

Systemic Antifungals and Antibiotics Correlated with Increased Likelihood of Childhood Food Allergies

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Key Findings:

- Children whose mothers were prescribed systemic antifungals in the year after birth are 16% more likely to develop a food allergy compared to those whose mothers were not prescribed an antifungal in the year after birth.
- Children prescribed systemic antibiotics in their first year of life are 12% more likely to develop a food allergy compared to those not prescribed antibiotics.

Antibiotics are commonly prescribed during pregnancy and in the early years of a child's life; their effect on the developing fetus and child can vary depending on the type of antibiotic used.¹ In previous studies, prenatal antibiotic exposure was found to be correlated with an increased risk of asthma, eczema, and non-food allergies in the affected child.² Additionally, studies have found that intestinal microbial composition is associated with the development of food allergies, and that systemic antifungals and antibiotics may play a role in this development.^{3,4,5,6} We sought to understand whether prenatal, postnatal, or childhood antifungal and antibiotic exposures are correlated with future food allergy development in children.

We studied 534,843 babies born between January 1, 2017, and November 3, 2021, to evaluate their risk of developing food allergies. We adjusted for the child's sex, race, ethnicity, and delivery method. We also adjusted for the mother's age and whether she had a food allergy.

We found that children whose mothers were prescribed systemic antifungals during the child's first year of life were 16% more likely to develop one or more food allergies than those whose mothers were not prescribed systemic antifungals, while those whose mothers were prescribed an antifungal prenatally had a 6% increased likelihood. There was not a statistically significant increase in the likelihood of developing food allergies for children prescribed antifungals in their first year of life.

Children whose mothers were prescribed systemic antibiotics during the year after the child's birth were 8% more likely to develop a food allergy than those whose mothers were not prescribed systemic antibiotics in the year after birth. If their mother was prescribed systemic antibiotics prenatally, the child was 3% more likely to develop food allergies than those whose mothers were not prescribed systemic antibiotics prenatally. Finally, children who were prescribed systemic antibiotics in the first year of life were 12% more likely to develop food allergies than those with no antibiotic prescription.

Change in Likelihood of Childhood Food Allergies with Antifungal and Antibiotic Use

