Postoperative anaerobic sepsis could be combated by prophylactic vaccination

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S11/01

Postoperative anaerobic sepsis could be combated by prophylactic vaccination

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Background: Postoperative sepsis is the leading cause of morbidity and mortality after major surgery, resulting in hefty financial costs in hospitals all over the world.

Material and Methods: 40 Fischer rats were injected intra-peritoneally with 0.05 ml Covexin 10 which contains toxoids from different clostridial species, 2 weeks prior to cecal ligation and puncture. Another 40 Fischer rats, as a control, underwent cecal ligation and puncture without vaccination.

Results: 16 of 40 vaccinated rats died (40%), peritoneal fluid cultures from the dead rats grew *E. coli* only, and 36 of 40 control rats died (90%), peritoneal fluid cultures from the dead rats were: 19 grew *E. coli* and *C. perfringens*; 12 grew *E. coli*, *C. perfringens*, and enterococci; 3 grew *E. coli* only; 1 grew *E. coli*, and enterocci; and 1 grew no organisms.

Conclusion: Prophylactic vaccination with clostridial toxoids prove effectiveness in preventing anaerobic infection, and reduce mortality in rats that underwent cecal ligation and puncture; the gold standard model for polymicrobial sepsis. Currently, a pilot study is underway in which human patients who will undergo major surgery are prophylactically vaccinated with clostridial toxoids, in an attempt to eradicate postoperative anaerobic sepsis.

S11/02

Persistence of fidaxomicin on *Clostridium difficile* spores, and subsequent effects on spore outgrowth, recovery and toxin production

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Objectives. Fidaxomixin is associated with lower recurrence rates of *Clostridium difficile* infection (CDI) compared with vancomycin therapy. We have evaluated whether fidaxomicin is more adherent to spores than vancomycin, and whether this affects outgrowth, germination and recovery.

Methods. *Clostridium difficile* spores were exposed to fidaxomicin, vancomycin or no antibiotic. After washing, residual antibiotic concentrations were determined. Recovery of antibiotic exposed or control 027 and 078 spores and vegetative cells was determined by viable counting. Relative rates of germination were determined via phase microscopy. Toxin production was assessed after 24 and 48 hours.

Results. Spores exposed to fidaxomicin exhibited antimicrobial activity after washing, whereas vancomycin and control preparations did not. 078 spores exposed to fidaxomicin exhibited a lower rate of germination than vancomycin exposed and control spores, and produced no toxin. These effects were not observed for 027 spores.

Conclusions. Fidaxomicin persists on *Clostridium difficile* spores after washing. Inhibition of outgrowth, recovery and toxin production was apparent for 078 spores exposed to fidaxomicin but not for 027 spores. Findings are consistent with evidence that fidaxomicin reduces the recurrence of CDI due to PCR ribotypes other than 027. Mechanisms via which inhibition of germination and toxin production occur require elucidation.

S11/03

Quorum sensing control of butanol production in *Clostridium acetobutylicum*

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Clostridium acetobutylicum has been shown to have several quorum sensing (QS) systems of both the agr and RNPP-type. The aim of this research is to understand these QS systems in greater detail, in particular, their relevance to butanol yields. There is relatively little understanding of QS in *Clostridia* including *C. acetobutylicum*. This is regardless of its use as an industrial strain for the acetone-butanol-ethanol pathway, and containing many identified QS systems. By eliminating QS genes in the organism, and characterising the resulting phenotype, it is possible to build a picture of what these systems control. As an industrially significant strain, understanding of the QS systems could lead to more efficient butanol production, whilst advancing the understanding of QS for gram positive bacteria.