The early reports on the use of Thephorin, a hydrogenated phenyl-pyridindene derivative, seemed to indicate that it was an ideal antipruritic, i.e., it effectively and consistently relieved the sensation of itching while producing relatively few or no untoward side effects. Lehmann et al. (1) reported that it is very potent in antagonizing important physiologic effects of histamine on smooth muscle, on arterial pressure, and on capillary permeability. Lehmann (2) proved—and Strauss (3) in reviewing antihistamine therapy, stated—that Thephorin is a more potent local anesthetic than procaine, which suggests the possibility that its local action may be more that of a local anesthetic than that of an antihistaminic.

In August, 1947, Kesten and Sheard (4) reported that Thephorin by mouth was effective in thirty-three of forty-one patients (80%) with dermatoses characterized by wheal formation and was a worthy adjuvant in allaying itching in twenty-two of thirty-nine patients (56%) with intensely pruritic dermatoses. They also found that the subcutaneous injection of Thephorin prevented itching in experimentally produced wheals. One year later, Woolridge and Joseph (5) reported on the treatment of atopic dermatitis (disseminated neurodermatitis) with Thephorin orally and locally. Seventeen of twenty-three patients (74%) showed more than 50 per cent clearing in from one to seven weeks. It was the opinion of these authors that the oral administration could be omitted without materially affecting the results. These reports mentioned side effects of irritability and sleeplessness as reactions to the oral use of the drug, which promptly subsided when Thephorin by mouth was discontinued. Woolridge and Joseph cited a patient whose eruption became worse under therapy, but who gave a negative response to patch test with Thephorin.

Shelmire (6) was the first to report sensitization dermatitis from the use of Thephorin. He reported on a series of 305 patients with pruritic dermatoses treated with five per cent Thephorin ointment. Of these a very high proportion, namely 233 patients (76.4%) showed benefit from the application of the salve; while a contact-type sensitization developed in only one patient. He states, however, that the skin sensitization index is higher than these figures would indicate. In an additional 150 patients treated with the salve, but who were not included in his first report because of an insufficient observation period, five additional cases of contact dermatitis due to Thephorin were encountered. Thus, Shelmire observed six instances of contact-type sensitization among 455 patients, an incidence of 1.31 per cent. He considered this low, because the

* Brand of Phenindamine (2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene hydrogen tartrate), supplied by Hoffmann-La Roche Inc.

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ointment was used by a great number of patients over a comparatively long time, the quantities of salve applied were often considerable, and large areas of the body were often covered.

Shelmire’s preliminary report (7) in April 1948 was so favorable that the present authors treated a series of patients with pruritic dermatoses with Thephorin locally in the form of a 5 per cent ointment in a Carbowax base or a 5 per cent lotion.

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>NUMBER OF PATIENTS</th>
<th>RESULTS</th>
<th>CLINICAL REACTION*</th>
<th>POSITIVE PATCH TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopic Dermatitis (Disseminated)</td>
<td>8</td>
<td>Good G</td>
<td>Fair F</td>
<td>Poor C</td>
</tr>
<tr>
<td>Lichen Simplex Circumscriptus</td>
<td>12</td>
<td>4</td>
<td>6</td>
<td>2</td>
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<tr>
<td>Pruritus Ani (Vulvae—Scroti)</td>
<td>10</td>
<td>6</td>
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<td>2</td>
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<tr>
<td>Lichen Urticatus</td>
<td>4</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Dermatitis with or without Lichenification</td>
<td>9</td>
<td>2</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Stasis Dermatitis</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Totals</td>
<td>50</td>
<td>13</td>
<td>13</td>
<td>24</td>
</tr>
</tbody>
</table>

* The eruption became worse with a tendency to spread.

The histories of the five patients in whom positive patch tests were obtained with the ointment, lotion, or a two per cent aqueous solution are briefly summarized:

**Case 1:** M. M., a white woman, was seen July 26, 1947 with a stasis dermatitis of the left leg. The initial treatment consisted of liquor aluminum acetate compresses, roentgen-rays, Nivea Skin Oil; later an ointment consisting of phenol, salicylic acid, liquor aluminum acetate in Qualatum was used. There were periods of remission and exacerbation, and by June 17, 1948 the dermatitis had spread to the right popliteal area, but there was no objective improvement. On July 30, 1948 the eruption was worse. On August 3, 1948 a patch test to Thephorin lotion produced a “two plus” reaction.

**Case 2:** R. K., a white man, was seen April 5, 1948 with a dermatitis on the dorsum of the toes of several weeks duration. Scrapings for fungi and patch tests to shoe lining were negative. Treatment consisted of roentgen-rays, liquor aluminum acetate soaks, and boric acid ointment. There followed periods of partial remission and exacerbation, during which time he also used Histadyl ointment. On July 28, 1948 Thephorin ointment was started and on August 25, 1948 the dermatitis was aggravated. Patch test September 4, 1948 to Thephorin ointment caused a “three plus” reaction.

