The Poison Ivy Picker of Pennypack Park: The Continuing Saga of Poison Ivy

William L. Epstein, M.D.
Department of Dermatology, University of California, San Francisco, San Francisco, California, U.S.A.

In 1958, Albert Kligman published three remarkable papers on the subject of poison ivy dermatitis and its prevention [1–3] (Fig 1) that established a benchmark for this modest, if annoying aspect of the clinical practice of dermatology. This review and tribute will attempt to place his contributions in perspective with advances that have occurred in the past quarter century. The paper is divided into scientific sections that subserve the observations made by Kligman.

BOTANY

Some may know that Dr. Kligman was trained in botany before getting his medical degree and that he was, in fact, a world authority on mushrooms, writing a definitive book on the subject that made him a consultant to the mushroom industry for many years. However, he was less well informed about the poison ivy/oak family of plants, and used the misnomer "Rhus" in the title of his papers. This no doubt followed the convention of earlier workers in the field and fit his penchant for brisk, Hemingway-like articulation. A serious botanist fully committed to this problem, William Gillis, investigated the distribution and taxonomy of these weeds and related plants during the 1960s and 70s, and corrected the misconceptions about the family and genus of these plants [4,5]. Poison ivy is correctly called *Toxicodendron radicans,* and poison oak, *Toxicodendron diversilobum;* whereas poison sumac is labeled *Toxicodendron vernix*. Obviously, these botanical tongue twisters are too much for any but an afficionado of the subject, so that most papers now refer to poison ivy/oak dermatitis.

Kligman [1] refers to the most common allergenic plants that cross-react with poison ivy—namely the Japanese lacquer tree; the marking nut of Southeast Asia; the mango rind, which accounts for the "Florida Grin;" and cashew nutshell oil, responsible for swizzel-stick dermatitis and most recently an epidemic of dermatitis in western Pennsylvania caused by Boy Scouts selling improperly prepared cashew nuts [6].

As Gillis [5] showed, although poison oak and poison ivy probably originated in North America, there seems to be a connection to the oriental cross-reacting plants, perhaps via the northern land bridge of ancient times. Also, there is increasing evidence that related plants have appeared in South America in great profusion so that recognition of the plants containing cross-reacting allergens has increased remarkably [7,8]. In addition, urusi (poison ivy) dermatitis has spread to the general population in Japan (Epstein, unpublished observation). The plant also has made its appearance in Europe as an ornamental flower, a vine to shore up the dikes in the Netherlands, and a wild plant in France and Germany responsible for an occasional bout of dermatitis [9].

As Kligman [1] pointed out, "Taxonomic confusion stems from the morphologic variability of the plant." However, because of the yeoman work of Gillis [4,5], it is clear that poison ivy grows mainly east of the Rocky Mountains and poison oak on the western side. In Canada, they tend to disappear as one travels north and the plants have not been reported in Alaska. On the other hand, in Texas, where the Rockies disintegrate, the two plants tend to intermingle. Perhaps the most important practical points are: (1) despite being botanically separable, the clinical reactions to poison oak and poison ivy are the same, and sensitivity to one confers equal sensitivity to the other; and (2) the appearance of these plants is so variable that the weed is distinctive only for a given region. Thus, poison oak from Northern California does not resemble poison oak in Southern California.

CHEMISTRY

Kligman's advantage over previous workers was that Dawson and his group at Columbia had chemically analyzed poison ivy carefully and demonstrated that it contains saturated and unsaturated urushiol with up to 3 double bonds in the carbon side chain attached to position 3 on the catechol ring [10,11]. In addition, Dawson's group had synthesized the saturated component, 3-*n*-pentadecylcatechol (PDC) [12], which was used by Kligman in most of his immunobiologic studies.

