

## Severe Cutaneous Adverse Reactions and their Prevention

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### Opinion Article

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### DESCRIPTION

A class of potentially fatal adverse medication events known as Severe Cutaneous Reactions (SCARs) affect the skin and mucous membranes of numerous body openings, including the eyes, ears, nose, mouth, and lips. SCARs can cause substantial harm to internal organs in more extreme circumstances. Toxic Epidermal Necrolysis (TEN), Stevens- Johnson/Toxic Epidermal Necrolysis Overlap Syndrome (SJS/TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome, also known as Drug-Induced Hypersensitivity Syndrome (DIHS), and acute generalised exanthematous pustulosis are the five syndromes included in SCARs (AGEP). The five illnesses share similar pathophysiologies, or disease-causing mechanisms, for which novel approaches are being developed or used to identify those inclined to experience the side effects of particular medications that cause SCARs. Although they are not included in the SCARs category, Maculopapular Rash (MPR) is a less well-defined and benign type of drug-induced adverse skin reactions. It has a pathophysiology with SCARs and is brought on by some of the same medications that do so.

Up to 20% of inpatients and 25% of outpatients are thought to experience serious therapeutic issues related to adverse medication reactions. Ninety percent of these negative effects are benign morbilliform rash hypersensitivity drug reactions, including MPR. They also incorporate more severe reactions, though: The Type I, Type II, and Type III hypersensitivity reactions of the adaptive immune system, mediated by IgE, IgG, and/or IgM antibodies and the Type IV hypersensitivity reactions of the innate immune system, SCARs and MPR, which are Type IV hypersensitivity reactions of the innate immune system initiated by lymphocytes of the T cell type and mediated by different leukocyte subtypes.

Off-target drug reactions also known as type IV hypersensitivity reactions, occur when a pharmacological toxicity affects a biological target that is not its intended target. They are T cell-initiated delayed hypersensitivity reactions that happen only in certain people who may be predisposed to them due to the Human Leukocyte Antigens (HLA) or T-cell receptors they express that are based on genetics, the effectiveness of how well they absorb, distribute to tissues, metabolise, and eliminate a drug or drug metabolite, or other less well-defined idiosyncrasies.

Before starting a course of treatment with a specific SCARs-inducing medication, it is advised that patients be tested for the expression of specific variant alleles of the HLA genes. The screening of populations with extremely low incidences of expressing the variant allele is seen as cost-ineffective, hence these guidelines normally only apply to certain populations that have a significant likelihood of expressing the suggested variation. Patients who display the HLA allele linked to medication sensitivity shouldn't be treated with the medicine.

- Before administering carbamazepine to specific Asian communities, the Taiwan and US Food and Drug Administrations advise HLA-B\*15:02 screening. This has been put into practise in numerous hospitals throughout Thailand and Mainland China, as well as in Taiwan, Hong Kong, and Singapore.
- Allopurinol: HLA-B\*58:01 screening is advised prior to allopurinol medication according to American College of Rheumatology guidelines for the management of gout. Numerous hospitals in Taiwan, Hong Kong, Thailand, and Mainland China offer this service.
- Abacavir: When treating HIV with abacovir in Caucasian populations, the US Food and Drug Administration advises HLA-B\*57:01 screening. This screening is frequently used. Additionally, it has been recommended that everyone who has been identified to express this HLA serotype forgo abacovir therapy.
- The cost-effectiveness of genetic testing for HLA-B\*13:01 to avoid dapsone-induced SCARs is currently being studied in studies in China and Indonesia. In Taiwan, similar studies are being conducted to stop phenytoin-induced SCARs in people who express the CYP2C9\*3 allele of CYP2C9 or a number of HLA alleles.