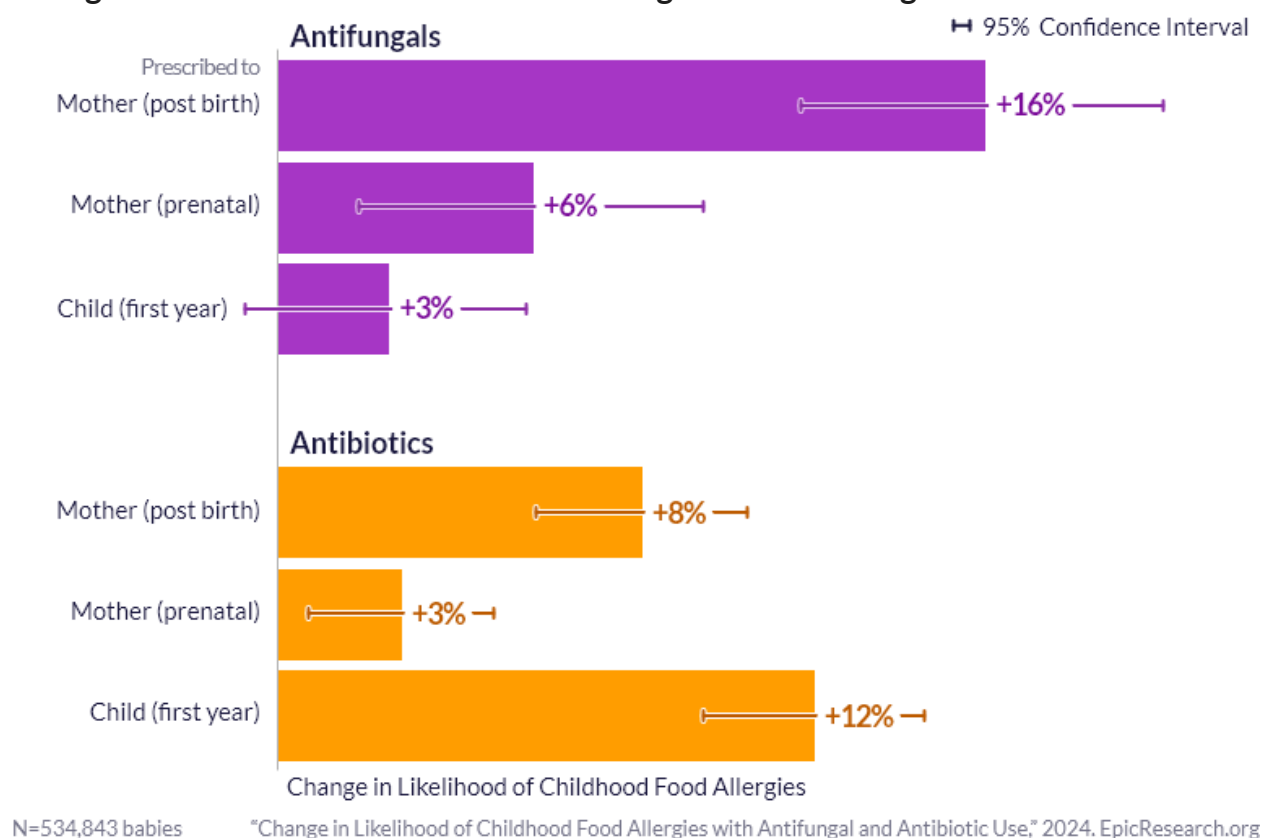


Figure 1. The difference in hazard of a child developing food allergies by maternal and childhood antibiotic and antifungal usage compared to children with no antibiotic or antifungal exposure.

Other factors that may impact the likelihood of developing food allergies, such as the indication for the antibiotics or antifungals, antibiotics or antifungals prescribed after the first year of life, breastfeeding status, and environmental factors, were not included in this analysis.

These data come from Cosmos, a collaboration of 236 Epic health systems representing more than 227 million patient records from 1,301 hospitals and more than 28,600 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. What antibiotics are safe during pregnancy? (2022, August 25). Mayo Clinic. <https://www.mayoclinic.org/healthy-lifestyle/pregnancy-week-by-week/expert-answers/antibiotics-and-pregnancy/faq-20058542>
2. Baron, R., Taye, M., der Vaart, I. B., Ujčić-Voortman, J., Szajewska, H., Seidell, J. C., & Verhoeff, A. (2020). The relationship of prenatal antibiotic exposure and infant antibiotic administration with childhood allergies: a systematic review. *BMC Pediatrics*, 20(1). <https://doi.org/10.1186/s12887-020-02042-8>
3. Blázquez AB, Berin MC. Microbiome and food allergy. *Transl Res*. 2017;179:199-203. doi:10.1016/j.trsl.2016.09.003
4. Lee KH, Song Y, Wu W, Yu K, Zhang G. The gut microbiota, environmental factors, and links to the development of food allergy. *Clin Mol Allergy*. 2020;18:5. Published 2020 Apr 2. doi:10.1186/s12948-020-00120-x

5. Love BL, Mann JR, Hardin JW, Lu ZK, Cox C, Amrol DJ. Antibiotic prescription and food allergy in young children. *Allergy Asthma Clin Immunol*. 2016;12:41. Published 2016 Aug 17. doi:10.1186/s13223-016-0148-7
6. About Harnessing Microbial Ecology for Public Health. Centers for Disease Control and Prevention. Published December 15, 2022. <https://www.cdc.gov/drugresistance/microbial-ecology.html>. Accessed January 5, 2024.

