EXPERIMENTS IN POISON IVY SENSITIVITY

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SENSITIVITY to poison ivy (*Rhus toxicodendron radicans*) and sensitivity to extracts of this plant have been the objects of numerous clinical and experimental studies. In 1922 Spain[1] and in 1927 Spain and Cooke[2] reported their observations with the use of an alcoholic extract of the dried leaves. These observers, using the patch test, found that 65 per cent of patients over eight years of age were sensitive to the active principle of poison ivy.

Straus,[3, 4] in experiments in infants, found that 72.9 per cent could be specifically sensitized by the application of poison ivy extracts to the normal or abraded skin.

Taking the figure reported by Spain, namely, 65 per cent of individuals with poison ivy sensitivity, it seems remarkable, in view of the frequency of exposure, that the incidence of clinical poison ivy dermatitis is not even greater than is actually the case. In a recent article, Spain, Newell, and Meeker[5] again called attention to the fact that the incidence of positive tests was, in their experiments, a function of the concentration of extract employed. Recent unpublished experiments performed by us have confirmed their findings on this point.

The following observations are reported as possibly throwing some light on certain other aspects of contact dermatitis in general and particularly on deliberate experimental poison ivy sensitization in an adult.

TECHNIC

We employed an acetone extract of poison ivy leaves, kindly prepared for us by Charles L. Cowles of Lederle Laboratories. The undiluted extract contained 8 per cent solids. In performing our tests (which were patch tests applied by the usual well-known technic—which now differs slightly from that employed by Spain and Cooke), we used the undiluted extract and acetone dilutions ranging from 1:10 to 1:1,000,000. All test sites were read at regular intervals of twenty-four hours, and were recorded as negative if no reaction appeared at any time within fourteen days after application.

The positive reactions were all eczematous in character, ranging from slight erythema to vesicular, bullous and edematous, highly inflamed sites with tendency to spreading and dissemination.

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EXPERIMENTS

A. *Experiment demonstrating the deliberate production of typical eczematous hypersensitivity to poison ivy in an individual who had no previous contact with poison ivy allergen.* In this study, one of us was the experimental object.

H. F., thirty years of age, had no history of poison ivy or other dermatitis, no atopic history, and no history of other pertinent findings. He had been born and had lived uninterruptedly in Germany. He arrived in America for the first time in March, 1934, and had no knowledge of contact with plants or shrubs while in this country.

On July 13, 1934, patch tests with poison ivy extract were applied on the left forearm in the following acetone dilutions: undiluted, 1:10, 1:1,000, 1:10,000, 1:100,000. Fresh poison ivy leaf was also applied. At twenty-four hours no reactions were observed, except the erythema at the site of the undiluted and the 1:10 dilutions. Such reactions were observed on almost all persons to whom these concentrations were applied, and are, therefore, considered nonspecific, primary irritant effects of the concentrated extract. These reactions at the sites of the two strongest concentrations increased in intensity up to the tenth day and then began to spread. At this time, a disseminate poison ivy dermatitis slowly appeared on various parts of the face, trunk, and extremities.

On the tenth day after test application—that is, on the day of the generalization of the dermatitis—the test sites of dilution 1:1,000 and of the leaf began to react (flare-up), and rapidly manifested four-plus reactions. At this time the sites of the higher dilutions evidenced no reaction. On June 22, 1935, that is, slightly under one year after the described experimental sensitization, H. F. was again tested with ascending concentrations of the ivy extract, in a manner identical with the first applications. This time, the reactions at the twenty-four-hour reading were as follows:

1:1,000,000	+
1:100,000	++
1:10,000	+++
1:1,000	+++
1:100	+++
1:10	+++
Undiluted (8% solids)	+++

Within the next twenty-four hours, the dilutions 1:1,000,000 and 1:100,000 also showed three-plus reactions.

