

CONTACT DERMATITIS DUE TO OIL OF CITRONELLA

REPORT OF 3 CASES WITH EXPERIMENTAL STUDIES ON INGREDIENTS AND RELATED SUBSTANCES¹

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Dermatitis due to the Graminae or tropical grasses, from which are obtained such important essential oils as oil of citronella and lemongrass, seems to be uncommon. Thus, the U. S. Public Health Service had no information regarding dermatitis due to these plants or their oils, including oil of citronella (1). In 1922 Lane (2) recorded an instance of dermatitis of follicular type, due to oil of citronella which had been used as a protection against mosquitoes. The value of this observation would have been considerably enhanced had patch tests been made, since oil of citronella is often combined with other substances. The only other report directly concerned with a related member of this family of grasses is that of Mendelsohn (1). Among a group of dock workers who had unloaded a cargo of lemongrass oil, Mendelsohn observed 8 instances of contact dermatitis due to this oil. Using pieces of pine which had been accidentally contaminated with lemongrass oil, positive patch tests were elicited in 4 of the affected persons. However, no tests were made with an uncontaminated specimen of this oil.

The occurrence of contact dermatitis due to oil of citronella is probably far more common than this scant literature seems to indicate. As these cases are observed chiefly during the summer, they are apt to be attributed to poison ivy or other plants. Moreover, the widespread use of this and related oils in many common commercial products poses questions of considerable interest and complexity. In the cases to be detailed in this paper, it was possible to carry out studies with the chief ingredients in oil of citronella and some related substances. These data provide an introduction to a more detailed analysis of the nature of the dermatitis due to oil of citronella and other essential oils containing similar or identical constituents. These data may be helpful to those who meet with cases of dermatitis due to perfumes in various commercial articles where information on the composition of these products is difficult to obtain.

REPORT OF CASES

Case 1: A man, 69 years of age, was observed in an acute attack of vesicular and edematous dermatitis which was diffusely distributed over the dorsa of the fingers, hands and forearms, with milder erythematous lesions on the anterior surface of the neck. The eruption had appeared four days before observation. No definite history of contact with possibly causative agents, including poison ivy, could be elicited.

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A routine series of patch tests gave negative results, except for a 3 plus vesicular reaction to gum turpentine (50 per cent in mineral oil). However, the patient denied contact with turpentine in any form. About a week later he brought in some oil of citronella which he had smeared over his windows as a protection against mosquitoes. This apparently had been his first experience with oil of citronella and he recalled that the eruption had started the day after he used the oil. He also recalled an attack of eczematous dermatitis on the dorsa of the hands while in the country about twenty-five years before, but did not know the cause of this eruption.

A patch test with oil of citronella compound (50 per cent in mineral oil) gave a vesicular and edematous reaction, graded as 4 plus, and this remained visible for at least ten days.

Additional patch tests were later made with ingredients of this oil and related compounds. With the exception of oil of lemon (10 per cent in acetone), the remaining substances were applied in a concentration of 1 per cent in acetone. The following results were obtained: citronellal, a vesicular reaction graded as 3-4 plus; citronellol, a mild papular response, graded 2 plus; hydroxycitronellal, a slightly more intense response graded 2-3 plus; geraniol, a mild papular erythema graded 1-2 plus; citral, a papular response graded 2 plus; geranyl acetate, 1-2 plus; and oil of lemon, about 2 plus.

The clinical signs of dermatitis faded in about a week under bland therapy. The application of the latter group of patch tests was accompanied by a mild focal itchy sensation on the hands and forearms.

Case 2: A man, 46 years old, a carpenter and maintenance man in a soap factory, acquired an itchy dermatosis about three weeks before observation. The eruption started in the interphalangeal areas and on the dorsa of the hands. Then it spread to the flexor aspects of the forearms and stopped short on the arms at a point just below the short sleeves. When observed, the lesions were erythematous and scaly and were in a stage of regression.

The history obtained was that he had recently handled a new poplar wood. Otherwise, the information elicited was unsatisfactory for the determination of the precise cause. He was therefore instructed to bring in all materials with which he might have come in contact during the preceding six weeks.