Since then, continuing advances in sophisticated technology, including gas/liquid chromatography and mass spectrometry [13], and further modifications [14] have allowed innumerable analyses of the chemicals in these weeds. The upshot of all this is that, in general, poison ivy has a C_{15} side chain; poison oak, a C_{17} side chain; and poison sumac, a C_{13} side chain. In the case of poison oak, the side chain is usually unsaturated, without a trace of heptadecylcatechol, even though it is easily synthesized [15]. Also, it has been confirmed that the side chain determines the specificity of the molecule [16,17], whereas initial binding to tissue proteins depends upon converting the hydroxyl groups at positions 1 and 2 on the ring of 3-*n*-alkylcatechol to quinones [17–19] (Fig 2), so that covalent bonds can be formed. Further analysis revealed that ring positions 4, 5, and 6 are free and available for nucleophilic attack. By selective methylation at the different reactive positions in the catechol ring, regiospecificity in the reactivity of urushiol was demonstrated [15]. Thus, the 6 position reacted only with sulfhydryl groups, whereas the 5 position reacted only with amino groups [15]. These binding preferences on the ring were found to determine the presence or absence of contact sensitization in animal experiments [19]. Thus, continuing analysis of the urushiol molecule has revealed some subtle binding characteristics that explain sensitization and can be used to produce desensitization or tolerance (see below).

Reprint requests to: William L. Epstein, M.D., Department of Dermatology, University of California, San Francisco, HSE 1092, Box 0536, San Francisco, California 94143.

Abbreviation:
PDC: 3-*n*-pentadecylcatechol

0022-202X/87/$03.50

Figure 1. Poison ivy picker of Pennypack Park. Picking poison-filled leaves, Dr. Kligman collects test material.

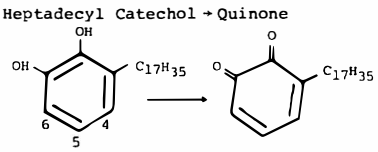

Figure 2. Urushiol in skin is converted in the presence of oxygen to a highly reactive quinone, which then becomes susceptible to regiospecific nucleophilic attack of the ring structure at sites 4, 5, and 6.

BIOLOGY

This section deals with the biologic effects on people of exposure to these poisonous plants, and here Kligman [1] is masterful. With the newer knowledge about the chemical and physical nature of urushiol, he was able to debunk many of the long-standing myths that crowd lay perception of poison oak/ivy dermatitis, and explain the numerous cryptic observations of his predecessors [20–23]. This is the historically classic section of the paper, which should be reread in the original by all young practitioners who wish to tell their patients the *truth* about this subject. A minor point comes up as to where urushiol is distributed in the plant. There is agreement that it is found in the resin canals that course through the roots, vines, and leaves. Whether or not it is distributed into the flowers and berries is less certain. Rodriguez [24], a phytochemist interested in plant allergens, believes that the point has not been rigorously tested. It is well known, however, that the honey produced by bees who feed on poison ivy/oak does not appear to contain allergenically active urushiol. Parenthetically, the honey is quite bitter.

EPIDEMIOLOGY

The earlier observations and Kligman's findings suggested that approximately 50% of the adult population in the United States are clinically sensitive to poison ivy/oak, and this has been borne out by subsequent studies [25]. The observation that blacks appear less reactive than whites, implying they are less readily sensitized by contact allergens, has not been totally supported by more recent conflicting reports [26,27], but clinical experience still insists that blacks are not as likely as whites to complain of acute allergic poison ivy dermatitis. An interesting controversy arose when Epstein and Clairborne reported that orientals born in Asia were less likely than their American compatriots to develop poison oak dermatitis when both groups worked in the United States [28]. This suggestion could hold significant meaning for so-called "natural tolerance" and implies that exposure early in life to cross-reacting, less allergenic chemicals in fruits and plants might induce a state of tolerance. Our studies with urushiol patch tests in new arrivals from the Orient and South America, unfortunately, gave many positive responses and did not support their contention [29].

