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Maggot debridement therapy (MDT) in diabetic foot wounds – Quorum sensing dependent bacterial niches may promote infection or MDT failure

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Background: Many diabetic patients with foot wounds are ideal candidates for MDT. The maggots gently and thoroughly remove necrotic tissue by mechanical action and by proteolytic digestion. The maggots secrete antimicrobial peptides into the wound, kill ingested bacteria in their gut and alkalinize the wound. However a few reports show that MDT in some cases subsequently facilitates an infection, when specific bacterial species are present in the wound prior to treatment. MDT has also been observed to fail in some cases due to the maggot's death in the wound environment i.e. Their bio surgical properties were not applicable.

Wounds and particularly diabetic wounds are susceptible to infection due to the development of microbial communities within and around the wound environment. It is now realized that chemically based cell-cell communication (denoted quorum sensing (QS)) and biofilm formation play important roles in a multitude of human infections. QS enables the bacteria to keep track of their numbers and pool their efforts in order to successfully cause disease. Bacterial biofilms show an inherent tolerance to a variety of antimicrobial treatments including the action of the immune system. This makes biofilm infections impossible to completely eradicate. Several pathogenic bacteria show QS mediated organisation and speculation regarding the role of QS and biofilm formation in wound healing is appealing. In this preliminary study we wish to investigate the possible role of QS in relation to infections related to MDT. **Methods:** In an in vitro setup using blood agar plates, we challenged *L. sericata* maggots with different concentrations of green fluorescent protein (GFP) tagged *Pseudomonas aeruginosa* wild type (PAO1 WT), a GFP tagged QS deficient mutant (PAO1 RR) and a *Staphylococcus aureus.* The survival of the maggots was determined and the clearing efficiency assessed during 3 day periods. The uptake of *P. aeruginosa* was determined using fluorescence microscopy. **Results:** The maggot survival and clearing efficiency was unaffected by *S. aureus* and PAO1 RR compared to negative controls, but maggot survival was significantly impaired by the PAO1 WT. Furthermore the florescence microscopy showed reduced uptake of PAO1 WT compared to the PAO1 RR. **Conclusion:** The results indicate that infections following maggot debridement therapy may originate from preferential feeding by the maggots creating micro niches in which bacteria survive and subsequently unchallenged cause infections and that this preference is QS dependent. Furthermore QS controlled virulence factors are toxic for the maggots. Therefore the presence of specific bacterial species may be counter indications for MDT. This suggests that QS inhibitors may be a useful future adjuvant for maggot debridement therapy in wounds harbouring specific bacterial species or as supplement to standard antibiotic therapy.