may not like it, I believe there is good reason to request full visual examination of blood smears to determine the presence of bandemia in selected circumstances. ■

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Rasburicase: Clearing Uric Acid from the Tumor Lysis Syndrome

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This article originally appeared in the March 2011 issue of Clinical Oncology Alert. *It was peer reviewed by V.R. Veerapali, MD. Dr. Veerapali is Staff Clinician, INOVA Fairfax Cancer Center, Falls Church, VA. Drs. Ershler and Veerapali report no financial relationships to this field of study.*

Uric acid as a weak organic acid (pKa 5.8) is poorly soluble at physiological pH. It presence in serum is derived both from diet and endogenous biosynthesis, and it is excreted primarily by renal (75%) mechanisms under normal circumstances. Humans, and some other primates, differ from lower animals by the absence of urate oxidase (uricase), an enzyme that catalyzes the oxidation of uric acid into water-soluble allantoin. Allopurinol, still considered a mainstay in the management of hyperuricemia, blocks the activity of the enzyme xanthine oxidase and, thereby, decreases the risk of uric acid crystallization, particularly in the kidneys and joints.[1,2] The concept of introducing urate oxidase function to metabolize uric acid under conditions of hyperuricemia was first introduced in the 1970s in Europe. At that time, enzyme was purified from cultures of *Aspergillus flavus* (Uricozyme™), but impurities in the preparation were associated with untoward reactions (primarily allergic), although the effect on uric acid levels was clearly demonstrable.[3] Using recombinant technology, uricase cDNA (cloned from *Aspergillus flavus*) was introduced into a genetically modified strain of *Saccharomyces cerevisiae*, a process that allows a high level of purification. This recombinant form of uricase (rasburicase, Elitek™) has been approved by the FDA, initially for use in children with leukemia and lymphoma, but now also for adults at high risk for tumor lysis syndrome (TLS).[4,5]

The decision to approve rasburicase was initially supported by pediatric trials. Pui et al[6] treated 131 children and young adults with newly diagnosed leukemia or lymphoma for a planned 5 to 7 days, but found that initial treatment was met with rapid drop in uric acid. For those who presented with hyperuricemia (n = 65), the mean uric acid level decreased from 9.7 mg/dL to 1.0 mg/dL within 4 hours of treatment, and for those who did not have hyperuricemia the levels dropped from 4.3 mg/dL to 0.5 mg/dL. Furthermore, the toxicity was negligible, and no patients required dialysis. When compared to allopurinol in controlling hyperuricemia in pediatric cancer patients, rasburicase proved more effective in reducing pretreatment uric acid levels.[7]

Two trials in adults with leukemia and/or lymphoma also support the efficacy and safety of rasburicase. In the first, Bosley and colleagues reported on a multinational study conducted over three years (1999-2001) in which patients at high risk for TLS (both pediatric and adult) were treated with rasburicase 0.2 mg/kg either twice a day for the first 3 days if they were considered high risk for TLS, or once per day for all others.[8] After the first 3 days, all patients were continued through a course that extended up to 7 days (median 5 days). All patients responded to treatment. For adults with hyperuricemia (pre-treatment), the uric acid fell from 13.1 mg/dL to 0.3 mg/dL, whereas those who presented without hyperuricemia had their plasma uric acid levels fall from 4.9 mg/dL to 0.3 mg/dL. As with children, toxicity was minimal and no major adverse events were observed. Published in the same year, Coiffier et al treated aggressive non-Hodgkin's lymphoma adult patients (n = 100; median age = 57 years) who were considered at risk for TLS on the basis of both clinical (large tumor burden, adverse IPI score) and laboratory markers (elevated uric

acid, LDH, creatinine) with 0.2 mg/kg rasburicase for 3 to 7 days.[9] Of the 100 patients, 95 had normalization of uric acid levels and this occurred usually within the first 4 hours of treatment. None of the patients went on to develop TLS. Grade 3 hepatotoxicity was observed, but rapidly reversed, and the drug was discontinued in one patient for clinical reasons other than drug toxicity.