Patch tests were made with machine oil, laundry soap, chip dust and Javanella, an oil used to give laundry soap a pleasant odor. All tests were negative except for Javanella which caused a papular erythematous reaction graded as 2 plus. The patient noted itching at the site of application of the Javanella about ten to twelve hours after the patches had been applied. The laundry soap gave an indefinite plus-minus erythema, such as is commonly produced by this soap in control subjects.

When the results of the patch tests were explained to the patient, he recalled that about a month before observation, he had accidentally knocked over a can of Javanella. The oil had smeared his hands which he wiped off with a cloth. He could not recall exactly when the eruption started in relation to this accident. However, two weeks before observation there was a flare-up of the rash after he handled the oil.

Case 3: A woman, 29 years old, was observed Sept. 1942 in a generalized attack of dermatitis venenata, which had occurred one day after going to the country. The case was thought at that time to be due to poison ivy. In July 1943 she came under my observation for the first time, with the history that an eruption had appeared one day after she sat in the grass in the park. There were vesicular lesions on the fingers with linear-like lesions and diffuse bands on the radial aspects of the forearms. Similar vesicular lesions were also present in the cubital spaces, legs, face, eyelids and neck. The eruption on the forearms gave the impression that something had been rubbed on them. On close questioning it was learned that she had used oil of citronella as a spray and also had rubbed it over various parts of the body as a protection against the mosquitoes.

Patch tests showed that the patient was hypersensitive to poison ivy (3-4 plus vesicular reactions to an acetone extract of *Rhus toxicodendron* and 1 per cent 3-geranyl catechol in acetone) (3). Undiluted oil of citronella gave a widespread edematous and vesicular re-

sponse graded as 4 plus. A 50 per cent dilution of Tick, an insecticide containing rotenone, gave a questionable reaction.

Patch tests with the ingredients of oil of citronella and related compounds in a 1 per cent concentration in acetone gave the following results: citronellal, a vesicular reaction graded 3 plus; geraniol, negative; citronellol, a papulovesicular response graded 2-3 plus; hydroxycitronellal, a similar 2-3 plus reaction; geranyl acetate, a mild papular response graded 1-2 plus; and citral, a vesicular reaction graded 3 plus.

The clinical course was one of rapid recovery within ten days.

CONTROL PATCH TEST STUDIES

The clinical features of the positive patch tests in these patients were of the nature of those observed in specifically hypersensitive patients. As further evidence for the specificity of the responses, the substances were applied as patch tests in 26 control subjects afflicted with a variety of skin ailments unrelated to contact dermatitis due to oil of citronella or apparently related materials. Of this group 14 persons were tested with citronellal, citronellol, geraniol, hydroxycitronellal, geranyl acetate, citral, and oil of lemon. These substances were applied in dilutions which had elicited responses in the sensitive patients, and all gave negative responses. The control group of 26 persons was patch tested with undiluted oil of citronella (Ceylon), oil of citronella (Java), Javanella and oil of citronella compound (brought in by case no. 1). The first three of the above substances gave negative responses in 23 of the 26 persons and mild erythemas (primary irritation) in the remaining subjects. The oil of citronella compound elicited negative reactions in 16 persons whereas the remaining 10 subjects showed somewhat more intense erythemas (primary irritation) than was produced by the first three specimens of oil of citronella. It should be stressed that in all cases these erythemas were mild and had to be carefully looked for and that they faded within ninety-six hours. In no instance was this simple erythema in any way comparable with the positive reactions obtained in the cases of dermatitis due to oil of citronella. These data indicate that materials labeled as "oil of citronella" are not necessarily identical, and it is likely that the oil of citronella compound was contaminated by another primarily irritating substances or substances.

One other control person, no. 27, was not included in the above discussion because positive reactions were obtained with some of the aforementioned substances. The details of this case will be given here as the data are of considerable interest.

