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Antibiotic Use in Total Knee Arthroplasty Periprosthetic Joint Infection

ESCMID Study Grp Implant-; Wouthuyzen-Bakker, Marjan; Lora-Tamayo, Jaime; Soriano, Alex

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advantages and potential risks of vaccines [1–5]. It is a frequently used argument by antivaccine campaigners that, before the 1960s, the decade during which the measles vaccine became available, everybody used to experience these back-then childhood diseases [6], an argument played out to create a connotation of normality and harmlessness concerning an antivaccination choice [1, 3].

However, such an argument contains bias. It is known that bias occurs if comparisons are made between groups that are systematically different with regards to certain characteristics [7]. For example, the act of remembering a specific event may be differential between those who had a disease (or an unfavorable clinical course of the disease) and those without the disease (or a mild course of the disease). Although those with unfavorable clinical courses of measles may be largely in favor of vaccinations, those with mild clinical courses may potentially be opposing it. This is an example of reporting bias [7]. However, as the bulk of measles-attributable population morbidity and mortality in high-income settings occurred before 1970, it is likely that today former patients may not correctly remember the severity of their individual episodes of measles, thus, constituting a form of recall bias [6].

Further, survivorship bias may play a role. It denotes the distorted perception of an exposure (eg, measles episode) when looking only at those with a favorable outcome (eg, survival). Explicit examples are numerous, such as the presumable ease to earn public reputation or fame: for every successful individual (in art, science, politics, etc.), there are, however, potentially hundreds having engaged in the same effort, not having succeeded and thus being lost to the formation of the public perception process [7, 8]. Similarly, in measles vaccination debates, the public opinion is virtually exclusively shaped by those who survived their measles episode in the pre-1970s or had benefitted from vaccination campaigns in the post-1970s. Contrarily, people with a fatal outcome in

their measles episode cannot contribute to the public debate anymore to advocate a provaccination choice.

A similar subtype of bias is the so-called visibility bias [9]. It refers to an increased awareness for an exposure (eg, measles) if its outcome is particularly salient or severe (eg, death). Despite a rising measles incidence, the average case-fatality rate of measles is 1:1000 and may still be too low in high-income settings to surpass the public perception threshold [6, 10]. Thus, the absence of public “visibility” of severe clinical outcomes may also be linked to decreased willingness to vaccinate.

Finally, one may even regard the composition of speakers in public debates to be subjected to selection bias. There is broad consensus among medical experts that the measles vaccine is highly efficacious, tolerable, and safe [6, 10]. Thus, a debate hosting the same number of favorers as there are opposers, conveys (whether willingly or unwillingly) a disproportionate medical reality to the audience and an overrepresentation of antivaccine campaigners.

Notes

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Johannes Mischlinger,^{1,2} Riko Muranaka,^{1,2,3} Silja Bühler,^{1,2} and Michael Ramharter^{1,2}

¹Department of Tropical Medicine, Bernhard Nocht Institute for Tropical Medicine and Department of Medicine I, University Medical Center Hamburg-Eppendorf, and ²German Centre for Infection Research (DZIF), Partner Site Hamburg-Luebeck-Borstel, Hamburg, Germany; and ³Graduate School of Kyoto University School of Medicine, Japan

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Correspondence: M. Ramharter, Bernhard-Nocht-Str. 74, 20359 Hamburg, Germany (ramharter@bnitm.de).

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Antibiotic Use in Total Knee Arthroplasty Periprosthetic Joint Infection

TO THE EDITOR—We have read with much interest the article by Shah et al [1], describing a 29% higher treatment success rate when patients are given an extended course of antibiotics compared with a 6-week treatment course for knee periprosthetic joint infections (PJIs) treated with surgical debridement (debridement, antibiotic therapy, and implant retention [DAIR]). The authors concluded that extended oral antibiotic therapy has

a superior infection-free survival rate, but because the beneficial effect of extended antibiotic use disappears after 1 year, antibiotics can be discontinued after that point. We would like to address some issues that should be considered to avoid misinterpreting the authors' observation.

First, although results of observational studies and a recent randomized controlled trial suggest that a 6–8-week antibiotic treatment course is as effective as longer treatments, these studies were performed mostly in early acute PJIs and using antibiotics with good antibiofilm properties [2–7]. However, in the study described by Shah et al [1], only 33% of patients had early acute PJIs, no details were provided about the exact antibiotic regimen, and some patients in the short treatment arm were treated for even less than 6 weeks. For this reason, we disagree with their conclusion that antibiotic therapy should be extended to 1 year without comparing such extended therapy to current recommendations (ie, 3–6 months of antibiotic treatment) [8].

There may also be a survival bias in the authors' analysis, because the length of therapy for a given patient was calculated from the moment of DAIR until the end of therapy or until failure, thus reversing the cause-effect relationship and self-fulfilling the authors' hypothesis. Failure itself may have led to discontinuation of antibiotics, whereas the absence of failure may have carried the opportunity for longer treatment. This phenomenon is indeed illustrated in the survival curve provided by the authors, demonstrating that a large percentage of patients in the "acute antibiotics" arm already had failure within 6 weeks. For this reason, to support conclusions about the efficacy of antibiotic duration per se, the analysis should be performed solely in patients that completed their total antibiotic course.

Finally, it is unknown whether the 2 groups were balanced with respect to other relevant variables with a recognized influence on outcome in patients undergoing DAIR, such as the exchange of removable components during debridement and the type of infection (acute vs

late chronic). For example, it is known that with the presence of persister cells in chronic infections, extending antibiotic treatment postpones rather than prevents failure [9, 10]. Shah et al did not state whether the cases without relapse after the end of antibiotic treatment at 1 year were all acute infections, which would also have been cured with a shorter course of antibiotics.

We hope the authors can provide answer to the questions we raise. Based on the data they provided, we believe that their recommendation to extend antibiotic treatment to 1 year should be based on more solid evidence.

Note

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Marjan Wouthuyzen-Bakker,¹ Jaime Lora-Tamayo,² and Alex Soriano³; ESCMID Study Group for Implant-associated Infections

¹Department of Medical Microbiology and Infection Prevention, University of Groningen, University Medical Center Groningen, The Netherlands; ²Department of Internal Medicine, Instituto de Investigación i+12, Hospital Universitario 12 de Octubre, Madrid, and ³Service of Infectious Diseases, Hospital Clínic, University of Barcelona, Spain.

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Correspondence: M. Wouthuyzen-Bakker, Internist-infectiologist, Department of Medical Microbiology and Infection Prevention, University Medical Center Groningen, University of Groningen, Hanzeplein 1, 9713 GZ, Groningen, the Netherlands (m.wouthuyzen-bakker@umcg.nl).

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Reply to Wouthuyzen-Bakker et al

TO THE EDITOR—Per the Infectious Diseases Society of America (IDSA) guidelines, patients with an acute total knee arthroplasty prosthetic joint infection (PJI) requiring debridement with prosthesis retention require 4–6 weeks of pathogen-specific intravenous or highly bioavailable oral antimicrobial therapy. Treatment may then be followed by indefinite chronic oral antimicrobial suppression. Those with staphylococcal PJI may benefit from the addition of rifampin. The guidelines limit the use of rifampin specifically to staphylococcal infections. Antibiotic treatment in our study followed these IDSA guidelines.

The decision to initiate indefinite oral antibiotic suppression is not straightforward, as evidenced by a lack of agreement on the use and duration of chronic suppression among the IDSA panel members themselves. As some data suggest up to a 4-fold increase in risk of treatment failure