

Sepsis: molecular or mass spectrometry-based diagnosis

Bacteremia and sepsis are severe infections for which adequate early antimicrobial therapy is very important. Rapid microbiological results are essential to determine the etiological agent and prompt antibiotic susceptibility testing is mandatory to ensure that effective antimicrobial therapy is given. Blood cultures remain currently the method of choice for the microbiological documentation of sepsis. However until recently, the major impact was the announcement of the result of Gram examination of bacteria isolated from blood, which allows to adapt or modify the empirical treatment. The bacterial identification and susceptibility testing had little impact because of the delay (1-3 days) in obtaining these results. Now the reduction of the turnaround time for the identification of a strain growing in blood culture bottle is possible thanks to MALDI-TOF on bacterial pellet allowing identification in < 1h. Moreover to accelerate the antibiotic susceptibility results, the same pellet can be used for susceptibility testing by means of an automated VITEK2 (bioMérieux) or, when positive for *S. aureus*, by MRSA GeneXpert PCR that gives methicillin susceptibility in < 1 hour. On such bacterial pellet various molecular tests including microarray can be done. When the patient was previously treated with antibiotics or for fastidious or intracellular bacteria, the use of pathogen-specific real-time PCR or broad-range PCR directly on the blood might be promising. Thus, in the context of endovascular infections such as endocarditis, *Coxiella burnetii*, *Bartonella* sp. and *Tropheryma whipplei* may be successfully detected in 20 to 50% of cases. But despite many technical progresses for the nucleic acid amplification and detection of amplified products, there is still a limitation of molecular approach to start with large volume of blood analyzed. Indeed, blood still represents the biggest challenge in the implementation of molecular techniques for the direct diagnosis of sepsis. Thus, direct detection by molecular approaches or indirect detection after a culture step may help reducing the turnaround time for diagnosis of sepsis.