

POISON IVY

A SUMMARY OF ONE HUNDRED CASES TREATED WITH AQUEOUS (ALUM PRECIPITATED PYRIDINE) EXTRACT

G. EVERETT GAILLARD, M.D., WHITE PLAINS, N. Y.

PROTECTION from dermatitis venenata by gradually increasing doses of the offending plant phenols has long been held to be practical.¹⁻⁶ The extracts available at the present time for the testing and treatment of sensitive individuals consist of a solution of the oleoresin in alcohol, as proposed by Spain and Cooke,⁷ and Syme,⁸ or in an oil such as almond,⁹ peanut, corn,¹⁰ or sesame. These materials are administered by the parenteral route.

Oral prophylaxis, either per se or in conjunction with parenteral injections, has been held to be effective since its inception among the Indians.¹¹ The thought has been upheld as practical by some workers,¹² even in recent years,¹³ since its popularization by Shamberg¹⁴ in 1917. The materials for use in oral therapy may be prepared from the alcohol, ether, acetone, or alum precipitated pyridine "extract" of the oleoresin. Later data,¹⁵⁻¹⁷ however, seem to indicate that this method of treatment is either not effective or too toxic for practical usage.

Current chemical and biologic evidence available today¹⁸ indicates that the same oleoresin is the active agent in the saps of the *Rhus* plants (ivy, oak, sumac, and Japanese lac), a point not wholly agreed upon by Cooke.²⁵ The works of Pfaff,¹⁹ Stevens and Tschirch,²⁰ Warren,²¹ and others²²⁻²⁴ have indicated that a variety of toxic compounds, all offensive to the sensitive individual, may be isolated from the ivy plants.

As previously mentioned, the material available today for the treatment of sensitive individuals consists of a solution of the toxic phenol in a fat solvent (such as acetone, ether, alcohol, etc.) or in an oil. All of these preparations have practical disadvantages in their employment. The alcoholic preparation must be specially handled, since the addition of even minute quantities of water to the extract will lead to the oxidation and destruction of the toxic principle.^{26, 27} In addition since the injection of strong alcoholic solutions produces great pain and local tissue irritation, it is necessary to dilute the extracts, preferably with physiologic saline, immediately before use. Even this procedure, however, necessitates the injection of a 5 to 10 per cent alcoholic solution which is not without considerable discomfort. This is especially inconvenient during the treatment of children or the treatment of individuals at a distance from the office. Similarly, when administering the extract in which the resinous principle is dissolved in oil, it is necessary to employ the intramuscular technique, which requires a long needle of fairly heavy gauge so that the material may be withdrawn and delivered. In addition, the presence of small quantities of protein in certain of these oils can cause severe reactions in allergic individuals.

Realizing the limitations of the currently obtainable extractions of the toxic resinous principle of the *Rhus* plants and other oils capable of producing dermatitis venenata, Strauss and Spain sought a product which would contain the active oleoresinous principle in an aqueous medium. A product fulfilling these requirements was developed, as noted in their paper.²⁸

The material which they describe is prepared by extracting the toxic phenols from poison ivy leaves with pyridine (a heterocyclic tertiary amine) and then precipitating the solution by the addition of aqueous alum, with or without an aqueous mineral acid. The material as supplied contains a green flocculent precipitate suspended in physiologic saline. From the evidence herein reported, the material is extremely stable; hence, there is no problem of storage or deterioration. In addition, since the precipitate is suspended in saline solution, there is no discomfort from an injection, other than that incurred by the needle. The suspension is of such low viscosity, even in the concentrated solution, that it is delivered with ease from a tuberculin type syringe with a 26-gauge $\frac{1}{4}$ inch needle. Furthermore, the syringe and needle are readily cleansed by washing with water.

Shelmire²⁹ showed that the oleoresin, obtained by drying the ether-extracted plant parts, was capable of withstanding prolonged contact with water exhibiting only slightly reduced activity. This furnishes at least presumptive evidence that an extract such as prepared by Strauss would be stable in the selected medium in which it is suspended. Further evidence along this line was obtained by the employment of this material for testing and treatment, after it had been allowed to stand at room temperature for one year.

