

## 'Sulfur allergy'

The term 'sulfur allergy' is confusing and may lead to patients believing that they are allergic to all sulfur-containing medications or preservatives, and even to sulfur, an important building block of life. We are often asked, "Can a patient with a sulfur allergy have medication containing sulfur?" and, "What other drugs is the patient likely to be allergic to?" The aim of this bulletin is to clarify the term "sulfur allergy" and the allergies sometimes grouped together under this mantle; sulfonamide, sulfite and sulfate allergies.

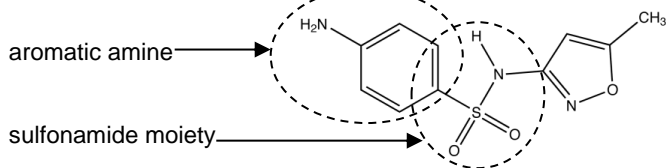
### Sulfonamide allergy- most common 'sulfur allergy'

Sulfonamide is the generic name for derivatives of sulfanilamide (PABA sulfonamide). It usually refers to the sulfonamide antimicrobials, which were introduced in the 1930s, such as sulfamethoxazole (often combined with trimethoprim as co-trimoxazole) and sulfacetamide (used topically e.g. to treat eye infections).

The incidence of this allergy is rare in the general population (<0.01% of treatment courses) but can be very high in patients with HIV (up to 60%). Hypersensitivity to sulfonamides usually develops 1 to 2 weeks after starting the drug, and is characterised by fever, rash and eosinophilia. Other immunological reactions to sulfonamides include angioedema, hypotension, immune thrombocytopenia, vasculitis and fixed drug eruptions.

The immunogenicity of sulfonamide antimicrobials may be due to the presence of an aromatic amine group (see figure below). Cross-reactivity may therefore occur with other sulfonamides with the same aromatic amine group.

Figure: sulfamethoxazole



### Cross reactivity with other sulfonamides

A number of other drug classes also contain a sulfonamide moiety and there is a concern that there may be a risk of cross-reactivity. The small number of case reports of possible allergy may be due to the fact that patients who have had an allergic reaction to one drug, are more likely to have allergic reactions in general. However, the majority of drugs that contain sulfonamides do not contain an aromatic amine (i.e. non aromatic amine sulfonamides, see table below), making cross reactivity unlikely (i.e. dissimilar chemical structure).

Table: Non aromatic amine sulfonamides

- unlikely to cross-react with sulfonamide antimicrobials	
Carbonic anhydrase inhibitors	acetazolamide brinzolamide dorzolamide
Cyclooxygenase 2 (COX-2) inhibitors	celecoxib
Loop diuretics	bumetanide furosemide
Sulfonylureas	glimepiride glipizide
Thiazide diuretics	chlorthalidone indapamide metolazone
Miscellaneous	sulfasalazine

### Sulfite allergy

There is no relationship between sulfite sensitivity and allergy to sulfonamide antimicrobials. However, sulfite allergy occurs in its own right.

Sulfites are used to preserve food, beverages and pharmaceuticals. They can be found in wine, dried fruit, dried vegetables and sometimes sausages and salads. Examples of sulfites used in industry include sulfur dioxide, sodium sulfite, sodium/potassium bisulfite and sodium/potassium metabisulfite. Sulfites can induce anaphylaxis, rash, asthma, seizures and death in sensitive patients. Approximately 10% of asthmatics are sulfite sensitive.

### Sulfate allergy

There is no relationship between sulfate sensitivity and allergy to sulfonamide antimicrobials.

Sulfates can be mildly irritant; however, true allergies are extremely rare. A diagnosis of sulfate allergy should be viewed with suspicion as they can be found in a variety of commonly encountered substances including medications and detergents such as soap, shampoo etc.

### Cautionary tale

There is at least one report in the literature of a sulfonamide allergic patient who started legal proceedings after she was told that her post-operative rash was caused by morphine sulfate and sulfates should not have been prescribed with her history of sulfonamide allergy. However, rashes associated with morphine are not usually allergic in nature but due to the drug itself causing histamine release as part of its pharmacological activity. The incorrect information given to this patient generated avoidable stress.

### Summary

The term "sulfur allergy" should be avoided as it is confusing. The exact agent involved and the patient's reaction to it should be recorded. If you have concerns regarding the use of a particular drug in a patient with a "sulfur" allergy, question the patient further as to the exact nature of their allergy. If the drug causing the "sulfur allergy" cannot be identified, it is possible the allergy is to sulfonamides and thus drugs suspected of cross-reactivity in sulfonamide-allergic patients should be used cautiously. If a patient has a sulfite allergy they will probably have much more detailed information regarding the cause and nature of the allergy because their exposure risk is much higher due to the presence of sulfites in foods etc.

Finally, it seems increasingly clear that patients allergic to one drug are more likely to be allergic to another, regardless of chemical structure.