Case 4: A man, 54 years old, a porter, had a scaly eczematous eruption on the dorsa of the hands and the flexor aspects of the wrists. The dermatosis had appeared several weeks before observation. The case was complicated by a history of eczema of the legs, for which the patient had been previously hospitalized some months before. At first, it was believed that the clinical picture could be attributed to hypersensitiveness to locally applied medications, and, in fact, patch tests showed moderately intense reactions to anaesthesin (ethyl p-amino benzoate) and to butesin picrate. However, the clinical course of the eruption on the hands and wrists seemed to be different from the condition of the legs, and, for this reason, inquiries were directed towards the materials handled by this man in his work. It was learned that he used benzine, floor wax and lemon oil in his job.

The patient was therefore patch-tested with the citronella compounds, with the following results: oil of citronella (Ceylon), 1 plus; oil of citronella (Java), 1 plus; Javanella, 1-2 plus; oil of citronella compound, 2 plus; turpentine (50 per cent in mineral oil), a bullous reaction with numerous vesicles in the periphery, graded 5 plus.

The following week patch tests were applied with geraniol, hydroxycitronellal, geranyl acetate, citronellol, citronellal, citral and oil of lemon in the concentrations used in case 1. These tests were negative, except for oil of lemon which elicited a papulo-vesicular reaction graded as 2-3 plus.

Since oil of lemon contains limonene, citral and citronellal and since the latter two substances gave negative patch tests, it seemed interesting to investigate the nature of this hypersensitiveness as well as that to turpentine. Patch tests were therefore made three days later, with the following results: citral, negative; dipentene (d-1 limonene), 10 per cent in acetone, a widespread erythema with intense edema graded as 1-2 plus; alpha pinene, 20 per cent in mineral oil, a papulo-vesicular reaction graded as 2-3 plus; beta pinene, 10 per cent in mineral oil, a vesicular reaction graded 3 plus; and benzene, 50 per cent in mineral oil, negative.

These data permit the following conclusions: (1) the hypersensitiveness to oil of lemon was directed essentially toward the content of limonene, perhaps also to other related terpenes, but not to the content of citral or citronellal; (2) the hypersensitiveness to oil of turpentine was directed chiefly to beta pinene and to a lesser extent to alpha pinene, both of which are close chemical relatives of limonene; (3) the mild positive reactions to the various citronella oils probably represented mild group responses due to their content of terpene constituents, since the other ingredients, including citronellal and geraniol derivatives as well as citral gave negative reactions.

The patient was advised to stop the use of oil of lemon in his work and the dermatosis on the hands and wrists quickly faded under bland therapy. The eruption on the legs pursued its own independent course.

GENERAL DATA ON THE CITRONELLA OILS

The oils of the Graminae family (tropical grasses) have been known since antiquity when they were used as a fragrance in wines, in ointments and in anointing oils. Large scale exportation to Europe first occurred during the early part of the nineteenth century (4).

Under the genus *Cymbopogon* are included a variety of grasses from which are obtained the oils of citronella, lemongrass, palmarosa, ginger grass and vetiver among others. These oils are utilized in soap perfumery, ointments, hair tonics, deodorizers, disinfectants, as a protection against mosquitoes, and as a cheap source of raw materials that are used alone or as a starting point in the manufacture of more complex perfumes. These oils are complex mixtures of ingredients and show variations in composition depending on various factors.

Among the most important oils in this group are the citronella oils. The chief sources of supply are Ceylon and Java, although similar products can be obtained from other countries. The ordinary commercial oil of citronella comes from Ceylon (*Cymbopogon Nardus*, Rendle), the bulk of which is steam-distilled by the natives. The United States is one of the largest consumers. The oil is colored a light yellow to a yellow brown, but occasionally it has a green hue due to copper impurities. It is a complex mixture of hydrocarbons, oxygenated constituents and terpenes. The chief ingredient is citronellal (6 to 20 per cent), an aldehyde which is largely responsible for the odor of the oil (4, 5). There are also alcohols, mostly in the free form, such as geraniol and citronellol, which also occur in small amounts as esters of acetic and butyric acids. Terpenes to the extent of 10 to 15 per cent are also present (camphene, 1-limonene, and dipentene among others), as well as small amounts of many other ingredients.

