

## EVALUATION OF TOPICAL DICHLOROXYQUINALDINE (STEROSAN) AS A THERAPEUTIC AGENT IN DERMATOLOGY\*

ARTHUR J. TRONSTEIN M.D.\*\*

While certain of the oxyquinoline derivatives, such as Vioform and Quinolor Compound, have been known to be useful as topical therapeutic agents in pyodermas and related conditions, the dichloroxyquinaldine products are not so well known in this country. This compound, commonly known as Sterosan, has been studied by European workers, and Sulzberger (1) has also suggested that it may have merit. In the European literature Hotz and Frutiger (2), Jadassohn et al. (3), Jadassohn and Fazler (4), Bruni (5), and Hirsch (6) have all reported upon its use as a therapeutic agent in dermatologic conditions due to infection.

### CHEMICAL NATURE OF DICHLOROXYQUINALDINE

The "parent" chemical of this material is oxyquinolin. This chemical has long been known to have some bactericidal value. Its action is most effective upon staphylococcus. Vioform, 5 chloro 7 iodo hydroxyquinoline, is much more effective than is oxyquinoline. However, it has been known to occasionally produce local irritation or sensitization effects. Jadassohn believed these side effects might be due to its iodine content. The well-known Quinolor Compound is a mixture of three closely related substances; 5 chlor 8 hydroxyquinoline, 7 chlor 8 hydroxyquinoline, and 5,7, dichlor 8 hydroxyquinoline. Quinolor Compound is also an effective bacteriostatic agent.

The replacement of one hydrogen in hydroxyquinoline by a methyl radical produces oxyquinaldine, a rather ineffective bacteriostatic agent. The dichloroxyquinaldine products have been shown to be decidedly efficient bacteriostatic products, especially against actively reproducing Gram positive organisms.

### PROPERTY OF SENSITIZATION

No detailed studies concerning sensitization to this material appear in the literature, to our knowledge. For our preliminary work we used the routine 48 hour patch test. These 48 hour tests were followed, whenever possible, by a repetitive patch test method now under study by the Department of Dermatology and Syphilology of the University of Cincinnati. Results of the various tests are shown in the following tables.

The single patient showing a doubtful reaction to the 5% ointment used for the tests showed a negative reaction to tests with the 5% powder and 5% paste forms. No bases alone were available for control use. Repetitive tests upon the same sites were also negative.

\* From the Department of Dermatology and Syphilology, College of Medicine, University of Cincinnati. Leon Goldman M.D., Director

\*\* Bristol Fellow in Antibiotics.

Dichloroxyquinaldine products for this study supplied by J. R. Geigy Co., N. Y.

Received for publication Dec. 10, 1948.

The single doubtful reaction has been noted before. The above tables do not include such experiences as developed in clinical use. Whenever sensitivity was suspected, every effort was made to verify it, but we have not as yet seen proven eczematous sensitization to the material.

Clinically, we found evidence of irritation in a young colored girl suffering from chronic discoid lupus erythematosus with secondary infection of one lesion. The ointment gave excellent results as far as the infection was concerned, but seemed to irritate the lupus erythematosus to a moderate degree. Patch tests gave negative results, and further use upon a non-infected lesion made no changes whatsoever.

TABLE 1  
*Results of routine 48 hour patch tests*

NO. PATIENTS	+	±	0
111	0	1	110

TABLE 2  
*Results of repetitive patch testing*

METHOD	NO. PTS.	0	±	+
Tested q. 48 hrs.—same site 4 times in approx. 21 days.....	26	25	1	0
Tested as above, but not within 21 days.....	66	66	0	0
Tested q. 48 hrs. 3 times in same site.....	4	4	0	0
Tested as above 2 times.....	7	7	0	0
Routine 48 hr. only.....	6	6	0	0
Totals.....	111	110	1	0

A local physician with nummular eczema reported by Goldman (7) was patch tested and showed a strong reaction to Vioform, but a negative reaction to 3 per cent iodine in carbowax and a negative reaction to dichloroxyquinaldine. Goldman also reports a patient with marked contact dermatitis of the hands who gave strongly positive reactions to Vioform and to 1 per cent iodine solution, but a negative patch test reaction to this material. In three other patients with eczematous dermatitis of the hands dichloroxyquinaldine could be used where Vioform could not be tolerated. In these patients no patch tests were done. In a few instances some "grease reactions" were noted. "Grease reactions" are seen often in stasis dermatitis, and are interpreted as vesicular flare ups due to increased surface temperature. These are not oil folliculitis of the skin nor eczematous reactions by the greases.

#### CLINICAL RESULTS

The materials used were employed in three forms: a bland ointment whose base is essentially a petrolatum and beeswax type; a water miscible paste whose

base is essentially triethanolamine, wool fat, and talcum, and a powder form with zinc oxide and talcum as essential components. The full formulae for these bases has not been stated by the manufacturer. In each preparation, there was a 5 per cent concentration of the active ingredient.