Data Definitions

Term	Definition
Study period	1/1/2017 - 11/11/2023
Study population	Babies born between 1/1/2017 and 11/3/2021 where the following are true: Mother has more than two face-to-face outpatient or telemedicine encounters in the nine months prior to birth. Mother has more than two face-to-face outpatient or telemedicine encounters in the year after birth. Baby has a face-to-face or telemedicine encounter during ages 0, 1, and 2.
Systemic antibiotics	A medication order for one of the following pharmaceutical classes with a route of "combination," "injection," "intramuscular," "intravenous," or "oral": Penicillin antibiotics; Cephalosporin antibiotics – 1st generation; Cephalosporin antibiotics - 2nd generation; Cephalosporin antibiotics - 3rd generation; Cephalosporin antibiotics - 4th generation; Cephalosporins - 5th generation; Macrolide antibiotics; Tetracycline antibiotics; Periodontal collagenase inhibitors; Quinolone antibiotics; Aminoglycoside antibiotics; Amebicides; Absorbable sulfonamide antibacterial agents; Chloramphenicol antibiotics and derivatives; Vancomycin antibiotics and derivatives; Lincosamide antibiotics; Antibiotics, miscellaneous, other; Polymyxin antibiotics and derivatives; Betalactams; Carbapenem antibiotics (thienamycins); Anaerobic antiprotozoal-antibacterial agents; Antiprotozoal drugs, miscellaneous; Antiparasitics; Cyclic lipopeptides; Streptogramin antibiotics; Oxazolidinone antibiotics; Rifamycins and related derivative antibiotics; Ketolide antibiotics; 2nd gen. Anaerobic antiprotozoal-antibacterial; Glycylcyclines; Lipoglycopeptide antibiotics; Nitrofurantoin derivatives antibacterial agents; Antibiotic, antibacterial, misc.; or Antitubercular antibiotics.
Systemic antifungals	A medication order for one of the following pharmaceutical classes with a route of "combination," "injection," "intramuscular," "intravenous," or "oral": Antifungal Agents or Antifungal Antibiotics.
Food allergy	• Dairy - A documented allergy that contains the text "milk," "dairy," "casein," "whey," "formula" + "inf," or "formula" + "baby," excluding those with the text "thistle," "milkwort," "coconut," "soy," "dairy digestive ultra," "dairy ease," or "dairy-aid". Alternatively, a diagnosis with ICD-10-CM code Z91.011. • Egg - A documented allergy that contains the text "egg," "albumen (egg white)," "egg yolk extract," "egg derived," "egg yolk," "egg extract," "egg white," or "eggshell membrane". Alternatively, a diagnosis with ICD-10-CM code Z91.012. • Fish – A documented allergy that contains the text "clams," "cod liver," "crab," "fish," "lobster," "mussel," "oyster," "scallop," "shrimp," "squid," or "tuna". Alternatively, a diagnosis with ICD-10-CM code Z91.013.

	• Fruit – A documented allergy that contains the text “apricot,” “apple,” “avocado,” “banana,” “blueberry,” “cantaloupe,” “cherry,” “coconut,” “honeydew,” “kiwi,” “mango,” “peach,” “strawberry,” or “watermelon”. • Legume – A documented allergy that contains the text “legumes,” “lentil,” or “peanut”. Alternatively, a diagnosis with ICD-10-CM code Z91.010. • Nut – A documented allergy that contains the text “almond,” “argan nut,” “Brazil nut,” “cashew,” “chestnut,” “hazelnut,” “kola nut,” “macadamia,” “nut – unspecified,” “nutmeg,” “pecan,” “pistachio,” “sesame,” “tree nut,” or “walnut”. • Soy – A documented allergy that contains the text “soy”. • Wheat – A documented allergy that contains the text “wheat” or “gluten”.
Time varying proportional hazard regression model	Independent variables: Baby’s sex, maternal age, maternal food allergy, baby’s race and ethnicity, prenatal systemic antibiotics or antifungal, maternal systemic antibiotics or antifungals in year after birth, child’s first year systemic antibiotics or antifungals, and birth delivery method. Patients are observed until the first of: a documented food allergy or the child’s last encounter in their last year of consecutive care observed.

Table 1: Change in Likelihood of Childhood Food Allergies with Antifungal and Antibiotic Use

Category	Group	Compared To	Prescribed to	Hazard Ratio	Lower CI	Upper CI
First Year Exposure	Maternal antifungals	No maternal antifungal	Mother (post birth)	1.16	1.12	1.20
Prenatal Exposure	Prenatal antifungals	No antifungal	Mother (prenatally)	1.06	1.02	1.10
First Year Exposure	Child antifungals	No child antifungal	Child (first year)	1.03	0.99	1.06
First Year Exposure	Maternal antibiotics	No maternal antibiotic	Mother (post birth)	1.08	1.06	1.11
Prenatal Exposure	Prenatal antibiotics	No antibiotic	Mother (prenatally)	1.03	1.01	1.05
First Year Exposure	Child antibiotics	No child antibiotic	Child (first year)	1.12	1.10	1.15