Regarding the persistence of sensitivity over time, Kligman [1] noted that "the incidence and intensity of poison ivy, usually acquired in childhood, appear to decline proportionally with age." Subsequent studies [30] showed that infants and young children below the age of 5 years are less readily sensitized to PDC than older children. This partially explains why the peak frequency of contact sensitivity to these weeds occurs between the ages of 8 and 14 years. It should be noted, however, that the actual level of skin sensitivity of an individual, as one grows older, is not so clearly known; so that depending upon activity and exposure, a person may become more or less reactive with increasing age [31]. In addition, the clinical finding that contact sensitivity to poison ivy/oak runs in families has been supported by experimental studies, which indicate that if both parents are contact sensitive, there is an approximately 80% chance that the children will also become sensitized [32].

IMMUNOLOGY

This portion of Kligman's treatise [1] is dated. The revolution in immunologic technology had not yet begun. Furious disputations were being waged among immunologists about whether lymphocytes could indeed make antibodies. Concepts about cell mediated immunity (CMI) lagged even further behind. A history of the research of CMI at that time is chronicled by Chase [33]. In total, the studies of poison ivy/oak, although confirmatory, have contributed relatively little to our basic understanding of the induction of CMI. Some careful and elegant immunologic studies in guinea pigs [34] sharply focused attention on the immunochemical nature of the antigenic determinants of urushiol [16,17]. An early study of passive transfer with leukocytes from poison ivy–sensitive donors proved to be the only situation in which positive transfers to a contact allergen in humans could be effected without repeated prior exposure of the recipients to the simple chemical [35–37]. Experimental studies of poison ivy did not materially affect the concept of antigen presentation by dendritic cells in the epidermis [38–40], nor did they deal with suppressor factors that occur during the induction of tolerance [41–43], but investigations in guinea pigs and mice have clearly shown that tolerance can be induced in naive animals by altering the route of exposure or by use of modified but related chemicals [18,19,44–48].

Baer's group [45] made the interesting observation that analogues substituted in the 6 position on the catechol ring of PDC could induce immunologic tolerance, and some of these were very poor sensitizers. This work has been extended to include analogues with substitutions at positions 4, 5, and/or 6 in mice [48], and more recently confirmed in guinea pigs [49]. Kligman had tried to prevent sensitization in children by daily feedings of PDC, but failed [1]. On the other hand, we were successful in producing partial, persistent tolerance in young children by in-

tramuscular injection of small amounts of purified urushiol [50]. Experimental studies of the past 25 years have indicated the feasibility of preventing sensitization to poison ivy/oak by injecting young, naive children with urushiol or potentially less toxic analogues.

SYSTEMIC PROPHYLAXIS

This is the one section where clinical observation manifestly foreshadowed scientific investigation. It had long been rumored that American Indians were protected against the undesirable effects of poison ivy/oak because they ingested the leaves of these weeds [51]. During the first years of the 20th century, several enthusiasts offered up a variety of extracts and concoctions as pabulum [2,3]. Shelmire and Howell, stalwarts of the clinical scene, supplied the best studies to support this rather vague idea [52,53], but it was left for Kligman to sift through the data and misinformation and chart a true course. He fed volunteers large doses of PDC over a long time and showed that this achieved a modest but definite reduction in patch-test reactivity in most subjects [2]. He also found that a similar regimen with cashew nutshell oil (cardol) was equally effective [3]. His control studies proved almost as meaningful. Persons on placebos reported clinical protection from poison ivy dermatitis, even though their patch-test reactivity did not change [2]. Unhappily, the uncertainty of the concept, the meager results of hyposensitization and Kligman's contumelious comments led practicing immunologists of the time to deny any scientific merit to the clinical findings. Undoubtedly this lack of official status created a vacuum and encouraged greedy and misguided companies to continue offering glorified placebos [51]. Further investigation [25,54,55], including a carefully controlled double-blind study [55], have confirmed Kligman's observations, which in the parlance of modern immunology are now considered a form of acquired tolerance, and are ascribed to the production of suppressor T cells and possibly other suppressor factors by the oral ingestion of purified urushiol [43,51]. The price for protection, however, is high in terms of untoward reactions such as pruritus ani, general itching, urticaria, and other rashes during the procedure using purified extracts [25,51,55], so that patients quit with the comment that the "treatment is worse than the disease."

