### **LETTER TO THE EDITOR**

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# Increasing allergy: are antibiotics the elephant in the room?

Rod A. Herman\*

#### **Abstract**

Antibiotics cause dramatic changes to the human microbiome. The composition of the microbiome has been associated with changes in the immune system and these changes are beginning to be linked to immune diseases. Thus, antibiotics have been implicated as a significant contributor to the continual rise of allergies and autoimmune disease in developed countries. This recognition will hopefully result in the development of post-antibiotic therapies that restore a healthy microbiome and reduce immune system disorders.

**Keywords:** Antibiotics, Microbiome, Immune system, Immune disease, Allergy

## Antibiotics → microbiome → immune system → allergy

The problem of pathogen resistance in response to antibiotic use is well known as is the propensity of individuals to develop allergies to various classes of antibiotics [1-3]. Perhaps less widely known is that widespread antibiotic use in developed countries may be contributing to the observed general increase in the frequency of immune diseases, including food, respiratory, and dermal allergy [4-7]. Evidence linking the biodiversity and makeup of the microbiome to human health is accumulating including studies linking the microbiome (Box 1) to the proper functioning of our immune system [8-11]. Furthermore, a correlation between our microbiome characteristics and autoimmune disease and allergy has now been established [6, 12, 13]. It is therefore not surprising that a positive correlation between certain types of allergy and antibiotic use has been observed [4, 14, 15]. For example, the use of antibiotics in early childhood is associated with an increased rate of asthma and allergy (assessed at up to 12 years later) [16–18]. Although the tremendous benefits of antibiotics to fight pathogenic bacteria and improve the outcomes of disease is undeniable, antibiotics also kill many non-pathogenic bacteria. Furthermore, one would expect dramatic effects on the microbiomes in our lungs and gut, as well as on our skin occur during, and persist for a time after, a course of systemic antibiotics [19, 20]. Since our microbiomes play a role in allergy development, it should also not be surprising that antibiotic use can, through modification of our microbiomes, affect allergy development [4-6, 21]. While antibiotics are certainly not the only factors affecting our microbiome, understanding the intricacies of the effects of antibiotics on our microbiome and fostering the recovery of healthy microbiomes after antibiotic use remain challenges, and widespread appreciation of this phenomenon by researchers is likely key to fostering development of post-antibiotic therapies that do not perpetuate immune disorders [22]. With their widespread use and significant impact on the human microbiome, antibiotics may be the elephant in the room in terms of the increased frequency of allergy occurring in the developed world.

#### **Box 1: Human microbiome**

The human microbiome refers to the microbial communities (bacteria, viruses, and fungi) that inhabit the human body including the gut, lungs, and skin (key sites of interaction between exogenous proteins and the immune system) [23]. The microbiome

<sup>\*</sup>Correspondence: rod.herman@corteva.com Corteva Agriscience, 9330 Zionsville Road, Indianapolis, IN 46268, USA



consists of the majority of the cells in the human body, and the sum of the genomes of these microbes is estimated at over 100-times greater than that of the human genome [4]. Humans and their microbiome have evolved together in often symbiotic relationships that facilitate good health [23, 24]. The makeup of the nascent microbiome is influenced by the mother (e.g., colonization from the vaginal microbiome) which can explain some immune diseases seen within families (e.g., asthma) [25]. However, whether specific changes to the microbiome cause disease, or are the result of disease, requires careful study. Environmental factors including diet are known to affect the composition of the microbiome, but perhaps no environmental factor has as dramatic an effect on the microbiome as antibiotics. Microbiome "transplants" from healthy to diseased individuals (e.g. fecal transplants) and probiotics are beginning to be used to treat certain diseases, including immune disease.

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#### References

- Lee CE, Zembower TR, Fotis MA, Postelnick MJ, Greenberger PA, Peterson LR, Noskin GA. The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance. Arch Intern Med. 2000;160(18):2819–22.
- Zaman SB, Hussain MA, Nye R, Mehta V, Mamun KT, Hossain N. A review on antibiotic resistance: alarm bells are ringing. Cureus. 2017. https://doi. org/10.7759/cureus.1403.
- Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH, Nisar MA, Alvi RF, Aslam MA, Qamar MU. Antibiotic resistance: a rundown of a global crisis. Infect Drug Resist. 2018;11:1645.