Of ten patients patch-tested with equal strengths of the aged extract and a freshly prepared extract, eight showed reactions of approximately the same degree; in one case, the fresh extract was capable of eliciting a positive reaction, while the aged extract test was negative. In the other case, the aged extract produced a weak but definitely positive reaction while the fresh extract test was negative. In addition, in the course of this investigation, two highly sensitive patients were encountered, to whom it was impossible to give a parenteral injection of the aqueous alum precipitated pyridine ivy extract in excess of 0.5 ml. of a 1 per cent (1:10) dilution without causing a generalized pruritus and/or generally distributed dermatitis venenata-like lesions. Both of these patients were subsequently treated with an aged extract in identical strength and dilution, and systemic reactions were obtained of an intensity equal to that obtained during the employment of the freshly prepared extract. The results obtained in these cases would seem to indicate that the alum precipitated pyridine ivy extract is of great stability.

The cases selected for this study were all obtained from a private practice, confined wholly to the treatment of allergic diseases. All were referred to the office for the treatment of poison ivy, or were patients regularly seen in the office for the treatment of other allergic diseases who requested treatment for poison ivy. All had either clinical poison ivy or a recent clinical history of

poison ivy of moderate to intense severity. In the majority of cases, the attacks had been repeated for several years. Most of the patients were children residing in suburban or semirural areas.

PATCH TESTING

Patch tests with serial dilutions of freshly prepared poison ivy extract of both the alcoholic and aqueous alum precipitated pyridine variety were performed simultaneously on thirty-six of the patients (Table I). These cases were selected at random with no regard for their hypersensitiveness, other than their clinical history or previous clinical findings. The patch tests were performed in the usual manner, employing the outer side of the arm as the test site. All negative tests were repeated with extracts of proved potency.

Twenty-three of these patients gave positive reactions to the alcoholic extract in the 1:1000 dilution, while in the same group, ten patients responded positively to the pyridine aqueous extract in the 1:1000 dilution; and twelve to the 1:100 dilution. One failed to respond at all to the aqueous extract. Seven of these patients gave positive reactions to the alcoholic extract in the 1:100 dilution, while in the same group, three patients responded positively to the pyridine aqueous extract in the 1:100 dilution and three to the 1:10 dilution. One patient failed to respond at all to the aqueous extract. Two of these patients gave positive reactions to the pyridine aqueous poison ivy extract in a 1:100 dilution and failed to respond at all to the alcoholic extract. Four patients yielded negative patch tests to both extracts. In other words, about one-half of the patients who were positive to the patch tests with the alcoholic ivy extract were also positive to the pyridine ivy extract in the same serial dilution, while the other half required a lesser dilution of the pyridine ivy extract to illicit a positive reaction.

The findings of lesser activity by patch testing with the pyridine ivy extract in the same strength are to be expected since the former is an alum precipitate and relatively insoluble in water, while the latter is soluble in water and contains a fat solvent (thus making it more readily absorbed by the skin). In all probability, the patch test cannot be construed as an accurate index of the relative potency of these dissimilar types of extracts. However, the potency of the pyridine ivy extract is assured by the presence of positive reactions to patch testing with the material.

TREATMENT AND RESULTS

The original plan of treatment for the prophylactic series included injections of the pyridine ivy extract of 0.1 ml., 0.2 ml., 0.4 ml., 0.8 ml. of the 1:50 dilution; then 0.4 ml., 0.7 ml., and 1.0 ml. of the 1:10 dilution given at five- to seven-day intervals. The 1.0 ml. doses were then repeated at monthly intervals. This schedule was followed without regard for the sensitivity of the individual as determined by the patch test.