This difficulty led Watson and colleagues to investigate diacetylated urushiol molecules as an analogue that might induce hyposensitization without the undesirable cutaneous side effects [56]. Her findings encouraged clinical trials with a so-called "blocked PDC," but several studies indicated that, although side effects were reduced, measurable hyposensitization by patch testing with dilutions of urushiol did not occur to the same degree as after ingestion of purified urushiol, and the product was withdrawn from clinical trials [57]. Other analogues with proven activity in animal models [19,47,48] undoubtedly will be considered for commercial development in humans. In addition, the Bureau of Biologics of the Food and Drug Administration proposed regulations in Federal Register (January 23, 1985 and August 9, 1985) to remove from the market all poison ivy/oak preparations that contain low doses of urushiol or offer short courses of prophylactic treatment, especially by the intramuscular route. In effect, this leaves only the high-potency, but potentially toxic oral preparations available. Physicians wishing to use these oral agents need to monitor their patients closely, especially in the beginning, because the dose given must be tailored to the patient's tolerance.

Before leaving this topic, we should consider the possibility of inducing renal damage by ingestion of urushiol. Abramowicz repeatedly notes this in his Medical Letter reviews [58], citing the one case seen at the University of California at San Francisco, where immune complex nephrosis occurred with circulating antibodies to urushiol [59]. Kligman [1] reviewed the suspected cases of his time and concluded that the evidence did not rule out the "more probable explanation—that the glomerulonephritis is a consequence of secondary bacterial infection." The patient with immune complex nephrosis seen by us likely developed the disease from repeated natural bouts of poison oak dermatitis rather than the 2 drops of dilute poison oak extract that he drank [59]. Furthermore, considering the large amounts of extract given over the years, this must be a very rare complication of the hyposensitization procedure [51].

PHARMACOTHERAPY

Despite a crescendo of activity and interest in pharmacology related to therapeutics, no specific treatment for allergic contact dermatitis has yet been discovered. Therapy remains empirical, and many questionable products vie for a slice of a moderately sized consumer market. As Kligman [1] found to his dismay and frustration, no topical product tested "influenced the course of acute poison ivy dermatitis when compared with standard, bland dermatologic treatment." Repeated and unpublished trials since then have affirmed the lack of activity of innumerable preparations, highly touted by their purveyors (Epstein, unpublished data). The single advance in topical therapy has been the development of high-potency fluorinated corticosteroids in a gel or optimized vehicle. Applied during the earliest stages of the rash, when the skin is red and not yet blistered, they materially decrease further evolution of dermatitis and prevent apparent spread of the disease. These preparations, however, can only be used in limited areas because of their high potency and the real possibility of systemic effects if used on large areas of the body. Systemic corticosteroids and adrenocorticotropic hormone had just become available for clinical use, and their magical effects on severe acute poison ivy dermatitis were well described by Kligman [1]. What has transpired since then is a running argument as to whether one should give moderate doses of systemic corticosteroids over 10 days to 2 weeks or single large doses at the onset of dermatitis to avoid a continued reaction [60].

PREVENTION

Preventive medicine has captured the public imagination and is reputed to be the central theme for reducing medical costs into the next century. It has long been a serious consideration in the case of poison ivy/oak dermatitis. Kligman investigated this issue in some detail [1]. Under experimental circumstances, he showed that washing off applied urushiol with water was effective for about 30 min if a person was only moderately sensitive; if they were highly sensitive it was not possible to remove sufficient chemical with water to prevent a severe reaction. Clinical experience has shown that, in moderately sensitive persons, washing liberally with water for up to 2 h after exposure seems to reduce the degree of reactivity. Also, experiments since then have demonstrated that the use of solvents such as acetone, alcohol, or xylene can effectively remove active allergen from the skin for at least 30 min after application (Epstein, unpublished observation), so that organic solvents potentially could be useful when a person leaves an area of high exposure to these weeds.

