Hospital Peer Review

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Hospital Peer Review is a monthly newsletter sponsored by the Rural Healthcare Quality Network to alert Critical Access Hospitals regarding findings from the Peer Review Program. Summarized are a few of the key findings and best practices that would be helpful for other critical access hospitals to be knowledgeable about. This newsletter is edited by Myron Bloom, Medical Director and he can be reached at drmbloom@msn.com.

Looking beyond the core measure – WHO NEEDS BLOOD CULTURES

The National Hospital Quality (Core) Measures developed by the Center for Medicare and Medicaid Services (and adopted by JCAHO) were to promote a paradigm shift to evidence-based care from anecdotal experience based practice. The initial Pneumonia Blood Culture Core Measure has recently been refined to read:

> *PN-3a Blood Cultures Performed Within 24 Hours Prior to or 24 Hours After Hospital Arrival for Patients Who Were Transferred or Admitted to the ICU Within 24 Hours of Hospital Arrival and PN-3b Blood Cultures Performed in the Emergency Department Prior to Initial Antibiotic Received in Hospital- (Discharges 10/01/2008-03/31/2009)*

So, the revised performance measure **does not** require blood cultures for all community acquired pneumonia patients, but **if** a culture is done, it should be done prior to administration of the first dose of antibiotics received in the hospital in order to meet the intent of the measures, as well as, being clinically relevant. The guidelines recommend that pretreatment blood cultures should be obtained from hospitalized CAP patients who are admitted to the Intensive Care Unit, have cavitary infiltrates, pleural effusion, leukopenia, asplenia, chronic severe liver disease, have a positive pneumococcal urinary antigen test (UAT), or have active alcohol abuse, citing as the reference *Clinical Infectious Disease,* 1;44 Supplement S28-S31, March 2007.

Although recommendations for blood cultures are controversial, due to the overall low yield, they can have a significant impact on the care of an individual patient and are important for epidemiologic reasons (changing antibiotic susceptibility patterns). The Joint IDSA/ATS Guidelines on the Management of Community-Acquired Pneumonia (CAP) in Adults recommend that certain patients with CAP should be cultured for pathogens that would alter decisions regarding empirical therapy, when the presence of these pathogens is suspected. However, doing blood (and urine) cultures after antibiotics have been administered decreases the yield by as much as 50%.

Studies have shown that annually there are between 500,000 to one million cases of sepsis and severe sepsis in American hospitals with a mortality rate between 15 and 30 percent, or as many as 200,000 deaths. Other patients will suffer permanent organ damage. Therefore, any patient admitted with severe sepsis should have two sets of peripheral blood cultures. Because the differentiation between bacteremia and a contaminated central line is problematic, blood cultures drawn through a central line are of questionable significance. However, potential sites of infection, especially central lines, should also be sampled.

What is some of the evidence about doing blood cultures in CAP?

A retrospective chart review was conducted at a community teaching hospital of ED patients 18 years old or older, with an admission and discharge diagnosis of pneumonia during calendar years 2001-2002. Of 684 eligible patients, 23 (3.4%) had true positive blood cultures and all were sensitive to the empiric antibiotics. Three risk factors were associated with positive blood cultures:

- ✓ oxygen saturation < 90%,
- ✓ serum sodium < 130, and
- ✓ respiratory rate > 30 breaths/min.

They found that positive blood culture rates were low and did not affect the routine clinical management of pneumonia patients. [Source: Benenson RS, Kepner AM, Pyle DN, Cavanaugh S. Selective Use of Blood Cultures in Emergency Department Pneumonia Patients. *Journal of Emergency Medicine.* 2007 July;33(1):1-8.]

