29th ECCMID Amsterdam, Netherlands 13 – 16 April 2019
The congress of ESCMID

P2391 Paradoxical reduction in antibiotic-mediated killing of *Staphylococcus aureus* in whole blood versus plasma

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Background: Persistent staphylococcal bacteraemia remains an important and frequent cause of morbidity and mortality, despite the availability of apparently effective antimicrobial therapy. An *ex vivo* whole blood model was used to study tolerance of methicillin sensitive *S. aureus* (MSSA) to antibiotics and the immune system. We hypothesised that *S. aureus* survives intracellularly within phagocytes and thereby evades antibiotic mediated killing.

Materials/methods: Wild-type (WT) *S. aureus* was incubated in whole human blood, broth and plasma (lacking immune cells), with human serum as a control. This was done with and without antibiotic (cloxacillin, gentamicin, vancomycin, ciprofloxacin, or clindamycin). Bacterial survival was measured at 0, 2, 4 and 6 hours. Key neutrophil processes- phagocytosis, the oxidative burst and acidification of the vacuole were inhibited using cytochalasin D, diphenyleneiodonium (DPI) and bafilomycin respectively.

Results: Antibiotic activity was as expected in broth and serum i.e. bactericidal or bacteriostatic. However, with the exception of gentamicin, the addition of antibiotic to blood, failed to increase bacterial killing compared to blood alone. Preincubation of WT bacteria in blood prior to the addition of ciprofloxacin, cloxacillin or gentamicin lead to significantly increased bacterial survival compared to the immediate addition of antibiotic. The anti-staphylococcal activity of plasma with or without antibiotic was greater than that of whole blood in combination with antibiotic or whole-blood alone, respectively. Blocking neutrophil processes; phagocytosis, the oxidative burst and acidification of the vacuole did not increase bacterial killing.

Conclusions: We demonstrated antagonism between whole blood and antibiotic activity. These results suggest some aspect of the interaction between *S. aureus* and immune cells may impede antibiotic ability to efficiently eradicate bacterial bloodstream infection. This supports other evidence that immune cells such as neutrophils may provide a protective niche that enables *S. aureus* to evade antibiotic-mediated killing.