Kligman [1] experimented with barrier creams and detoxicants and found them disappointing. However, it is known that a large number of substances, including albumin [15], silica, aluminum salts can bind avidly to urushiol, and experiments in humans have shown that topical applications of these preparations can reduce but not totally prevent experimental poison oak/ivy dermatitis in moderately sensitive persons [61]. In that series of experiments, the most active binding agent was an activated clay, Tixogel (United Catalysts, Inc., Louisville, Kentucky), which is commonly found in many spray-on preparations. Its application to skin in a double-blind study indicated that it is effective in reducing reactivity for up to 24 h after application [61]. Along the same vein, Orchard and coworkers [62] have reported that polyoxypropyleneamine salts of linoleic acid dimer, when applied topically, completely prevented experimental poison oak der-

matitis for up to 24 h. Whether these preparations will have practical value in field trials remains to be determined.

CONCLUSION

This review emphasizes the several areas of science that relate to poison ivy/oak sensitivity in humans. In the past quarter century the botanical aspects have been well studied and it is apparent that a continuing recognition of cross-reacting plant allergens, particularly from South America, is in the offing. The biology has been well described; yet there is a recurring need to instruct laymen and physicians alike so as to reduce morbidity from exposure to these weeds. The chemistry and especially immunochemistry have been deeply plumbed and integrated with the rapid advances in understanding of the basic science of cell-mediated immunity, so that strategies can now be planned to turn the thrust of immunologic exposure to urushiol from hypersensitivity to one of immune tolerance. Perhaps a modern "vaccine" will emerge from these investigative forays. Pharmacotherapy and preventive medicine have attracted some interest, but advances lag behind the other, better defined sciences. "The narrow path twists ever upward past lands of vast deep experience until through the majestic portals he passes into immortality." (Anonymous, circa 1985)