A retrospective cohort study, from Boston University Medical Center, examined the utility of routine performance of blood cultures in 289 immunocompetent adults aged 22-100 (mean, 56.6) hospitalized with an ED and discharge diagnosis of CAP. The study excluded patients with a history of hospital admission within seven days prior to presentation, nursing home residence, or suspected aspiration pneumonia. All were treated with empiric intravenous ceftriaxone and oral azithromycin, or levofloxacin in penicillin-allergic patients. Blood cultures were true-positive in 13 patients (4.5%) and false-positive in 13 patients (4.5%). Eleven of the true-positive blood cultures yielded S. pneumoniae and two yielded H. influenzae. The empiric antibiotic regimen was judged to be appropriate in all 13 patients with true-positive blood cultures, and a change in antibiotics based on blood culture results was documented for only one. The direct laboratory cost for the processing of negative blood cultures was $6,660. The potential savings associated with switching to a narrower-spectrum antibiotic based on blood culture results was only $170. [Source: Ramanujam P, Rathlev NK. Blood Cultures Do Not Change Management in Hospitalized Patients with Community Acquired Pneumonia. *Academic Emergency Medicine.* 2006 July;13(7):740-745.]

Brigham & Women's Hospital and Beth Israel Deaconess Medical Center authors prospectively examined findings in 414 adults presenting to an urban university ED with pneumonia who had blood cultures performed prior to initiation of empiric antibiotics. The blood cultures were positive in 29 patients (7%). Cultures prompted broadening of antibiotic therapy due to resistant organisms in four cases (1%) and in eleven cases (2.7%), cultures prompted a narrowing of antibiotic therapy. Empiric therapy was unchanged in the remaining patients. In a sensitivity analysis, it was estimated that blood cultures would need to be performed in 125 patients with pneumonia to identify one patient with a resistant infection. Their conclusion was that the findings do not support the practice of routinely performing blood cultures for patients presenting with pneumonia. [Source: Kennedy M, Bates DW, Wright SB, et al. Do Emergency Department Blood Cultures Change Practice in Patients with Pneumonia? *Annals of Emergency Medicine. 2005 Nov;*46(5):393-400.]

So besides pneumonia patients destined for the intensive care unit, who else might benefit form blood cultures?

A study from Harvard Medical School derived (in 2,466 patients) then validated (in an additional 1,264 patients) a prediction rule for blood culture testing utility. Blood cultures were true-positive in 8.3% of the derivation patients and 8.0% of the validation patients. The independent predictors from the regression model were divided into "major" or "minor" criteria. A blood culture was indicated if at least one "major" or two "minor" criteria were present; otherwise patients were classified as "low risk." Major predictors included suspected endocarditis (3 points), a temperature above 39.4C (103F) (3 points), and an indwelling vascular catheter (2 points). Minor predictors each scored 1 point: temperature 101-102.9 degrees F, age >65, chills, vomiting, hypotension (SBP < 90), neutrophil % >80, WBC >18k, bands >5%, platelets <150k, suspicion of a urinary track infection, or creatinine >2.0. Patients were divided into groups at low (0-1 points), moderate (2-5 points), and high risk (6 points or more) for bacteremia. Rates of bacteremia in the derivation and validation patients of the three groups were 0.6% and 0.9%, 6.8% and 9.1%, and 25.6% and 15.4%, respectively. If blood cultures were obtained only in patients with one major or two or more minor criteria, the prediction rule would have had a sensitivity of 98% in the derivation and 97% in the validation patients, a specificity of 29% in both groups, and a negative predictive value of 99% resulting in a 27% reduction in the use of blood cultures. This would have missed positive cultures in seven patients but treatment would have been influenced in only two of the seven. [Source: Shapiro NI, Wolfe RE, Wright SB, et al. Who Needs a Blood Culture? A Prospectively Derived and Validated Prediction Rule. *Journal of Emergency Medicine*. 2008 Oct;35(3):255-264.]

How about Pyelo?