In 1945, forty-six patients were treated with the previously outlined schedule (Table II). Fifteen (or 33 per cent) of these had no recurrence

TABLE I. COMPARISON OF PATCH TESTS

PATIENT NO.	ALCOHOLIC IVY EXTRACT		ALUM PRECIPITATED PYRIDINE IVY EXTRACT		
	1:1000	1:100	1:1000	1:100	1:10
1	P		N	P	
2	P		N	N	N
3	P		P		
4	P		N	P	
5	P		PN	P	
6	P		N	P	
7	P		N	P	
8	P		PN	P	
9	P		P		
10	P		P		
11	P		N	PN	P
12	P		PN	P	
13	P		PN	P	
14	P		N	P	
15	P		N	P	
16	P		P		
17	P		N	P	
18	P		N	P	
19	P		N	P	
20	P		N	P	
21	P		N	P	
22	P		PN	P	
23	P		P		
24	N	P	N	N	P
25	N	P	N	N	N
26	N	P	N	N	P
27	N	P	N	N	P
28	N	P	N	P	
29	N	P	N	PN	P
30	N	P	N	P	
31	N	N	N	P	
32	N	N	N	PN	P
33	N	N	N	N	N
34	N	N	N	N	N
35	N	N	N	N	N
36	N	N	N	N	N

P = positive.

N = negative.

of the poison ivy during 1945; eighteen (or 39 per cent) experienced mild poison ivy, but of definitely less severity than in previous years, while thirteen (or 28 per cent) were no better than in previous years. In other words, 72 per cent of the patients had definite benefit from the treatment, while 28 per cent were not helped.

Nine of these patients had been treated in 1944 with the alcoholic ivy extract with no relief of symptoms. Five of these were greatly improved and one moderately improved in 1945, after treatment with the alum pyridine ivy extract. The remaining three were not helped. It is interesting to note that the six patients who registered improvement with the pyridine ivy extract had been unable to tolerate injections of the alcoholic ivy extract in doses exceeding 0.05 ml. of the 1:50 dilution but were capable of receiving injections of the pyridine ivy extract in doses of from 0.5 ml. to 1.0 ml. of the 1:10 dilution.

Four of the patients among the original forty-six treated were unable to follow the outlined schedule. These developed systemic reactions when their injection dosage exceeded 0.5 ml. of the 1:10 dilution of the pyridine ivy

extract. All of the patients had successful seasons. It may be noted that the top dose attained by the more sensitive of these patients was the equivalent of a dose of 0.05 ml. of the concentrated alcoholic ivy extract, a dosage rarely if ever used in treatment with this material.

In 1946, twenty-five of the original forty-six patients continued treatment with the pyridine ivy extract (Table III). This treatment was consummated by the administration of injections at monthly intervals. The dosage administered varied from 0.5 ml. of the 1:10 dilution to 0.5 ml. of the concentrated extract, depending upon the sensitivity of the individual. Twenty-three of these patients (or 92 per cent) had excellent seasons, experiencing no poison ivy. One patient developed mild poison ivy which remained localized at the point of known contact and which subsided readily by the use of a patent remedy. The remaining patient had a severe case of poison ivy of no less intensity than before treatment.

TABLE II. RESULTS OF ONE YEAR OF TREATMENT

NUMBER OF CASES	YEARS OF TREATMENT	NO POISON IVY	MILD POISON IVY	SEVERE POISON IVY
46	1945	15 (33%)	18 (39%)	13 (28%)
36	1946	16 (44%)	13 (36%)	7 (19%)
31	1947	13 (41%)	13 (41%)	5 (17%)
TOTALS				
113	One year	44 (39%)	44 (39%)	25 (22%)

In 1947, thirteen of the original forty-six patients continued their treatment through a third year (Table IV). The treatment plan was a continuation of the annual treatment with the injections given at monthly intervals. During the winter months, seven of the patients skipped a month but were able to tolerate their top injection dosage after two-month intervals with no apparent discomfort. This may indicate that bi-monthly injections may eventually be successfully incorporated in the plan of treatment. Twelve of these patients had extremely successful seasons, none of whom experienced even mild poison ivy. The remaining patient had one moderate attack of ivy dermatitis which remained localized at the point of contact. Four were patch-tested with the pyridine ivy extract in dilutions up to the 1:5. All of the tests were negative. These cases had, in 1945, reacted positively to patch tests in a 1:1000 dilution of the same material.