Repetition of these tests on July 3, i.e., eleven days later, gave identical results. The reactions were again positive, even to the high dilutions, after a lapse of twenty-four to forty-eight hours. A patch test with a fresh leaf was also strongly positive within sixteen (!) hours.

This experiment shows that high concentrations of an acetone extract of poison ivy can sensitize an adult not previously sensitive, when applied by means of skin tests. The higher concentrations employed were manifestly primary irritants and could be shown to cause non-sensitization types of irritation of the skin in practically all persons.

The period of incubation of sensitivity was approximately ten days, as shown by the interval between the application of the first tests and the appearance of the generalized dermatitis, as well as of the reaction to the higher, not primary irritant, dilutions, and of the reaction to the leaf itself.

On retesting with higher dilutions, the reaction time was from twenty-four to forty-eight hours, as is normal for reactions to patch tests on skin previously sensitized.

These findings in an adult correspond closely to those of Straus[3, 4] in experimental rhus sensitization in infants, and are identical with those of Sulzberger and Wise[6], in butesin picrate dermatitis, regarding (a) the period of incubation of sensitivity, and (b) the reaction time.

B. *Experiment demonstrating the variability in response to patch tests in one and the same specifically hypersensitive individual.*

During the course of our investigations of the poison ivy sensitivity of experimentally sensitized H. F., we applied quantitative patch tests with the various acetone dilutions of poison ivy extracts at different times and to different skin areas. These repeated tests brought to light an astonishing and extreme variability in response. For example, tests performed with dilutions of 1:1 to 1:1,000,000 on the right forearm elicited marked reactions to all concentrations within forty-eight hours. Corresponding tests applied to the left forearm several days later gave reactions to the higher concentrations only, and even these were of very slight intensity. About one week later, the same tests applied simultaneously to the right and left arm (symmetrical areas on the forearms) again showed varying results. This time, the left arm reacted more strongly, showing reactions up to and including a 1:1,000,000 dilution, while the right arm reacted less strongly, there being no response at a 1:1,000,000 or 1:100,000 dilution.

In addition to these chronologic fluctuations in hypersensitivity, there were variations in the reaction to patch tests apparently dependent not on the time, but entirely upon the site or locality to which the test was applied. For example, tests applied with the following concentrations, 1:1,000, 1:10,000, 1:100,000, 1:1,000,000 on the right forearm, showed no reaction at the site to which 1:100,000 had been applied, while all the other areas reacted. This experiment, repeated in identical areas fifty-three days later, gave identical results. That is to say, while all other areas reacted to the applied tests, the pre-

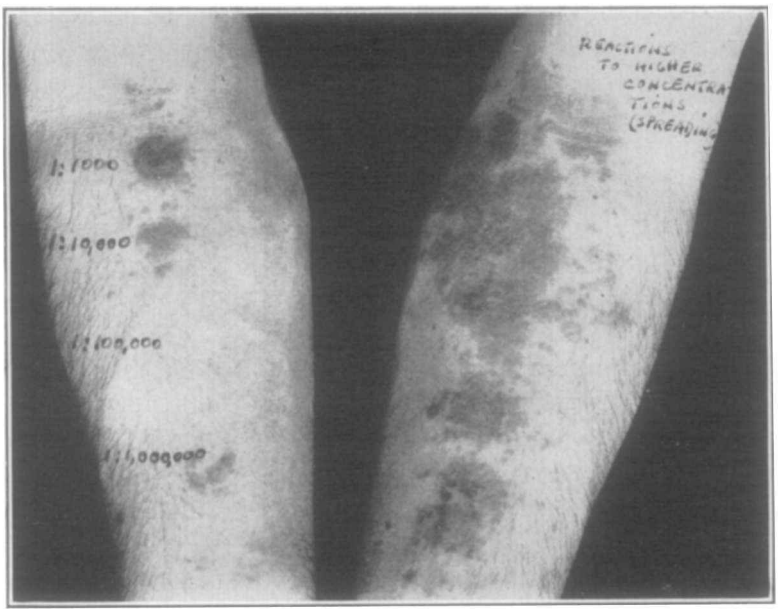

Fig. 1.—Patch test reactions to dilutions of poison ivy extract in H. F. Note flexor surface of right forearm with complete lack of reaction at 1:100,000 site. Tests forty-eight hours old and read on August 2, 1934.