A prospective study involving 642 patients with febrile urinary tract infection (UTI) found antimicrobial pretreatment (OR, 3.3), an indwelling urinary catheter (OR, 2.8), and malignancy (OR, 2.7) to be independent risk factors for bacteremia with an uropathogen that was <u>not</u> recognized or cultured in the urine. [Source: van Nieuwkoop C, Bonten TN, Wout JW, et al. Risk Factors for Bacteremia with Uropathogen Not Cultured from Urine in Adults with Febrile Urinary Tract Infection. *Clinical Infectious Diseases.* 2010 June 1;50(11):e69-72.]

Authors from the University of Pennsylvania reviewed the English-language literature finding only four research articles addressing whether the management of pyelonephritis is altered by obtaining blood cultures. In one prospective study of 583 adult women with clinical symptoms of acute, uncomplicated, community- acquired pyelonephritis, 2.4% had discordant blood and urine cultures, and blood cultures were used to determine oral antibiotic therapy in 2% of the women with a negative urine culture. In a retrospective study of 194 patients aged 4-91 with a discharge diagnosis of pyelonephritis, 29% of blood cultures were positive but none prompted a change in empiric antibiotics. In another retrospective study of 338 patients with a discharge diagnosis of pyelonephritis and a positive urine culture, blood cultures were positive in 18% of those in whom they were performed. There were three true-positive blood cultures that did not match urine culture results, and there was no change in initial antibiotic therapy. In a final retrospective study of non-pregnant women admitted for pyelonephritis, the blood culture positivity rate was 36% among the 64 patients undergoing such testing with the blood culture results matching urine culture results in all but two cases (women with E. coli bacteremia but a negative urine culture). In view of the high bacteremia rate, these authors advocated routine blood cultures for pyelonephritis but did not address the influence of blood cultures on patient management and this would suggest that blood cultures do not alter the management of immunocompetent non-pregnant adults with uncomplicated acute pyelonephritis. [Source: Mills AM, Barros S. Are Blood Cultures Necessary in Adults with Pyelonephritis? *Annals of Emergency Medicine.* 2005 Sep;46(3):285-287.]

So blood cultures are strongly indicated in urinary tract sepsis with outpatient antibiotic failures, indwelling urinary catheters, and cancer, as well as for the immune-incompetent or pregnant ladies with pyelonephritis.

What about anaerobic cultures?

To determine the number of patients with bacteremia and fungemia and to evaluate the utility of routine anaerobic blood cultures as part of the work-up for suspected bacteremia, a retrospective review of microbiology data followed by selective chart review at a university-affiliated Veterans Affairs Medical Center was conducted for the blood cultures drawn from January 1, 1994 to December 31, 1996, and the number of anaerobic, aerobic, and fungal isolates. There were 6,891 sets of blood cultures processed through the laboratory, resulting in 1,626 patients with positive results. Anaerobic isolates were recovered from 36 patients (2.2%) in 48 bottles. Aerobic isolates were recovered from 1,550 patients (95.3%), and fungal isolates were recovered from 40 patients (2.5%). Seven patients (0.4%) had true anaerobic bacteremia and all had an obvious source of anaerobic infection that was known or suspected before the cultures were drawn. Antibiotic changes were made in four of these patients after the positive anaerobic results were known, resulting in clinical improvement in one patient. They concluded that anaerobic blood cultures rarely results in clinically important diagnostic or therapeutic benefits, based on the low incidence of anaerobic bacteremia in patients who are not at increased risk, and therefore anaerobic blood cultures should only be selectively ordered in patients at risk for anaerobic infections. [Source: Ortiz E, Sande MA. Routine Use of Anaerobic Blood Cultures: Are They Still Indicated? *American Journal of Medicine.* 2000 Apr 15;108(6):445-447.]

