

## DIFFERENTIAL DIAGNOSIS – NEGATIVE REACTIONS

Negative reactions to patch testing are common. Between 38% and 77% of patients can test negative to the 28 common allergens and allergen mixes included in T.R.U.E. TEST (Cohen *et al.*, 1997; Marks *et al.*, 1998). Therefore, patients should be informed about the possibility of negative test results during pretest counseling. Physicians should also discuss with patients the value of negative tests, which can be helpful in diagnosing a patient's skin condition.

**True Negatives:** When performed and read according to international guidelines, true negative reactions provide important information to help diagnose a patient's condition and guide treatment. True negatives are characterized by no reaction to a test allergen, and the absence of history or symptoms suggesting a contact allergy to that substance.

### **True negative T.R.U.E. TEST results can add the following clinical value:**

- Indications that patients are not allergic to common allergens responsible for most cases of allergic contact dermatitis
- Redirection of the clinical investigation toward other irritants, allergens or underlying conditions (e.g., contact urticaria)
- Reassurance for patients that their skin condition is not caused by common allergens
- Fewer restrictions on patient; use of products that contain these common allergens

The percentage of patients that are truly negative with no clinical evidence of allergy (i.e., patch test specificity), has been estimated at 80% (Nethercott, 1994). However, patch test specificity varies greatly with the type of allergen, test conditions and test frequency.

In some patients, T.R.U.E. TEST reactions are negative or doubtful, but their symptoms and history strongly suggest a contact allergy. Physicians should also consider other possibilities, including other potential allergens or conditions such as atopic dermatitis or irritant dermatitis.

Remember that even when individual allergens and mixes are considered, T.R.U.E. TEST only includes 51 of 3700 known allergens. Therefore, consideration should be given to patch testing patients with additional allergens using Finn Chambers. As needed, refer patients to a specialist with training and experience in contact allergy testing (e.g., members of the American Contact Dermatitis Society).

**When discussing negative T.R.U.E. TEST results, provide patients a copy of “A Negative Test Result” (Section 9) and advise them that:**

- Their skin condition is not caused by common allergens, which reduces restrictions on their use of consumer, commercial and health care products;
- Negative results are common and occur in more than 25% of patients who undergo patch testing;
- Negative results can still help diagnose their condition and refine their treatment;
- Reactions can still occur to other allergens, possibly requiring additional testing;
- Skin may still be irritated by substances and environments at home or at work, requiring alternative products or avoidance strategies;
- Skin must be cared for properly, taking into consideration alternative skin care products; and
- To contact a physician if they suspect product-related reactions again.

**False Negatives:** Not all negative reactions are true negatives. Based on generalized estimates (Nethcott, 1994), false negative results may occur in 30% of patch-tested patients. To minimize the risk of false negatives, T.R.U.E. TEST uses standardized amounts of allergens and allergen mixes and controls the composition, concentration and associated vehicles. Consistent with this, studies have shown that T.R.U.E. TEST results are very reproducible, with discordant reactions observed in less than 5% of patients (Ale & Maibach, 2004).

**False negative reactions to T.R.U.E. TEST may occur for several reasons, including the following:**

- Lack of a second and later reading (especially neomycin and *p*-phenylenediamine)
- Test panel was removed too soon, (before 48 hours)
- Use of topical corticosteroids on the test site
- Use of oral corticosteroids (equivalent to 15 mg of prednisolone)
- Insufficient contact between the allergen patch and skin
- Effect of UV light (photosensitization or tanned skin)
- Absence of adjuvant factors involved in eruptions
- Allergen concentration is too low for a reaction

The duration of patch test exposure and reaction development can be critical: Because some positive allergic reactions only appear after the third day, it is essential to perform additional readings at later time points. In patients who sweat heavily or wet T.R.U.E. TEST panels while bathing, skin contact with test panels may be reduced, influencing the validity of test results.

Physicians may consider retesting the patient depending on patient history, symptoms and testing conditions. Retesting may be of greater value when patch test application or care is suspect and reactions are likely to be clinically relevant.

If the reaction has little clinical relevance, interpret doubtful reactions with caution. Remember that the safety and efficacy of repetitive testing are unknown, and that the benefit of repeat testing should be weighed against the possible risk of sensitization.

If patients undergo a second series of patch tests immediately, select a new test site for T.R.U.E. TEST application. Alternatively, the same site may be retested after a 3-week clearing period, provided the site remains free of significant scarring, skin disease, tanning or other conditions that might effect test results.

Skin condition and immune responsiveness are important factors: Both are adversely influenced by ultraviolet light exposure (e.g., tanning and photosensitization). Some pharmacologic agents can have immunosuppressive activity and results should be interpreted carefully in patients taking these medications. Patients must also stop using topical corticosteroids on test sites and avoid using oral corticosteroids for at least 2 weeks prior to testing.

Occasionally, the concentration of the allergen used is too low to elicit a detectable skin response. This may be especially true for some weakly sensitized patients in whom the focal allergen application in patch tests may be below their symptom elicitation threshold. In real life, patients often react to allergen exposure occurring over large areas of skin or through broken skin.

## DIAGNOSTIC PATH FOR NEGATIVE REACTIONS