**Case 3:** A. A., a 32 year old white woman, was seen March 30, 1948 with a pruritic dermatitis of the nape of the neck of eight months duration. In the occipital area, within the hairline, there was a well defined lichenified plaque 5.0 cm. in diameter. Treatment was
started with Domolene and roentgen-ray therapy. Since the patient still complained of pruritus, on May 20, 1948, Thephorin lotion was prescribed. She returned two months later, namely, July 23rd, 1948 and in the interim, she had continued to use Thephorin lotion; progress had been satisfactory until a few days previously when the affected area became worse and exudation was noted for the first time. A patch test with two per cent aqueous Thephorin solution produced a “two plus” reaction.

**Case 4:** M. A., a 33 year old white man, was first seen January 30, 1948 with a history of recurrent pruritus of the scrotum for one year. Examination revealed a scaly, lichenified, erythematous dermatitis of the scrotum. Treatment was started with a lotion containing phenol, liquor aluminum acetate, bentonite, olive oil and liquor calcis. By June 14, 1948 he had shown some improvement, but still complained of pruritus. The institution of Thephorin lotion resulted in decreased itching and was continued until August 5, 1948 when the patient presented an acute dermatitis of the scrotum. Patch tests resulted in “two-plus” reactions to Thephorin lotion and to a two per cent aqueous solution made from a crushed Thephorin tablet.

**Case 5:** A. S., a 52 year old white woman, had been previously successfully treated for a stasis dermatitis from October 19, 1943 to April 17, 1944. She returned on July 2, 1948 because of a recurrence in the formerly affected area where she now had a well defined scaly pruritic plaque on the left ankle. Treatment with Thephorin ointment and roentgen-rays was instituted. There was gradual improvement until September 8th, 1948, when she complained of increased itching and the use of Thephorin ointment was discontinued. On September 23, 1948, the eruption on the legs became purpuric and by September 30, 1948 she presented a generalized erythematous, papulovesicular dermatitis. The patient was hospitalized from October 2, 1948 to October 21, 1948; when she was discharged there was only a mild erythema. During the final week of hospitalization a patch test was performed with a two per cent solution of Thephorin, which had been prepared several weeks previously from a crushed tablet. The test was negative. On November 9, 1948, she was patch tested with a freshly prepared two per cent aqueous solution of Thephorin; the result was a “three plus” positive reaction.

**DISCUSSION**

The interval between institution of local therapy with Thephorin and appearance of contact-type sensitization in the above five cases was a long one, namely 28 to 68 days (average 50 days). While this may seem to be a relatively protracted period of use, it should be remembered that the patients in whom Thephorin has proved of especial value have been those with chronic dermatoses; i.e., atopic dermatitis, lichen simplex circumscription, chronic contact dermatitis, pruritus ani, and pruritus vulvae. Shelmire considers the use of Thephorin ointment to be contraindicated in cases of acute dermatitis, where its application is attended by marked stinging and burning without relief of itching.

**SUMMARY**

While 26 of a series of fifty patients with chronic pruritic dermatitis treated locally with Thephorin lotion or ointment experienced substantial relief from itching, fourteen became worse or developed a reaction to the drug when using this medication for a long period (average 50 days). Nine of these fourteen patients were not tested because their dermatitis was too acute and extensive (reaction?) when seen and the patients would not cooperate and return for
testing later. There were positive patch tests to the particular Thephorin-containing medicament, (i.e. the Thephorin plus the vehicle) in all the five remaining patients who could be tested. Three of these five patients evidenced positive patch tests to a solution of crushed Thephorin tablets or aqueous solution of Thephorin.

CONCLUSION

In a series of fifty patients treated locally with Thephorin for chronic pruritic dermatoses, after a long period of use (average 50 days) clinical reactions developed in fourteen cases (28 per cent). Only five could be patch tested, but all these, i.e., 10 per cent of the entire series, had contact allergic eczematous sensitivity proven by positive patch tests to Thephorin in the vehicle employed; and three patients, i.e., 6 per cent, were proven sensitive to the drug itself. If only the latter figure is accepted as the sensitizing index or even if further reports substantiate that Shelmire’s larger series with a figure of 1.3 per cent contact sensitivity indicates the average sensitizing index, it is the opinion of the present authors that the local use of Thephorin requires caution similar to that advocated (8) in the case of other “antihistaminics and many other valuable topical agents;” and presents certain risks as a routine agent in the protracted treatment of chronic pruritic dermatoses, in spite of its effectiveness as an anti-pruritic in these diseases.

REFERENCES

7. Shelmire, B.: Round Table Discussion, Amer. Dermatological Asso., Sixty-eighth Annual Meeting, Coronado, California, April 1948.