- Riiser A. The human microbiome, asthma, and allergy. Allergy Asthma Clin Immunol. 2015;11(1):35.
- Pascal M, Perez-Gordo M, Caballero T, Escribese MM, Longo MNL, Luengo O, Manso L, Matheu V, Seoane E, Zamorano M. Microbiome and allergic diseases. Front Immunol. 2018;9:1584.
- Noverr MC, Huffnagle G. The 'microflora hypothesis' of allergic diseases. Clin Exp Allergy. 2005;35(12):1511–20.
- Hirsch AG, Pollak J, Glass TA, Poulsen MN, Bailey-Davis L, Mowery J, Schwartz BS. Early-life antibiotic use and subsequent diagnosis of food allergy and allergic diseases. Clin Exp Allergy. 2017;47(2):236–44.
- 8. Shi N, Li N, Duan X, Niu H. Interaction between the gut microbiome and mucosal immune system. Mil Med Res. 2017;4(1):14.
- Plunkett CH, Nagler CR. The influence of the microbiome on allergic sensitization to food. J Immunol. 2017;198(2):581–9.
- Hoskin-Parr L, Teyhan A, Blocker A, Henderson A. Antibiotic exposure in the first two years of life and development of asthma and other allergic diseases by 7.5 yr: a dose-dependent relationship. Pediatr Allergy Immunol. 2013;24(8):762–71.
- Yamamoto-Hanada K, Yang L, Narita M, Saito H, Ohya Y. Influence of antibiotic use in early childhood on asthma and allergic diseases at age 5. Ann Allergy Asthma Immunol. 2017;119(1):54–8.
- 12. Proal AD, Albert PJ, Marshall TG. The human microbiome and autoimmunity. Curr Opin Rheumatol. 2013;25(2):234–40.
- Fujimura KE, Lynch SV. Microbiota in allergy and asthma and the emerging relationship with the gut microbiome. Cell Host Microbe. 2015;17(5):592–602.
- Seo J-H, Kim HY, Jung Y-H, Lee E, Yang S-I, Yu H-S, Kim Y-J, Kang M-J, Kim H-J, Park KS. Interactions between innate immunity genes and early-life risk factors in allergic rhinitis. Allergy Asthma Immunol Res. 2015;7(3):241–8.
- Ong M-S, Umetsu DT, Mandl KD. Consequences of antibiotics and infections in infancy: bugs, drugs, and wheezing. Ann Allergy Asthma Immunol. 2014;112(5):441–445.e441.
- Droste J, Wieringa M, Weyler J, Nelen V, Vermeire P, Van Bever H. Does the use of antibiotics in early childhood increase the risk of asthma and allergic disease? Clin Exp Allergy. 2000;30(11):1548–53.
- Fischer PR. Antibiotic use in infancy associated with allergic disease during childhood. Infect Dis Alert. 2018. https://doi.org/10.1186/s1288 7-12019-11594-12884.
- Kuo C-H, Kuo H-F, Huang C-H, Yang S-N, Lee M-S, Hung C-H. Early life exposure to antibiotics and the risk of childhood allergic diseases: an update from the perspective of the hygiene hypothesis. J Microbiol Immunol Infect. 2013;46(5):320–9.
- Hong B-Y, Maulén NP, Adami AJ, Granados H, Balcells ME, Cervantes J. Microbiome changes during tuberculosis and antituberculous therapy. Clin Microbiol Rev. 2016;29(4):915–26.
- 20. Ferrer M, Méndez-García C, Rojo D, Barbas C, Moya A. Antibiotic use and microbiome function. Biochem Pharmacol. 2017;134:114–26.
- Wypych TP, Marsland BJ. Antibiotics as instigators of microbial dysbiosis: implications for asthma and allergy. Trends Immunol. 2018;39(9):697–711.
- Kang Y, Cai Y, Zhang H. Gut microbiota and allergy/asthma: from pathogenesis to new therapeutic strategies. Allergol Immunopathol. 2017;45(3):305–9.
- 23. Marsland BJ, Salami O. Microbiome influences on allergy in mice and humans. Curr Opin Immunol. 2015;36:94–100.
- 24. Lloyd-Price J, Abu-Ali G, Huttenhower C. The healthy human microbiome. Genome Med. 2016;8(1):51.
- Mueller NT, Bakacs E, Combellick J, Grigoryan Z, Dominguez-Bello MG. The infant microbiome development: mom matters. Trends Mol Med. 2015;21(2):109–17.

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