REFERENCES

1. Kligman AM: Poison ivy (rhus) dermatitis. Arch Dermatol 77:149–180, 1958
2. Kligman AM: Hyposensitization against rhus dermatitis. Arch Dermatol 78:47–72, 1958
3. Kligman AM: Cashew nut shell oil for hyposensitization against rhus dermatitis. Arch Dermatol 78:359–363, 1958
4. Gillis WT: Systematics and ecology of poison-ivy and poison-oaks. Rhodora 73:72–159; 161–237; 370–443; 465–540, 1971
5. Gillis WT: Poison ivy and its kin. Arnoldia 35:93–123, 1975
6. Marks JG, DeMelfi T, McCarthy MA, Witte EJ, Castagnoli N, Epstein WL, Aber RC: Dermatitis from cashew nuts. J Am Acad Dermatol 10:627–631, 1984
7. Goldstein N: The ubiquitous urushiols. Cutis 4:679–685, 1968
8. Hurtado I, Medina JD, Dao L, Urbina C: Studies on the skin-sensitizing properties of the "pepeo" tree, *Mauria puberula*. J Am Acad Dermatol 7:341–345, 1982
9. Ippen H: Contact allergy to anacardiaceae. A review and case reports of poison ivy allergy in central Europe. Derm Beruf Umwelt 31: 140–148, 1983
10. Dawson CR: The toxic principle of poison ivy and related plants. Recent Chemical Progress 15:39–53, 1954
11. Dawson CR: The chemistry of poison ivy. Trans NY Acad Sci 18: 427–443, 1956
12. Loev B, Dawson CR: Synthesis of urushenol, the mono-olefinic component principles of poison ivy and Japanese lacquer. J Org Chem 24:980–985, 1959
13. Craig JC, Waller CW, Billets S, Elsohly MA: New GLC analysis of urushiol congeners in different plant parts of poison ivy. J Pharm Sci 67:483–485, 1978
14. Yamauchi Y, Murakami T, Kumanotani J: Separation of urushiol by high-performance liquid chromatography on an 8% octadecylsilare chemically bonded silica gel column with electrochemical detection. J Chromatogr 214:343–348, 1981
15. Liberato DJ, Byers VS, Dennick RG, Castagnoli N: Regiospecific attack of nitrogen and sulfur nucleophiles on quinones derived from poison oak/ivy catechols and analogues as models for urushiol–protein conjugate formation. J Med Chem 24:28–33, 1981
16. Baer H, Watkins RC, Kurtz AP, Byck JS, Dawson CR: Delayed contact sensitivity to catechols. J Immunol 99:370–375, 1967
17. Baer H, Dawson CR, Kurtz AP: Delayed contact sensitivity to catechols. IV. J Immunol 101:1243–1247, 1968
18. Baer H, Dawson CR, Byck JS, Kurtz AP: The immunochemistry of immune tolerance. II. J Immunol 104:178–184, 1970
19. Dunn IS, Liberato J, Castagnoli N, Byers VS: Contact sensitivity to urushiol: role of covalent bond formation. Cell Immunol 74: 220–233, 1982
20. Knowles FC, Decker HB, Pratt AG, Clarke JA: Susceptibility of allergic and non-allergic persons to rhus toxicodendron. Arch Dermat Syph 38:773–779, 1938
21. Shelmire B: Contact dermatitis from weeds: patch testing with their oleoresins. JAMA 113:1085–1090, 1939
22. Shelmire B: The poison ivy plant and its oleoresin. J Invest Dermatol 4:337–348, 1941
23. Howell JB: Solubility of the dermatitis producing fraction of poison ivy. Arch Dermat and Syph 44:665–666, 1941
24. Rodriquez E: Personal communication. Sept. 1985
25. Epstein WL, Baer H, Dawson CR, Khurana RG: Poison oak hyposensitization: evaluation of purified urushiol. Arch Dermatol 109:356–360, 1976
26. Weigand DA, Haygood C, Gaylor JR, Anglin JH: Racial variations in the cutaneous barrier, in Current Concepts in Cutaneous Toxicity. Edited by VA Drill, P Lazar. New York, Academic Press, 1980, pp 221–235
27. Andersen KE, Maibach HI: Black and white human skin differences. J Am Acad Dermatol 1:276–282, 1979
28. Epstein E, Claiborne ER: Racial and environmental factors in susceptibility to rhus. Arch Dermatol 75:197–201, 1957
29. Epstein WL: What factors determine unresponsiveness to poison oak/ivy, in Controversies in Dermatology. Edited by EE Epstein. Philadelphia, WB Saunders, 1984 pp 424–427
30. Epstein WL: Contact-type delayed hypersensitivity in infants and children: induction of rhus sensitivity. Pediatrics 27:51–53, 1961
31. Epstein WL: Poison oak and poison ivy dermatitis as an occupational problem. Cutis 13:544–548, 1974
32. Walker FB, Smith PD, Maibach HI: Genetic factors in human allergic contact dermatitis. Int Arch Allergy 32:453–462, 1967
33. Chase MW: Immunology and experimental dermatology. Ann Rev Immunol 3:1–29, 1985
34. Baer H: Chemistry and immunochemistry. Poisonous Anacardiaceae. Clin Dermatol 4:152–159, 1986
35. Epstein WL, Kligman AM: Transfer of allergic contact-type delayed sensitivity in man. J Invest Dermatol 28:291–304, 1957
36. Bloom BR, Chase MW: Transfer of delayed-type hypersensitivity. Prog Allergy 10:151–255, 1967
37. Epstein WL, Byers VS: Transfer of contact sensitivity to beryllium using dialyzable leukocyte extracts. J Allergy Clin Immunol 63: 111–115, 1979
38. Rowden G: The Langerhans cell. CRC Crit Rev Immunol 3:95–180, 1981
39. Wolff K, Stingl G: The Langerhans cell. J Invest Dermatol 80(suppl): 17–21, 1983
40. Schuler G, Steinman RM: Murine epidermal Langerhans cells mature into potent immunostimulatory dendritic cells in vitro. J Exp Med 161:526–546, 1985
41. Claman HN, Miller SD, Sy MS, Moorhead JW: Suppressive mechanisms involving sensitization and tolerance of contact allergy. Immunol Rev 50: 105–132, 1980
42. Iijima M, Katz SI: Specific immunologic tolerance to dinitrofluorobenzene: modulation by suppressor T cells. J Invest Dermatol 81:325–330, 1983
43. Nishioka K: Allergic contact dermatitis. Int J Dermatol 24:1–24, 1985
44. Bowser RT, Baer H: Contact sensitivity and immunologic unresponsiveness in adult guinea pigs to a component of poison ivy extract. J Immunol 91:791–794, 1963
45. Baer H, Hooton ML, Dawson CR, Lerner DI: The induction of immune tolerance in delayed contact sensitivity by the use of chemically related substances of low immunogenicity. J Invest Dermatol 69:215–218, 1977
46. Watson ES, Murphy JC, Wirth PW, Elsohly RL, Kierkowski P: Immunological studies of poisonous anacardiacea: production of tolerance in guinea pigs using 3-*N*-pentadecylcatechol—"modified" autologous blood cells. J Pharm Sci 70:785–789, 1981
47. Watson ES, Murphy JC, Wirth PW, Waller CW, Elsohly RL: Immunologic studies of poisonous anacardiaceae: production of tol-

