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Same Exposure but Two Radically Different Responses to Antibiotics: Resilience of the Salivary Microbiome versus Long-Term Microbial Shifts in Feces

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Editor Alex van Belkum, bioMérieux

ABSTRACT

Due to the spread of resistance, antibiotic exposure receives increasing attention. Ecological consequences for the different niches of individual microbiomes are, however, largely ignored. Here, we report the effects of widely used antibiotics (clindamycin, ciprofloxacin, amoxicillin, and minocycline) with different modes of action on the ecology of both the gut and the oral microbiomes in 66 healthy adults from the United Kingdom and Sweden in a two-center randomized placebo-controlled clinical trial. Feces and saliva were collected at baseline, immediately after exposure, and 1, 2, 4, and 12 months after administration of antibiotics or placebo. Sequences of 16S rRNA gene amplicons from all samples and metagenomic shotgun sequences from selected baseline and post-antibiotic-treatment sample pairs were analyzed. Additionally, metagenomic predictions based on 16S rRNA gene amplicon data were performed using PICRUSt. The salivary microbiome was found to be significantly more robust, whereas the antibiotics negatively affected the fecal microbiome: in particular, health-associated butyrate-producing species became strongly underrepresented. Additionally, exposure to different antibiotics enriched genes associated with antibiotic resistance. In conclusion, healthy individuals, exposed to a single antibiotic treatment, undergo considerable microbial shifts and enrichment in antibiotic resistance in their feces, while their salivary microbiome composition remains unexpectedly stable. The health-related consequences for the gut microbiome should increase the awareness of the individual risks involved with antibiotic use, especially in a (diseased) population with an already dysregulated microbiome. On the other hand,

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doi: 10.1128/mBio.01693-15
10 November 2015 mBio vol. 6
no. 6 e01693-15

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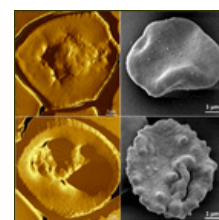
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understanding the mechanisms behind the resilience of the oral microbiome toward ecological collapse might prove useful in combating microbial dysbiosis elsewhere in the body.

IMPORTANCE Many health care professionals use antibiotic prophylaxis strategies to prevent infection after surgery. This practice is under debate since it enhances the spread of antibiotic resistance. Another important reason to avoid nonessential use of antibiotics, the impact on our microbiome, has hardly received attention. In this study, we assessed the impact of antibiotics on the human microbial ecology at two niches. We followed the oral and gut microbiomes in 66 individuals from before, immediately after, and up to 12 months after exposure to different antibiotic classes. The salivary microbiome recovered quickly and was surprisingly robust toward antibiotic-induced disturbance. The fecal microbiome was severely affected by most antibiotics: for months, health-associated butyrate-producing species became strongly underrepresented. Additionally, there was an enrichment of genes associated with antibiotic resistance. Clearly, even a single antibiotic treatment in healthy individuals contributes to the risk of resistance development and leads to long-lasting detrimental shifts in the gut microbiome.

FOOTNOTES

Citation Zaura E, Brandt BW, Teixeira de Mattos MJ, Buijs MJ, Caspers MPM, Rashid MU, Weintraub A, Nord CE, Savell A, Hu Y, Coates AR, Hubank M, Spratt DA, Wilson M, Keijser BJF, Crielaard W. 2015. Same exposure but two radically different responses to antibiotics: resilience of the salivary microbiome versus long-term microbial shifts in feces. *mBio* 6(6):e01693-15. doi:10.1128/mBio.01693-15.

Received 30 September 2015 Accepted 8 October 2015 Published 10 November 2015

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