Sepsis: Does the Bug Matter?

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In this issue of the journal, Turan et al provide a nice study looking at this problem.[1] They find that whether sepsis was due to Gram positives or Gram negatives does look not to play a role. Indeed, the reaction of the host, who develops or not the acute (and excessive?) inflammatory process targeted by the micro-organism is an important determinant of death. This is the rationale of the concept of severe sepsis. However, the type of micro-organism plays probably a role as well, but many more patients would be needed to demonstrate it. In animal models,[2] drugs like steroids or anti-inflammatory agents have very different effects according to the micro-organism. Anti-INF, for example does not work in pneumoccal experimental sepsis. Meningococcal sepsis, like purpura fulminans seems also to be different from other kind of sepsis, with an extremely high bacterial inoculum in the blood, and active systemic coagulation with thrombosis and distal ischemia.

In human studies, drugs like activated protein C or Tissue Factor Pathway Inhibitor (Tfpi) seem to work more clearly in patients with pneumonia, in particular when due to *Pneumococcus pneumoniae*.[3,4] This is the rationale for the ongoing study of Tfpi in community acquired pneumonia. Whether the acute inflammatory process is activated by virulence factors or the whole bacteria is likely to be an important factor. The best clinical examples should be toxic shock syndrome, and severe pneumonia due to community acquired *Staphylococcus aureus* harbouring the Panton Valentine Leucocidin (PVL). For those reasons, some authors proposed recently to target new therapies on specific mode of activation of the inflammatory process.[5] Drugs like anti- TNF or activated protein C should be administrated only if the pathophysiological process can be demonstrated at inclusion in the trial with convincing biological markers.

Very logically, inappropriate initial antibiotic therapy is an important factor as demonstrated again by the authors of the paper. The choice of antibiotic, both initially (then often empiric therapy) and a few days later, when bacteriological information is back is a key factor of success.[6] Infections diseases specialists or clinical microbiologists could be of paramount help for intensive care specialists for appropriate therapy of severe sepsis.

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