Routinely using half the collected blood volume for getting an anaerobic culture should be challenged. The records of 61 patients who had an anaerobic isolate recovered only from an anaerobic bottle were examined to define clinical settings in which such isolates occur. Fifty-six patients (92%) had clinically important isolates, but the source of infection was obvious at the time of culture in 47 of the 56 (84%). Of the 56 patients, 36 (64%) had abdominal signs and symptoms, including 12 with recent abdominal surgery. Of nine patients without an obvious source of infection, six were on high-dose steroids. Relative yields were compared for three methodologies: (i) one aerobic bottle and one anaerobic bottle (5 ml to each) for all blood cultures; (ii) two aerobic bottles (5 ml to each); or (iii) two aerobic bottles plus an extra anaerobic bottle (only for clinically suspected anaerobic sepsis) (5 ml to each). The third approach had the highest yield (475 isolates) because the routine use of two aerobic bottles recovered more Candida spp., Enterobacteriaceae, and non-fermenters than did the first approach (448 isolates) ($P < 0.02$), and clinically directed culturing for anaerobes would recover anaerobes missed with the second approach (458 isolates). The data suggested that the use of two aerobic bottles with more selective culturing for anaerobes could increase the number of clinically relevant isolates by at least 6% compared with the current practice of inoculating an aerobic bottle and an anaerobic bottle with equal volumes of blood. [Source: Morris AJ, Wilson ML, Mirrett S, et al. Rationale for Selective Use of Anaerobic Blood Cultures. *Journal of Clinical Microbiology* 1993 Aug;31(8):2110-2113.]

Blood cultures are useful in Neutropenic Fever

Blood cultures in management of high-risk neutropenic fever was evaluated by an analysis of 2,520 blood cultures obtained from 126 consecutive patients with neutropenic fever between January 2000 and June 2004 (265 episodes of neutropenic fever, each lasting ≥10 days) in patients being treated for acute lymphoblastic or myeloid leukemia or autologous stem cell transplantation for other hematological malignancies. The cultures yielded bacterial pathogens in 219 (8.7%) instances (gram positive in 78.5% of these instances; gram negative in 21.5%) and fungal pathogens in 13 (0.5%). The rates of fungal and gram-positive bacterial isolates were significantly increased in patients with central venous catheters. The positivity rate was significantly higher for cultures obtained before antibiotic initiation than for those obtained afterward (14.3% vs. 7.0%). In half the positive blood culture cases, the antimicrobial regimen was modified accordingly, most often after detection of coagulase-negative staphylococci, *Pseudomonas,* or yeasts. [Source: Hummel M, Warga C, Hof H, et al. Diagnostic Yield of Blood Cultures from Antibiotic-Naïve and Antibiotically Treated Patients with Haematological Malignancies and High-Risk Neutropenia. *Scandinavian Journal of Infectious Diseases.* 2009;41(9):650-650.]

And dialysis patients

Bacteremic infections are a major cause of mortality and morbidity in chronic hemodialysis patients. A prospective study was carried out involving 988 adults on chronic hemodialysis at 19 French dialysis to determine the incidence of and risk factors for bacteremia. The incidence of bacteremia was 0.93 episode per 100 patient months. Significant risk factors for bacteremia were: vascular access (catheter versus fistula RR=7.6); history of bacteremia (2 or more events versus none: RR=7.3); and immunosuppressive therapy (current versus not: RR=3.0). Catheters, especially long-term implanted catheters, were found to be the leading risk factor of bacteremia in chronic hemodialysis patients. Staphylococcus aureus (n=20) and coagulase-negative staphylococci (n=15) were responsible for most of the 51 bacteremic episodes recorded, but the trend toward recurrence of bacteremia was not associated with chronic staphylococcal nasal carriage. [Source: Hoen B, Paul-Dauphin A, Hestin D, Kessler M. EPIBACDIAL: a Multicenter Prospective Study of Risk Factors for Bacteremia in Chronic Hemodialysis Patients. *Journal of the American Society of Nephrology.* 1998 May;9(5):869-876.]

And what about blood cultures for ambulatory patients?