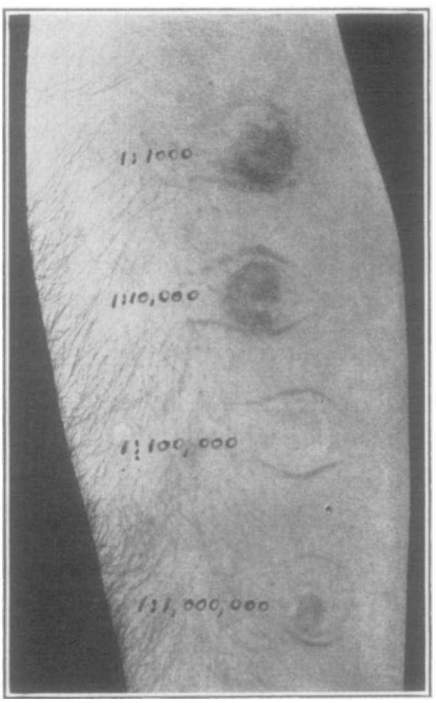

Fig. 2.—Experiment of Fig. 1 repeated on September 24, 1934, with identical result. Note that the same skin area on the right forearm has again failed to react.

viously refractory area again remained immune and showed not the slightest reaction. (Figs. 1 and 2.)

Similar phenomena of apparently immune areas were observed in patch tests on other parts of the body.

DISCUSSION

The above experiments bring to light a variation in response to patch tests even in an individual experimentally sensitized and known to have become hypersensitive and to have remained hypersensitive to the allergen for a period of about one year's duration.

These variations in response seem to depend, first, upon chronologic fluctuations in the degree of sensitivity, which varied greatly at different times in one and the same area. Second, certain irregularly disseminated, circumscribed skin areas seemed to be consistently less sensitive than others.

This makes it apparent that the result of a patch test may depend to a great degree (a) upon the site chosen for testing, and (b) upon the time of application of the test (phase of sensitivity). It is obvious that the recognition of these variations serves to corroborate many observations continually puzzling the users of the patch test. Among these may be mentioned the discrepancies between reactions observed by one investigator and not seen by the next one even though employing an identical and correct technic on the very same patient; also, the differences of reaction seen in the same patient by the same observer at different times and at different sites; and, still more important, it may explain certain false negatives obtained with patch tests even though applied and read correctly—by chance, the test may have been applied to relatively immune (refractory) skin area. Unfortunately these unpredictable spontaneous chronologic fluctuations, as well as the variations of sensitivity dependent on localization, would seem to make it nearly impossible to evaluate variations in response even to the most careful quantitative testing, unless the tests are repeated many times and in many different areas, as they were in our case.

SUMMARY

A person presumably never previously in contact with poison ivy was experimentally sensitized by the application of skin tests with an 8 per cent acetone extract of the leaf. The incubation period required for the development of this induced eczematous hypersensitivity was nine to ten days.

When this same individual was patch tested after the skin had become sensitized, the time required for the development of the clinically manifest skin reaction was regularly approximately twenty-four to seventy-two hours, depending somewhat upon the concentration of the extract applied.

The sensitization was of such degree that this individual, previously not reacting at forty-eight hours even to concentrations as high as 1:100, later reacted strongly to a 1:1,000,000 dilution of the extract employed.

The test person in this experiment showed marked variations in reaction to the same extracts on repeated patch testing. There were (a) variations depending upon the time of test; and also (b) constant variations depending on the skin area tested.

This result not only warns against drawing too definite conclusions from one or a few patch tests applied at the same time, but also serves to explain certain discrepancies of results and unexplained variations in reactions, as well as false negatives.

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