Commentary and update: Cutaneous sensitivity to monoglyceryl para-aminobenzoate

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Para-aminobenzoic acid (PABA) and its esters are used extensively in commercial sunscreen lotions. The most widely used esters include monoglyceryl PABA, amyl dimethyl PABA (Padimate A), and octyl dimethyl PABA (Padimate O). These compounds absorb ultraviolet light in the 290–320 nm wavelength spectrum. This property is the basis of their photoprotective effect in sunscreens, since it effectively shields the surface of the skin from ultraviolet light in the principal sunburning spectrum.

Curtis and Crawford[1] were among the first to recognize that PABA and its esters were important potential allergic contact sensitizers. They based their conclusions on 48-hour occlusive patch tests, with a single reading at 72 hours. Their studies have subsequently expanded to include allergic photocontact dermatitis.[2–5] It seems paradoxical that a substance that "photoprotects" may cause photoallergic contact dermatitis. However, the ability to absorb ultraviolet light is prerequisite to the development of photoallergy. The sunscreen vehicle may also influence its development.[5] Photoallergic sensitization can occur independently of simple contact dermatitis. Controlled study requires covering the patch-test site with a light impermeable material until the time of the final reading, a procedure not followed in Curtis and Crawford's[1] case report. Experience has since shown that inadvertent light exposure between removal of a patch test and the time of final reading may be sufficient to convert a control, "nonlight exposed" patch test into a positive one, if the substance is a true photosensitizer. Either should be suspected when underlying endogenous photodermatitis, treated with sunscreens, fails to improve or clinically worsens.

Curtis and Crawford[1] attempted to define clinical cross-reactivity in their patient, found positive patch test reactions to benzocaine, PABA, aniline, and paraphenylenediamine (in addition to monoglyceryl PABA), then compared their experience to that of other investigators. Their observations, and those of others, form the basis for defining the clinical spectrum of cross-sensitivity for this important class of compounds. Chemical substances that have been reported to cross-react with PABA and its esters include a wide range of therapeutic agents, both oral and topical: anesthetic agents based on esters of aminobenzoic acid (benzocaine, tetracaine, procaine, proparacaine, benoxinate); para-amino type azo dyes (paraphenylenediamine, aniline); sulfonamide antibiotics; sulfonamide-based hypoglycemics; thiazide diuretics; and artificial sweeteners (saccharin, sodium cyclamate). However, benzoic acid esters (parabens, cocaine, piperocaine), lacking an amine group in the para position, have never demonstrated clinical cross-reactivity.

The problems of determining clinical cross-reactivity on the basis of patch testing have since proved to be enormous. For convenience, multiple patch tests of "related" chemicals are usually applied at one time. We now know that simultaneous positive patch test reactions may include false-positive reactions, due to the nonspecific influence of inflammation at one patch-test site on the reactivity at another. This phenomenon has been dubbed the "angry back" or "excited

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skin" syndrome.[6,7] To differentiate such false-positive reactions, multiple positive reactions must be retested individually after inflammation has subsided. This is extremely time consuming and inconvenient. Undoubtedly, the results of many early studies of cross-reactivity of PABA were affected by this phenomenon. It is difficult to predict how certain sulfa derivatives (diuretics, hypoglycemics, sweeteners), which lack an amine group in the para position of their aromatic rings, might cross-react, but practical experience has not shown this to be a problem. Fisher[8] reported that residual impurities in substances synthesized from PABA may result in "cross-reactivity" from a single allergen impurity, in contradistinction to true cross-reactivity between related substances. He found an almost 100% cross-reactivity between benzocaine and monoglyceryl PABA. Consultation with the manufacturer of the PABA ester revealed small amounts of benzocaine in the commercial monoglyceryl PABA preparation. Removal of residual benzocaine from this preparation virtually eliminated "cross-reactivity."[9]

Curtis and Crawford[1] observed an eczematous reaction in their patient following ingestion of 100 mg of PABA; this appears to be the only such report. PABA is available in "health food" stores, in tablet form as a food supplement. As our society becomes increasingly "health conscious," PABA consumption is almost certain to increase. We would do well to remember the experience of Curtis and Crawford.

References

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