The oil of citronella obtained from Java (*Cymbopogon Winterianus*) is colorless or slightly yellow. It is essentially similar to the Ceylon variety and differs only in the percentage composition of the ingredients. Thus, the Java oil of citronella contains a higher

percentage of the aldehyde, citronellal (40-60 per cent) and relatively less of the alcoholic ingredients, such as geraniol (25-30 per cent). There is also a small amount of citral (0.2 per cent). Due to its higher content of citronellal, it has a more intense odor and is more expensive than the variety from Ceylon. For the latter reason, it is less apt to be used in soap perfumery except during wartime when the supply of the cheaper type is exhausted or difficult to obtain.

The quantity of pure oil sold is almost negligible (6). Almost the whole supply is sold in a contaminated form, with the addition of such materials as petroleum products, fatty oils and alcohol among others (4-7). This is important to bear in mind when considering the problem of primary irritation and sensitization in relation to the oils of citronella. It may be noted that the amounts of these oils used in soaps to give a pleasant fresh odor depends on the original odor of the soap itself. Therefore, the amount of essential oil found will vary with different soaps and probably with different batches of the same soap, although the limits of concentration are likely to be narrow. It may be noted also that sometimes oil of citronella may be used to contaminate other essential oils, such as oil of lemongrass.

INGREDIENTS OF OIL OF CITRONELLA AND SOME RELATED SUBSTANCES (8)

Citronellal is the representative aldehyde in oil of citronella and other oils. It is used in lotions, toilet waters and perfumes. Its stability makes it useful in soap perfumery.

Hydroxycitronellal is a synthetic substance and is used in perfumes, cosmetic powders, creams and soaps.

Citronellol, the alcohol corresponding to citronellal, is prepared artificially from rose and geranium oils.

Geraniol is found in many essential oils. It is isolated chiefly from oil of citronella, although the best grade is said to be derived from palmarosa oil. It is extensively used in perfumery and soaps owing to its alkali-resistance. It is sometimes utilized in flavoring for confectionery and candies.

Geranyl acetate occurs in many essential oils and is prepared artificially from geraniol. It is used mainly in soap perfumery, occasionally as a flavoring agent.

Citral is chiefly found in lemongrass oil, to a lesser extent in oil of lemon. The former is the commercial source for citral which is extensively used in the synthesis of the important ionone perfumes. It is also utilized in soap perfumery, cheap colognes as well as in fine perfumery. The specimen used in these studies was probably a mixture of alpha and beta citral, the aldehydes corresponding to the stereoisomeric geraniol and nerol.

Lemon oil is obtained from the peel of *Citrus limonum* (family Rutaceae), which is grown mainly in the Mediterranean countries. The specimen used in my studies came from California. Lemon oil is chiefly composed of terpenes as d-limonene with small amounts of citral and traces of citronellal among many other substances. The odor is due to the relatively small percentage of citral. It is not widely used in soap perfumery, as it must be fixed, otherwise it quickly undergoes resin-formation with loss of odor.

RELATION OF THE INGREDIENTS IN OIL OF CITRONELLA TO DERMATITIS

The detailed studies in cases 1 and 3 revealed clearly that the essential allergen in oil of citronella was the aldehyde, citronellal. The synthetic hydroxycitronellal, which is not present in the oil, also gave positive, though less intense reactions, probably because of its close chemical similarity to citronellal. The unsaturated alcohol, geraniol, which is one of the major constituents in oil of citronella, elicited a weakly positive reaction in case 1 and a negative response in case 3. Geranyl acetate gave relatively mild papular reactions in these cases. On the other hand, citronellol, an unsaturated alcohol similar to geraniol but more closely related to citronellal, elicited far more intense reactions than

geraniol. This is of interest since citronellol is less unsaturated (one double bond) than geraniol (two double bonds). These data may be interpreted as further evidence for the importance of citronellal and derivative configurations.

Citral, the aldehyde corresponding to geraniol, gave moderately positive reactions in cases 1 and 3. It is apparently present in small amounts only in the Java variety of oil of citronella. These reactions are difficult to interpret since the data obtained were inadequate for evaluation of this point. In general, positive responses of this type are due to sensitization to essential oils containing citral or related substances.

GROUP REACTIVITY

The problem of group reactivity among essential oils is complicated by such factors as the variations in composition in natural materials, the frequent contamination of products with other essential oils, the degree of hypersensitiveness of the patient, the chemical relations between the substances in question and other factors. Nevertheless, there are many points of interest which arise from data obtained in such studies.