For the most part we selected cases in which no prior therapy had been employed. Some were cases in which prior therapy had failed. A few of the patients had been treated before for similar conditions, and had suffered recurrences. In

TABLE 3

DIAGNOSIS	CLINICAL RESULTS				
	No. Pts.	Cured or markedly improved	Improved but not cured	No change	Worse under therapy
Impetigo.....	49	47	2	0	0
Superficial pyoderma, ecthyma, etc.....	36	33	2	1	0
Sycosis vulgaris.....	3	2	1	0	0
Psoriasis.....	3	0	1	2	0
Infected acne.....	5	0	0	1	2
Infectious eczematoid dermatitis.....	28	9	16	2	1
Diaper dermatitis, folliculitis.....	9	9	0	0	0
Infected neurodermatitis.....	5	0	5	0	0
Infected lower leg ulcer syndrome.....	16	8	6	2	0
Infected superficial mycoses.....	24	13	7	2	2
Pompholyx.....	2	0	0	2	0
Infected seborrhea.....	8	2	2	4	0
Conjunctivitis.....	4	3	1	0	0
Infected lupus erythematosus.....	2	0	0	2	0
Impetiginized factitia.....	4	0	4	4	0
Pemphigus vulgaris.....	1	0	0	1	0
Infected ivy dermatitis.....	5	5	0	0	0
Infected scabies.....	3	0	3	0	0
Nodular periphlebitis with ulceration...	2	0	0	2	0
Perleche.....	3	2	1	0	0
Pruritus ani.....	4	0	2	1	1
Dermatitis herpetiformis.....	2	0	0	2	0
Unclassified.....	8	2	5	1	0
Totals, 23 types.....	224	135 60%	61 27%	22 10%	6 3%

some instances we used "rightist-leftist" methods for comparison. This method is one in which one extremity is treated with one mode of therapy while the other extremity, having lesions of similar intensity, is treated by a different method, and results compared. In no cases were systemic agents such as sulfonamides, antibiotics, etc., used, nor were any physical agents, radiations, etc., employed while the patients were under therapy with this material.

If the product seemed to be ineffective within a reasonably short time (6-7 days), all therapy was discontinued for several days before beginning any other form of treatment. Occasionally, in order to satisfy the patient, we used a placebo

during this interval. This waiting period would be of value to judge any latent results, and would give a better chance for comparison of results of the next form of treatment.

It is evident that those dermatitides caused entirely by, or aggravated by pyogenic infection had excellent response to Sterosan.

As has been stated before, any case in which we suspected sensitization or local irritation to be taking place, was carefully studied by patch tests. No proved cases of these reactions were found. In an occasional instance we felt that the apparent aggravation of symptoms was due to the "grease reaction" from the base.

When controlled comparison with other therapeutic agents, such as penicillin ointment (500 U/Gm.), 2-5% ammoniated mercury ointment, 5% boric acid ointment, etc., could be made, the results were very favorable. Comparison of results between the various forms (ointment, paste and powder) did not show any particular variation.

In a few cases we used the material simply as an anti-pruritic agent. Results were inconclusive. Whatever relief was obtained could well have been attributed to the base material as well as to the active ingredient. No work was done combining the agent with such medicaments as tar, phenol, salicylic acid, etc., but we see no reason why this could not be done.

No pigmentary changes were noted following its use on the skin, but when used on the blonde hair of one child, slight discoloration was claimed by the parents. In this case, other factors may have been present and may have produced the discoloration. Simple tests upon linens, clothing, etc., do not indicate any harmful effects. The ointment is a tan color, but is easily removed from clothing by the usual laundry methods. The other mixture forms are white in color.

#### CONCLUSIONS

Dichloroxyquinaldine (Sterosan) appears to be a satisfactory addition to the field of topical therapy in dermatology. Its usefulness is greatest when employed in those conditions in which infection by Gram positive, actively reproducing microorganisms is the specific etiological agent, or where such infection plays a major role. It offers adequate bacteriostatic action in most of such cases with little or no evidence of serious side reactions.

In our experience it appeared to be less sensitizing than a related oxyquinoline derivative, 5 chlor 7 iodo 8 hydroxyquinoline (Vioform).

Further study of dichloroxyquinaldine and related compounds seems indicated.

#### REFERENCES

- (1) SULZBERGER, MARION B.: Therapy of Mycosis of the Feet; Yearbook of Dermatology and Syphilology 1948, page 60 (1948) Yearbook Publishers, Chicago, Ill.
- (2) HOTZ, A. AND FRUTIGER, U.: Sterosan, ein neues Mittel z zur Behandlung des Pemphigus neonatorum and anderer Staphylokokkenkrakungen im Kindersalter; Schweiz. Med. Wehnschr.: 74, 6, 680 (1944).
- (3) JADASSOHN, W. ET AL.: ein neuess Mittel zur Behandlung von Pyodiermen (G. 1204, Sterosan): Schweiz. Med. Wehnschr. 74, 6, 168.

- (4) JADASSOHN, W. AND FAZLER, J.: Sterosan; *Therapeutische Umschau* #10; 1-3 (1945) Mediziner Verlag Hans Buber, Bern, Switzerland.
- (5) BRUNI, G.: Sterosan, ein neues Mittel zur Behandlung von verschiedenen Hautaffektionen, (*Praxis*), *Schweiz. Rundschau für. Med.*, 43 (1945).
- (6) HIRSCH, J.—personal communication to the author.
- (7) GOLDMAN, L.—personal communication to the author.