

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

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4 **Roger Bayston, Waheed Ashraf**

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6 Sir, we thank Dr Mounier and colleagues for their response ¹ to our comments. ² We
7 consider that they have not fully addressed three important areas: laboratory methods,
8 clinical evidence of efficacy and longevity of effect.
9 Mounier et al say that most of our laboratory experiments “rely on 5min to 1h bacterial
10 challenge”... “this model of short term exposure” ...but in our papers we expose the
11 antimicrobial catheters for 1 h *every 2 weeks for 42 days* in constant flow conditions to
12 mimic repeated bacterial challenge of the external ventricular drain (EVD). ³ This could
13 hardly be said to be a short - term exposure. The 1h contact for bacterial attachment
14 resulted in heavy colonization of control catheters; the antimicrobial catheters remained
15 free of colonization even after 42 days, which is inconsistent with their zone plate findings.
16 Mounier et al say that clinical evidence does not support claims of benefit from
17 antimicrobial EVD catheters. One study by Ramirez et al which they cited showed Bactiseal
18 failures only when *Acinetobacter baumannii* or *Klebsiella pneumoniae* were involved, and
19 this is understandable as Bactiseal has no activity against Gram negative bacilli ⁴. Some of
20 the other studies cited that show no difference in infection rate also used systemic
21 antibiotics throughout the EVD period of use, ^{5,6,7} and this is acknowledged to reduce
22 ventriculitis rates. However, the risk of this approach is also evidenced in the literature, the
23 study by Wong et al (REF) being an example, where antimicrobial EVD catheters without
24 systemic antibiotics were compared with plain catheters with systemic antibiotics. While the
25 ventriculitis rates were low (1.1% and 3.2% respectively), there were three cases of
26 *Clostridioides difficile* infection in the antibiotics group (with one total colectomy) but none

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

31 Finally, Mounier et al say that the activity of antimicrobial EVDs decreases with time in use.
32 This is to be expected, but as we pointed out previously, ² the amount of antimicrobial
33 released should not be taken to indicate potential protective activity. We have shown that
34 the amount of rifampicin and clindamycin decreases sharply from 3mg/L and 25mg/L resp
35 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
36 released on Day 21. ⁸ It is important to point out that these concentrations are those
37 released into surrounding fluid phase and are not indicative of the continuing surface
38 activity at these time points. Indeed, the protective activity was sustained at these time
39 points.

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

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44 No funding was received in connection with this letter

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46 Transparency declarations

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

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