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maximization test: a procedure for screening and rating contact sensitizers. J. Invest. Dermatol. 47:393-409, 1966.

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A new bioassay method, termed the "maximization test," is described and its application to the testing of a number of well-known substances is recorded. [The SCI® indicates that this paper has been cited in over 320 publications since 1966.]

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Human skin is exposed to an enormous variety of chemical substances. Ordinary skin care entails contact with complex perfumes, multiple-ingredient creams, soaps, shampoos, sunscreens, deodorants, antiperspirants, and other substances. Moreover, skin disorders are common and are treated with many different topical drugs.

Adverse reactions to cosmetics, toiletries, and drugs are frequent. Of these, contact sensitization is the most distressing and may persist indefinitely unless the allergen is identified. Virtually all substances can sensitize some persons. It is important to be able to determine the allergenic potential of topical agents prior to their entrance into the channels of commerce.

When I began my work, the accepted procedure was the Draize test, which required repeated, occlusive exposures on panels of 200 persons each.1 This is onerous and expensive. Draize worked for the FDA and, not surprisingly, this situation gave authority and semi-legal status to his test, a procedure used worldwide for decades. Everyone rather reasonably supposed that Draize had tested a variety of known allergens and had developed his "repeated-insult" methodology on the basis of its proven capability for detecting contact allergens. Curiously, not a scrap of data had been presented for public scrutiny. I could not find out how he had arrived at the number of 200 subjects nor the specification of 10- to 48-hour exposures. I could not quiet my suspicion that the Draize test was often performed on paper; it was especially difficult to imagine how busy practitioners could test 200 subjects 10 times (2,000 visits).

My suspicion was confirmed on several occasions, the most spectacular relating to the incorporation in toiletries of tetrachlorsalicylanilide, a bacteriostat and a potent contact and photo-contact sensitizer.² The manufacturer averred that five Draize tests had been conducted (1,000 subjects!) by testing laboratories with no instances of sensitization. A conscientious test on 20 subjects would have revealed the allergenic capacity of this malevolent chemical that caused havoc in England.

Being a constitutional iconoclast, I set about to find out whether the Draize test could identify topical agents that dermatologists had come to recognize as significant allergens, including neomycin, benzocaine, nitrofurans, ammoniated mercury, penicillin, substituted hydroquinones, and others. The result was unequivocal: the test lacked sensitivity and could not pick up familiar troublemakers. The Draize test could not stand up to testing.

My next task was to develop a procedure that could reliably identify contact allergens on a small number of volunteers. I took advantage of the fact that damaged skin is more easily sensitized. I pretreated the test sites with an anionic surfactant, sodium lauryl sulfate; this provoked an inflammatory response and also made the skin highly permeable to the test materials. I was able to show that even mild allergens could be reliably identified by 5- to 48-hour exposures on a panel of 25 subjects. I and others have modified the procedure but the basics remain.3 The popularity of the test rests on its feasibility and reliability.

The moral of this story is that regulatory procedures issuing from government institutions cannot be exempt from one of the holiest structures of the scientific enterprise, namely, repeatability by other persons.

How could an insensitive method be so widely accepted? My dark answer is because of its insensitivity. A negative result is reassuring. It spells safety and is comforting to the manufacturer. Silence is tranquilizing. The maximization test, by contrast, is a vexation. It often results in one or more of the test subjects becoming sensitized. This is a troublesome result because one must then undertake an analysis of risk. The data have to be passed through the human mind and judgments have to be made. The maximization test only measures sensitizing potential and does not tell what percentage of people will become sensitized under actual use conditions. The maximization test is by no means a darling among producers of topical skin care products. Some would prefer not to know.

Draize J H. Woodard G & Calvery H O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther. 82:377-90, 1944. (Cited 275 times since 1955.)

^{2.} Wilkinson D S. Photodermatitis due to tetrachlorsalicylanilide. Brit. J. Dermatol. 73:213-19, 1961, (Cited 115 times,) Kligman A M & Epstein W. Updating the maximization test for identifying contact allergens. Contact Dermatitis 1:231-9, 1975. (Cited 100 times.)