Comment on: Durability of antimicrobial activity of antibiotic-impregnated external ventricular drains: a prospective study.

Roger Bayston, Waheed Ashraf

Sir, we thank Dr Mounier and colleagues for their response [1] to our comments. [2] We consider that they have not fully addressed three important areas: laboratory methods, clinical evidence of efficacy and longevity of effect.

Mounier et al say that most of our laboratory experiments "rely on 5min to 1h bacterial challenge"… "this model of short term exposure" …but in our papers we expose the antimicrobial catheters for 1 h *every 2 weeks for 42 days* in constant flow conditions to mimic repeated bacterial challenge of the external ventricular drain (EVD). [3] This could hardly be said to be a short - term exposure. The 1h contact for bacterial attachment resulted in heavy colonization of control catheters; the antimicrobial catheters remained free of colonization even after 42 days, which is inconsistent with their zone plate findings.

Mounier et al say that clinical evidence does not support claims of benefit from antimicrobial EVD catheters. One study by Ramirez et al which they cited showed Bactiseal failures only when *Acinetobacter baumannii* or *Klebsiella pneumoniae* were involved, and this is understandable as Bactiseal has no activity against Gram negative bacilli [4]. Some of the other studies cited that show no difference in infection rate also used systemic antibiotics throughout the EVD period of use, [5,6,7] and this is acknowledged to reduce ventriculitis rates. However, the risk of this approach is also evidenced in the literature, the study by Wong et al (REF) being an example, where antimicrobial EVD catheters without systemic antibiotics were compared with plain catheters with systemic antibiotics. While the ventriculitis rates were low (1.1% and 3.2% respectively), there were three cases of *Clostridioides difficile* infection in the antibiotics group (with one total colectomy) but none

in the antimicrobial catheter group. The message from these studies is not that there is no difference in ventriculitis rate between Bactiseal EVD and plain catheters, but that Bactiseal EVD gives the same protection as longterm systemic antibiotics but without the adverse effects.

Finally, Mounier et al say that the activity of antimicrobial EVDs decreases with time in use. This is to be expected, but as we pointed out previously, [2] the amount of antimicrobial released should not be taken to indicate potential protective activity. We have shown that the amount of rifampicin and clindamycin decreases sharply from 3mg/L and 25mg/L resp on Day 1 to 0.8mg/L and 1.2mg/L resp on Day 2, but 0.01mg/L and 0.2mg/L are still being released on Day 21. [8] It is important to point out that these concentrations are those released into surrounding fluid phase and are not indicative of the continuing surface activity at these time points. Indeed, the protective activity was sustained at these time points.

Antimicrobial biomaterials are still imperfectly studied and incompletely understood, but it is important to use assessment methods that are as nearly relevant as possible to clinical use conditions.

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Transparency declarations

RB is the named inventor of Bactiseal but has not received any royalties. He has received speaker fees from Codman, but these have been paid to his university and were not for personal gain. WA has none to declare.

References

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