In 2001 and 2002, 3,102 sets of cultures were drawn from 1,732 ambulatory outpatients in the Calgary Health Region (a fully integrated, publicly funded health system serving a population of 1 million, annual rate = 89.4 per 100,000 population). Significant isolates were identified from 73 (2.4%) sets of cultures from 51 patients, including *Escherichia coli* in 18 (35%) and seven (14%) each of *Staphylococcus aureus* and *Streptococcus pneumoniae*. Of the 24 patients with an aerobic Gram-negative rod bacteremia, a urine culture was not done in seven cases, had discordant (negative) results in seven cases, and was concordant (positive with identical isolate) in 10 cases. The one patient with an extended spectrum beta-lactamase producing *E. coli* had a concordant urine sample. The one patient with *Pseudomonas aeruginosa* bacteremia had no other cultures collected. In eight (16%) patients with positive cultures, the anaerobic bottle was independently positive and the organisms were all facultative anaerobes (*E. coli* in five and one each of *Klebsiella pneumoniae*, *Proteus mirabilis*, and *S. aureus*). Seven cases of urinary tract infections had positive blood cultures and negative urine cultures as a consequence of antibiotic therapy before the collection of urine cultures. The anaerobic bottle was the only positive bottle in 8/1732 (0.5%) patients cultured, but in 5 of the 6 cases, the diagnosis was urinary tract infection and the etiology may have been available from urine cultures. All isolates of *S. aureus* were methicillin susceptible. The conclusion was that blood cultures drawn in outpatient settings are not commonly positive (2.4%) and of questionable cost effectiveness. [Source: Laupland KB, Church DL, Gregson DB. Blood Cultures in Ambulatory Outpatients *BMC Infectious Diseases.* 2005, 5:35doi:10.1186/1471-2334-5-35.]

How much blood for blood cultures in children?

Investigators in Australia placed laminated posters in all blood-collection areas with the recommended blood volumes and culture set by age (≥0.5 mL for infants younger than 1 month, >1.0 mL for children aged 1 to 36 months, and >4.0 mL for patients older than 36 months) and compared the results of 1,358 blood cultures from 783 children taken before (1,067) and after (291) implementation. They found cultures with adequate blood volume were significantly more likely than those with inadequate volume to yield true positive cultures (5.2% vs. 2.2%). [Source: Connell TG, Rele M, Cowley D, et al. How Reliable is a Negative Blood Culture Result? Volume of Blood Submitted for Culture in Routine Practice in a Children's Hospital. *Pediatrics.* 2007 May;119(5):891-896.]

In conclusion, let's be more selective when ordering blood cultures!

Evidence Based Clinical Indicators for Drawing Blood Cultures

The guidelines and the clinical evidence recommends that pre-treatment blood cultures should be obtained from hospitalized CAP (or other sepsis) patients who are admitted to the Intensive Care Unit, or have:

- ✓ Cavitary infiltrates,
- ✓ Pleural effusion,
- ✓ Leukopenia,
- ✓ Chronic severe liver disease,
- ✓ Asplenia,
- ✓ Pneumococcal urinary antigen test (UAT),
- ✓ Active alcohol abuse,
- ✓ Oxygen saturation < 90%,
- ✓ Serum sodium < 130, and/or
- ✓ Respiratory rate > 30 breaths/min.

For all types of patients with one MAJOR predictor such as:

- ✓ Neutropenic fever,
- ✓ Suspected endocarditis,
- ✓ Temperature above 39.4C (103F),
- ✓ Indwelling vascular catheter, or
- ✓ Dialysis.

Or two or more MINOR predictors:

- ✓ Temperature 101-102.9 degrees F,
- ✓ Hypotension (SBP < 90),
- ✓ WBC >18k,
- ✓ Neutrophil % >80,
- ✓ Bands >5%,
- ✓ Platelets <150k,
- ✓ Creatinine >2.0
- ✓ Urinary tract infection,
- ✓ Chills,
- ✓ Vomiting, and/or
- ✓ Age >65.