erance and desensitization to poison ivy and oak urushiol using esterified urushiol derivatives in guinea pigs. J Invest Dermatol 76:164–170, 1981

48. Dunn IS, Castagnoli N, Byers VS: Influence of chemical reactivity of urushiol type haptens on sensitization and the induction of tolerance. Cell Immunol 97:189–196, 1986
49. Stampf J-L, Benezra C, Byers V, Castagnoli N: Induction of tolerance to poison ivy urushiol in the guinea pig by epicutaneous application of the structural analogue 5-methyl-3-pentaclecyl cathechol J Invest Dermatol, (in press)
50. Epstein WL, Byers VS, Baer H: Induction of persistent tolerance to urushiol in humans. J Allergy Clin Immunol 68:20–25, 1981
51. Epstein WL: Allergic contact dermatitis to poison oak and ivy: Feasibility of hyposensitization. Dermatology Clinics 2:613–617, 1984
52. Shelmire B: Hyposensitization to poison ivy. Arch Dermat Syph 44: 983–998, 1941
53. Howell JB: Evaluation of measures for prevention of ivy dermatitis. Arch Dermat Syph 48:373–378, 1943
54. Epstein WL: Current status of immunologic prophylaxis for poison oak/ivy hypersensitivity in dermatoses due to environmental and physical factors. Edited by RB Rees. Springfield, CC Thomas, 1962, pp 197–200
55. Epstein WL, Byers VS, Frankart W: Induction of antigen-specific hyposensitization to poison oak in sensitized adults. Arch Dermatol 118:630–633, 1982
56. Watson ES, Murphy JC, El Sohly A: Immunologic studies of poisonous anacardiaceae: oral desensitization to poison ivy and oak urushiols in guinea pigs. J Invest Dermatol 80:149–155, 1983
57. Manner R: Personal communication. April 1985
58. Abramowicz M: Hyposensitization to poison ivy. Med Lett Drugs Ther 23:40, 1981
59. Devich KB, Lee JC, Epstein WL, Spitler LE, Hopper J: Renal lesions accompanying poison oak dermatitis. Clin Nephrol 3:106–113, 1975
60. Epstein WL: Contact dermatitis, Current therapy in internal medicine. Edited by TM Bayless, MC Brain, RM Cherniak. Philadelphia, BC Decker, 1984, pp 102–106
61. Epstein WL: Topical prevention trials, written report to USDA Services Equipment Development Center, Missoula, MT, June 6, 1985
62. Orchard SM, Fellman JH, Storrs FJ: Poison ivy/oak dermatitis. Use of polyamine salts of a linoleic acid dimer for topical prophylaxis. Arch Dermatol 122:783–789, 1986