DIISOCYANATES PANEL

Scientific Information Statement (with references)

Patch Testing For TDI

Dermatitis may occur as a result of exposure to chemicals in the workplace. Approximately 30 percent of cases of chemical dermatitis are classified as allergic contact dermatitis (ACD). Irritant contact dermatitis (ICD), due to the irritant effect of chemicals, is much more common.1,2 Toluene diisocyanate (TDI) is one of many chemicals that is both a weak skin sensitizer and an irritant.3 Patch testing is widely used to establish a causal relationship between ACD and a specific causative agent, and to differentiate between ACD and ICD, which often is not possible on clinical or even histological grounds.3

Background

There currently are three widely used, standardized patch tests: 1) Finn Chamber, 2) True Test, and 3) Epiquick. There is approximately 67 percent concordance of results among these methods.4 In these tests, the suspected sensitizing agent is dissolved in a solvent and diluted to a concentration that will not cause irritation. A patch containing the diluted agent is applied to the skin and read at 48, 72 and 96 hours. The patch test is interpreted based on the observation of redness, itching and hardening of the skin at the site of the patch.3,4 Given the importance of patch testing in diagnosing ACD, organizations, such as the International Contact Dermatitis Group, have recommended the use of a standard methodology for the test and its interpretation.3 However, standardized test concentrations have been published only for the most common of the approximately 100 environmental substances that are frequently associated with ACD.4 This is in contrast to the 2200 chemicals (out of 2-3 million chemicals) that have been identified as sensitizers.4 Diisocyanates, including TDI, although associated with dermal sensitization are not among the commonly implicated substances for which standardized concentrations have been developed. At most, there have been only a handful of reports of ACD due to diisocyanates. TDI, in particular, is a known skin irritant 6 and has been characterized as a very week skin irritant and sensitizer, causing dermatitis only as a consequence of grossly insufficient workplace hygiene.5 In a series of 360 patients whose skin was tested for ACD to plastics and glues, TDI was found to elicit an allergic response in 0.8% while inducing an irritant reaction in 1.9% of the cases.9

Accuracy and Validity of Patch Testing

The accuracy or validity of the patch test is determined by its ability to truly diagnose those individuals with ACD, which defines the sensitivity of the test, and to eliminate those without it, which is the specificity of the test. A number of factors effect the accuracy of patch testing, including pre-selection of patients by a physician, selection of allergen, appliance vehicle, and, finally, proper technique.4 Even when the test is performed using the recommended methodology and standard series of allergens with a high pre-test probability that the patient has ACD, false positive and false negative results may be encountered.3 There is greater uncertainty in interpreting patch test results when less common allergens are used,

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* Material Safety Data Sheets, available from TDI suppliers, provide additional health and safety information regarding this chemical.
particularly if the test substance is also an irritant.\textsuperscript{2} It is well known that TDI is a weak skin irritant.\textsuperscript{5} The concentration that is used in the procedure is vitally important for the following reasons:

- At a given concentration of a material there might be 5 percent of individuals that will show a response but do not have ACD (false positives) and 5 percent of individuals with ACD to the material that will not respond (false negatives). This is considered to be good test performance.\textsuperscript{3}

- If an irritating concentration of the chemical is used in the testing, there will be an overlap of the irritant and the allergic responses. This overlap results in a much higher percentage of false positives, unless the concentration is set very low, which increases the risk of false negatives.\textsuperscript{3}

- Standard panels of allergens have been studied in diseased and reference populations. This is not often the case with less commonly used substances. To establish the validity of the test concentrations for such chemicals, “it is common practice to test 20 [control] subjects,” taking steps to ensure that they will not be injured by the test.\textsuperscript{3}

- There may be a risk of sensitizing someone through patch testing, especially if it is not conducted using standard concentrations. Accordingly, “such patch tests must not be applied indiscriminately since the induction of ACD may result in chronic disability for the test subject.”\textsuperscript{3}

Diisocyanates are among the substances for which no generally accepted, standardized patch test method has been adopted. Various concentrations have been recommended and used. For TDI, concentrations have ranged from 0.1\textsuperscript{7} to 2 percent.\textsuperscript{8} As an example of the difficulty of interpreting patch testing results, one case has been reported to have a negative result with TDI at 0.1 percent while at 0.5 percent concentration a positive result was seen.\textsuperscript{5} Irritant reactions have also been reported to be more common than allergic responses.\textsuperscript{9}

**Summary**

Patch testing can be used effectively as a diagnostic test if patients are properly selected, and tested against standard antigens. There are real limitations in the validity of the test results if non-standard antigens are used without hands-on experience with the test methodology. Care in performing the test is important to reduce spurious irritant responses. In the case of an irritant chemical, such as TDI, it is not always possible to differentiate between irritant and allergic contact dermatitis through patch testing. In diagnosing ACD, patch test results should always be correlated with the patient’s symptoms and a dermatologist’s examination.

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References