RECOMMENDATIONS: TLS PREVENTION AND TREATMENT

TLS is a life-threatening condition that occurs in patients with rapidly proliferating, highly chemosensitive tumors. The identification of high-risk patients, and early recognition of the syndrome, is of paramount importance. In this regard, consensus guidelines have been published for diagnosis and treatment.[4] Included in these recommendations are treatment with rasburicase for those considered at high risk, and especially for those who are diagnosed with TLS. The current recommended dose is 0.2 mg/kg/day administered intravenously with the first dose given prior to chemotherapy. Expectations are that uric acid levels will fall promptly, but repeated doses for 3-5 days have been commonly administered. Nonetheless, the recently published experience from a single institution suggests that one dose (at 6 mg) is often sufficient to prevent the occurrence of TLS for most patients.[10]

Hyperuricemia is only one manifestation of TLS, and treatment with rasburicase or allopurinol is itself insufficient to either prevent or treat the disorder. In this regard, aggressive hydration with the maintenance of high urine output and attention to electrolyte, renal, and cardiac function all assume critical importance. ■

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CME Questions

1. **In the prospective observational study by Dixon, et al, the addition of daily bathing in the ICU with 2% chlorhexidine-impregnated cloths to other unusual interventions for reducing central-line associated bloodstream infections (CLABSI) led to which of the following outcomes?**

a. Increased incidence of cutaneous candidal infections.
b. Increased nosocomial transmission of *C. difficile* within the ICU.
c. A greater than 75% reduction in CLABSI rate during the course of the study.
d. No significant change in the CLABSI rate during the course of the study.

2. **According to the study of 101 bacteremic patients by Geissal and colleagues, the use of an automated complete blood count analyzer followed by a quick visual examination of the blood smear:**

a. Accurately detected all patients with bandemia (an elevation of band forms > 13%).
b. Failed to detect bandemia in over half the bacteremic patients with normal total WBC counts compared to a complete manual review of the blood smear.
c. Failed to detect bandemia in nearly 25% of all bacteremic patients compared to a manual review of the blood smear.
d. B and C

3. **Based on the recent report by Krasuski et al of patients presenting with prosthetic valve thrombosis, treatment with thrombolysis led to:**

a. clinical outcomes similar to surgical therapy.
b. statistically significant reduction in complications compared to surgical therapy.
c. increased risk-adjusted hospital length of stay.
d. increased risk of 30-day and 90-day mortality compared to surgical therapy.

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. ■

CME Instructions

1. Read and study the activity, using the provided references for further research.

2. Log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. *First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice, or renewal notice.*

3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.

4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.

5. Once the evaluation is received, a credit letter will be sent to you. ■

AHC Media

Dear *Hospital Medicine Alert* Subscriber:

This issue of your newsletter marks the start of a new continuing medical education (CME) semester, and provides us with an opportunity to tell you about some new procedures for earning CME.

Hospital Medicine Alert, sponsored by AHC Media, provides you with evidence-based information and best practices that help you make informed decisions concerning treatment options. Our intent is the same as yours — the best possible patient care.

The objectives of *Hospital Medicine Alert* are:

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

The American Medical Association, which oversees the Physician's Recognition Award and credit system and allows AHC Media to award *AMA PRA Category 1 Credit*™, has changed its requirements for awarding *AMA PRA Category 1 Credit*™. Enduring materials, like this newsletter, are now required to include an assessment of the learner's performance; the activity provider can award credit only if a minimum performance level is met. AHC Media considered several ways of meeting these new AMA requirements and chose the most expedient method for our learners.

HERE ARE THE STEPS YOU NEED TO TAKE TO EARN CREDIT FOR THIS ACTIVITY:

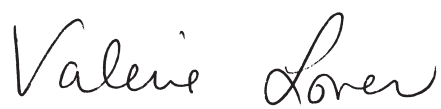
1. Read and study the activity, using the provided references for further research.
2. Log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. *First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice, or renewal notice.*
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the evaluation is received, a credit letter will be sent to you.

This activity is valid 36 months from the date of publication. The target audience for this activity is hospitalists, intensivists, and acute care clinicians.

If you have any questions about the process, please call us at (800) 688-2421, or outside the U.S. at (404) 262-5476. You can also fax us at (800) 284-3291, or outside the U.S. at (404) 262-5560. You can also email us at: customerservice@ahcmedia.com.

On behalf of AHC Media, we thank you for your trust and look forward to a continuing education partnership.

Sincerely,



Valerie Loner
Continuing Education Director
AHC Media