The positive response to California oil of lemon in case 1 could be explained on the basis of its chemical composition. Oil of lemon contains mostly limonene, with small amounts of citral and traces of citronellal among other ingredients. This patient gave a moderately positive reaction to citral and an intense reaction to citronellal. Important also in this case was the patient's intense hypersensitivity to American gum turpentine. The chief allergenic ingredients of this oil, according to my observations, are the pinenes, alpha and beta, which are chemically related to limonene.

More instructive were the data furnished in case 4 where the patient was intensely hypersensitive to oil of lemon, turpentine and, to a far lesser degree, to the citronella oils. Patch test studies showed that the hypersensitiveness to oil of lemon was due to its content of limonene (negative reactions to citral and citronellal); the hypersensitiveness to gum turpentine was due chiefly to beta pinene and alpha pinene, whereas the mild reactions to the citronella oils were probably based on their content of related terpenes. In general, such relationships can be established only by fractional patch tests, but the data obtained must be carefully evaluated. Thus, in case 3 the positive response to 3-geranyl catechol represented a group reaction commonly observed in persons sensitive to poison ivy to which this patient also gave a positive reaction (9). It is likely that the linkage of a geranyl radicle to a benzene ring, as in 3-geranyl catechol, diminishes or eliminates the possibility of group reactions between this aromatic compound and the aliphatic geranyl derivatives. I have elsewhere (3) recorded an instance showing intensely positive reactions to rhus extract and 3-geranyl catechol but completely negative responses to the ingredients of oil of citronella and some related derivatives.

Several points of practical import arise from studies of this type: 1. Persons sensitive to oil of citronella will probably be unable to tolerate the essential oils obtained from other members of the same family, such as lemongrass oil and, probably also, palmarosa and gingergrass oils. This cross-reactivity ex-

tends also to other essential oils derived from plants of unrelated botanical origin, as *Eucalyptus citriodora* (almost entirely composed of citronellal), geranium oil (contains esters of geraniol) and other oils. This is apart from the factor of contamination by other essential oils.

2. There is considerable evidence to support the view that hypersensitiveness to one essential oil promotes sensitivity to other essential oils containing related chemical ingredients (10).

3. The relationship between sensitivity to oil of citronella and the commercial products which contain this oil can best be considered from a quantitative point of view. Thus, in case 2 the patient was hypersensitive to Javanella (Java oil of citronella) but not to the soap in which it was present in small percentage. This patient had been in contact with the concentrated oil, as a result of which he became only moderately sensitive to Javanella as shown by the moderate response to this substance on patch testing. The soap itself had only a small amount of the oil, about 1 per cent or less, according to the manufacturer. The grade of hypersensitiveness exhibited by this patient was probably not sufficiently pronounced to produce positive responses to the small amount of Javanella in the soap. In all likelihood, however, persons intensely sensitive to Javanella would be unable to tolerate even the small concentration of this oil in the soap. It is also possible that the grade of hypersensitiveness in this patient may increase in time to produce definite intolerance to this soap.

4. Finally, the extent of group reactivity may be as variable in the group of essential oils as it is in persons sensitive to poison ivy or to resorcinol and so forth (9, 11, 12a and b). This point may be determined only by systematic fractional patch tests. For example, sensitivity to limonene and alpha pinene are commonly found in the same patient, but there are instances where cross-reactivity is absent (10).

SUMMARY

Three cases of eczematous contact-type hypersensitiveness to oils of citronella are recorded. In two instances detailed patch test studies were made with the ingredients of oil of citronella and some related substances. The essential allergen in oil of citronella seems to be citronellal, an aliphatic aldehyde with one double bond.

The relationship between oil of citronella and other essential oils are briefly discussed from the point of view of botanical origin, group reactivity and fractional patch tests with the ingredients of oil of citronella and some related substances.

Dermatitis due to oil of citronella is probably far more common than has been suspected heretofore. The widespread use of this and related essential oils in many commercial products poses questions of considerable interest and complexity, and some of these problems are discussed in the article.

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