

### Article of Interest

Strom B, et al. Absence of Cross-Reactivity between Sulfonamide Antibiotics and Sulfonamide Nonantibiotics. *New England Journal*. 2003. [\(Click to Access\)](#)

### Context and Study Objective

Allergic reactions to antibiotics with a sulfonamide ("sulfa") component are associated with hypersensitivity reactions to sulfa-containing nonantibiotics (e.g. thiazide and loop diuretics). Consequently, medication packaging inserts recommend against diuretic administration to this population. This paper sought to establish if those with an allergy to sulfa-containing antibiotics (e.g. sulfamethoxazole or trimethoprim-sulfamethoxazole) would be more likely to suffer a drug reaction to sulfonamide-containing nonantibiotics than those without an established sulfa sensitivity.

### Design, Setting, and Participants

In a retrospective manner, persons exposed to sulfonamide-based medications were identified from the United Kingdom General Practice Research Database, a validated archive of doctor-patient encounters. Among individuals prescribed an agent of interest, diagnostic codes consistent with a drug allergy were culled if they occurred within 1 month of medication receipt. Identification of allergic reactions relied upon patient reporting. Pfizer supported the study.

### Results

- Study characteristics: 20,250 persons included. 70% women. Prescribed agents included sulfamethoxazole, thiazides, and loop diuretics. Further population characteristics were lacking.
- Including all-comers, 5% reported a hypersensitivity reaction after sulfonamide antimicrobial ingestion and 2% after receipt of a sulfonamide nonantimicrobial.
- Among those who tolerated the sulfa antimicrobial, 1.5% reported a reaction to the ensuing sulfa nonantimicrobial. Among those with an allergic reaction to the sulfa antibiotic, 10% exhibited a hypersensitivity response when given a sulfa nonantibiotic.
- If an individual tolerated the sulfa antimicrobial, she had a 2% chance of experiencing an allergy to penicillin. If she developed a reaction to the sulfa antibiotic, there was a 14% chance of having a similar reaction to penicillin.
- These associations was preserved after adjusting for confounders.

### Clinical Perspective

- This paper has allowed me to exercise greater discretion in the prescription of diuretics to patients with a sulfa allergy. As the [American College of Allergy](#) states, "There is no evidence to suggest allergic cross-reactivity between sulfonamide antibiotics and nonantibiotic sulfonamides."
- While many of us sidestep this dilemma by writing for ethacrynic acid, an agent devoid of sulfa, it is inferior to traditional diuretics.
- My practice is to elicit a thorough drug allergy history and assess for further risk factors (e.g. prior history of allergic drug reactions, female sex, etc.). If uncertain, I refer the individual to an allergist. This ensures that only those with severe reactions will be disqualified from receiving a thiazide or loop diuretic, therapies indispensable for blood pressure and volume control.
- How can one explain the study's findings? If both the antibiotic and nonantibiotic share a sulfonamide component, why would the rates of hypersensitivity to each differ among treatment-naive individuals? It is because "sulfa" is an imprecise term referring to multiple compounds. If this were the case then magnesium sulfate (containing sulfuric acid) and omeprazole (containing elemental sulfur) would be contraindicated. Rather, it is believed that the presence of both a sulfonamide and an arylamine component are necessary to generate an immunologic response. While sulfa antibiotics contain both, diuretics contain only the sulfonamide portion.
- If the above is true, then why did persons with allergies to sulfa antibiotics react more frequently to sulfa nonantibiotics? The higher incidence of an allergic response reflects an immunologic predisposition to medication allergies. This would account for the observation that patients with a sulfa allergy experienced a higher rate of hypersensitivity to penicillin, a structurally unrelated compound.
- Disclosures: I have no conflicts to declare.