In 1946, an additional thirty-six cases were treated with the pyridine ivy extract. At this time, the plan of treatment was altered to include injections of 0.4 ml., then 0.8 ml. of the 1:50 dilution, then 0.2 ml., 0.6 ml., and 1.0 ml. of the 1:5 dilution, given at five- to seven-day intervals and followed by monthly injections of 1.0 ml. of the 1:5 dilution of the pyridine ivy extract. By this procedure, it was possible to attain a top dose of 1.0 ml. of the 1:5 dilution in 5 injections, while with the previous schedule, 7 injections were required to attain 1.0 ml. of the 1:10 dilution. Thirty-five of these patients were able to tolerate this dosage schedule without experiencing either local or systemic reactions. The remaining patient developed a moderate degree of local

reaction and a generally distributed pruritis without visible lesions, following the injection of 0.6 ml. of the 1:5 dilution. The patient was later comfortably stabilized on a dosage of 0.4 ml. of the same dilution.

On this routine, twenty-nine of the thirty-six patients (or 80 per cent) had satisfactory seasons (Table II). Sixteen of the twenty-nine were wholly free from poison ivy, while thirteen experienced one or more mild attacks of definitely less severity than in previous years. The remaining seven patients were not benefited by the treatment.

In 1947, twenty-nine of the thirty-six cases treated in 1946 continued their treatment through a second year (Table III). The plan of treatment again was of the annual variety with injections of the top dose being administered at monthly intervals. Eighteen (or 85 per cent) of these patients had little or no poison ivy throughout the season. The three remaining patients were among the group who had not done well in 1946. All of them, however, felt they were enough improved from their original status to warrant continuation of their treatment.

TABLE III. RESULTS OF TWO YEARS OF TREATMENT

NUMBER OF CASES	YEARS OF TREATMENT	NO POISON IVY	MILD POISON IVY	SEVERE POISON IVY
25	1945 and 1946	23 (92%)	1 (4%)	1 (4%)
21	1946 and 1947	14 (66%)	4 (19%)	3 (15%)
TOTALS				
46	Two years	37 (80%)	5 (11%)	4 (9%)

TABLE IV. RESULTS OF THREE YEARS OF TREATMENT

NUMBER OF CASES	YEARS OF TREATMENT	NO POISON IVY	MILD POISON IVY
13	1945, 1946 and 1947	12 (92%)	1 (8%)

In 1947, an additional thirty-one new cases were treated (Table II). The plan of treatment was the same as had been employed in 1946, whereby a top dose of 1 ml. of a 1:5 dilution of the pyridine ivy extract was reached in 5 injections at weekly intervals, followed by monthly injections of the top dosage. All of the patients accepted the outlined schedule without experiencing either local or systemic reactions. Twenty-six (or 83 per cent) of these patients had successful seasons. One-half of these had no poison ivy, while the other half had one or more mild attacks of less severity than in previous years.

None of the cases referred for acute poison ivy were placed on phylactic therapy. A colleague of the writer has been able to treat the acute problems more rapidly and effectively by local treatments. No oral therapy was attempted.

SUMMARY

1. A total of one hundred thirteen patients, hypersensitive to poison ivy, were treated with pyridine ivy extract during the years 1945, 1946, and 1947.

2. Patch tests performed on thirty-six of these cases indicate that the pyridine ivy extract is slightly less active than the alcoholic ivy extract in the production of positive tests.

3. The pyridine ivy extract is simple to use, produces no discomfort, and is very stable.

4. The pyridine ivy extract, because it is slowly absorbed, may be administered in larger, more rapidly increasing doses than the alcoholic extract.

5. Of the one hundred thirteen cases, eighty-eight (or 77 per cent) had satisfactory results the first season of treatment.

6. Of forty-six cases treated for two years, forty-one (or 84 per cent) had success the second season of treatment.

7. Of thirteen cases treated for three seasons, twelve had success the third season of treatment.

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