

Repeat Blood Cultures after 3 Days in Patients with *Staphylococcus aureus* bacteremia

Victor L. Yu, M.D.

Background

The differentiation from *Staphylococcus aureus* bacteremia versus endocarditis has been an important clinical problem for many decades. The accepted risk factors for endocarditis include origin from the community (as compared to acquisition in the hospital), presence of preexisting heart disease especially valvular heart disease, intravenous drug use, and history of prior endocarditis. In the absence of typical Oslerian manifestations (such as changing murmur, splenomegaly, embolic lesions), the clinical diagnosis can be challenging. And, in the current era of widespread empiric antibiotics, Oslerian manifestations are rarely seen in U.S. hospitals today.

New Data

In a large-scale observational, multi-collaborative study involving over 500 consecutive patients, persistent bacteremia during the course of therapy was significantly associated with presence of endocarditis, both by univariate and by multivariate analysis. Likewise, mortality was also significantly associated with persistence of bacteremia. Persistent bacteremia occurred significantly more often in endocarditis caused by MRSA compared with MSSA. It should be noted that persistence of bacteremia was only validated for positive blood cultures following three days of initiation of antistaphylococcal antibiotic therapy.

Recommendation

We now recommend that in all patients with *S. aureus* bacteremia, repeat blood cultures should be drawn 3 full days after initiation of anti-staphylococcal antibiotic therapy. If these blood cultures yield *S. aureus*, the likelihood of underlying *S. aureus* endocarditis becomes high, *even if echocardiography is unrevealing*. We have encountered four patients with persistent bacteremia despite three days of antistaphylococcal antibiotic therapy in which both transthoracic and transesophageal echocardiogram were negative. Subsequent autopsy or open-heart surgery showed that these patients did indeed have endocarditis.

Subsequent blood cultures do not have to be drawn unless there is evidence of metastatic infection, hypotension, persistent fever or clinical signs of antibiotic failure. Note that this dictum refers only to *S. aureus*. In general, blood cultures do not need to be repeated for other etiologies of bacteremia/fungemia unless there are clinical indications that therapy is inadequate.

For all patients who have persistent bacteremia three full days after initiation of antistaphylococcal therapy, we would recommend changing the patient's anti-

staphylococcal regimen to a more “potent” regimen, for example, 3-drug therapy with a cell active agent, nafcillin for MSSA or vancomycin for MRSA, low dose gentamicin, and rifampin. It is also important to advocate surgical removal of the infected foci (intravascular catheter or infected heart valve). Note that vancomycin has been shown to be inferior as monotherapy for MSSA bacteremia in numerous studies. The comparative efficacy of linezolid, daptomycin, and quinopristin/dalfopristin (Synercid) has not been evaluated in controlled trials of humans, but combinations of all three agents *in vitro* with rifampin and gentamicin show additivity as determined by susceptibilities performed by E-test or kill curves studies, although the numbers of MSSA or MRSA isolates tested were small.

REFERENCES

1. Chang FY, MacDonald BB, Peacock JE Jr, Musher DM, Triplett P, Mylotte JM, O'Donnell A, Wagener MM, Yu VL. A prospective multicenter study of *Staphylococcus aureus* bacteremia: incidence of endocarditis, risk factors for mortality, and clinical impact of methicillin resistance. *Medicine* 2003; 82:322-332.
2. Chang FY, Peacock JE Jr, Musher DM, Triplett P, MacDonald BB, Mylotte JM, O'Donnell A, Wagener MM, Yu VL. *Staphylococcus aureus* bacteremia: recurrence and impact of antibiotic treatment in a prospective, multicenter study. *Medicine* 2003; 82:333-339.