

## Sulfur Allergy

There is much confusion about what constitutes "sulfur allergy" and its clinical significance. 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?" This bulletin discusses the meaning of "sulfur allergy" (note sulfur is the internationally agreed spelling of sulfa or sulphur) and the allergies often grouped together under this mantle. i.e.

- Sulfonamide allergy
- Sulfite allergy
- Sulfate allergy

### Sulfonamide allergy

The most common "sulfur allergy" is that to a sulfonamide drug. Sulfonamide is a generic name for derivatives of sulfanilamide (PABA sulfonamide). It usually refers to sulfonamide antimicrobial agents that include sulfamethoxazole, often combined with trimethoprim as co-trimoxazole, and sulfacetamide, used topically to treat eye infections. Patients who are allergic tend to react to the aromatic amine portion in the sulfonamide molecule and the incidence is < 0.01% of treatment courses. Hypersensitivity to sulfonamides usually develops 2 to 8 weeks after starting the drug, and fever is often the first clinical sign, followed by rash and internal organ involvement. Other immunological reactions to sulfonamides include angioedema, hypotension, immune thrombocytopenia, vasculitis and fixed drug eruptions.

### Cross reactivity

Sulfonamide allergic patients are thought to have a higher risk of allergic reactions to other derivatives of sulfanilamide such as sulfonyleureas, thiazide diuretics, loop diuretics, carbonic anhydrase inhibitors and possibly celecoxib. Possible cross-reacting drugs are:

<b>Carbonic anhydrase inhibitors</b>	acetazolamide, dorzolamide
<b>Loop Diuretics</b>	bumetanide, frusemide
<b>Sulphonamides (systemic or topical)</b>	sulfacetamide, sulfadiazine sulfamethoxazole, sulfasalazine
<b>Sulfonyleureas</b>	glibenclamide, gliclazide, glipizide, tolbutamide
<b>Miscellaneous</b>	celecoxib

### BUT

Recently it has been suggested that sulfonamide-allergic patients have a higher risk of allergic reactions to drugs in general e.g., penicillin, rather than only drugs containing a  $\text{SO}_2\text{NH}_2$  moiety, and that cross-reactive "sulfonamide allergy" is "based on myth at best". However, until better information is available it is probably still prudent to avoid those drugs suspected of having cross allergenicity, where possible.

### Sulfite allergy

Some patients react to sulfites that are used to preserve food, beverages and pharmaceuticals. 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

Sulfate allergies are extremely rare and sulphates are so common that this diagnosis should be interpreted with caution.

### 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.

### Postscript

It is also interesting that the rate of allergic reactions to sulfonamides is 10 times higher in the HIV positive population than in the general population.

### Summary

It is probably best to avoid the term "sulfur allergy" as it is confusing. It is better to record the exact agent involved and the patient's reaction. 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.