THERAPEUTIC ASSAYS OF THE NEW YORK SKIN AND CANCER UNIT, NEW YORK POST GRADUATE MEDICAL SCHOOL AND HOSPITAL

ASSAY I—BISTRIMATE FOR LUPUS ERYTHEMATOSUS, LICHEN PLANUS AND OTHER DERMATOSES

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The therapeutic effects of Bistrimate\(^2\) (sodium bismuth triglycollamate (Smith)) were studied over a period of nine months from November 1946 to August 1947 under the direction of Dr. Frances Pascher in charge of the treatment unit of the New York Skin and Cancer Unit, New York Post Graduate Medical School and Hospital. Four staff members participated in the study and their independent observations were used as the basis of this report. A total of 92 patients was treated with Bistrimate for periods ranging from four weeks to five months.

The following dermatoses were treated:

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lupus erythematosus</td>
<td>45</td>
</tr>
<tr>
<td>Discoid</td>
<td>40</td>
</tr>
<tr>
<td>Subacute disseminated</td>
<td>2</td>
</tr>
<tr>
<td>Congestive</td>
<td>2</td>
</tr>
<tr>
<td>Telangiectatic</td>
<td>1</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>32</td>
</tr>
<tr>
<td>Exanthematic</td>
<td>21</td>
</tr>
<tr>
<td>Hypertrophic</td>
<td>9</td>
</tr>
<tr>
<td>Oral</td>
<td>2</td>
</tr>
<tr>
<td>Granuloma annulare</td>
<td>3</td>
</tr>
<tr>
<td>Scleroderma (diffuse)</td>
<td>1</td>
</tr>
<tr>
<td>(circumscribed)</td>
<td>2</td>
</tr>
<tr>
<td>Mosaic wart</td>
<td>1</td>
</tr>
<tr>
<td>Lichen nitidus</td>
<td>1</td>
</tr>
<tr>
<td>Mycosis fungoides</td>
<td>1</td>
</tr>
<tr>
<td>Psoriasis (guttate)</td>
<td>1</td>
</tr>
<tr>
<td>(chronic lichenoid)</td>
<td>1</td>
</tr>
<tr>
<td>Psoriasis arthropathica</td>
<td>3</td>
</tr>
<tr>
<td>Keratoderma blenorrhagica</td>
<td>1</td>
</tr>
</tbody>
</table>

\(^1\) From the New York Skin and Cancer Unit, Department of Dermatology and Syphilology—New York Post Graduate Medical School and Hospital, Dr. Marion B. Sulzberger, Director.

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\(^2\) We are indebted to Carrol Dunham Smith Pharmacal Co. for the supply of Bistrimate for this investigation.
RESULTS

A. Results in lupus erythematosus

The discoid cases (group of 40) were subdivided into two groups:

1. Early discoid (duration less than 6 months)

- Healed. ......................................................... 1/6
- Improved. ..................................................... 5/6

2. Discoid, of long duration (from 7 months to many years)

- Healed ......................................................... 4/34
- Improved ...................................................... 21/34
- Unimproved .................................................. 7/34
- Relapse ....................................................... 2/34

The results in the other forms of lupus erythematosus treated were:

- Subacute disseminated Improved ........................................ 2/2
- Telangiectatic Unimproved ........................................ 1/1
- Congestive Improved ........................................... 2/2

The results for the entire group of lupus erythematosus were as follows:

- Healed ......................................................... 5/45 or 11+%
- Improved ...................................................... 30/45 or 67-%
- Unimproved .................................................. 8/45 or 17+%
- Relapse* ....................................................... 2/45 or 4+%

B. Results in lichen planus

The exanthematic cases (group of 21) were subdivided into two groups: duration less than or over two months.

- Exanthetic (early)
  - Healed ......................................................... 1/6
  - Improved ..................................................... 2/6
  - Unimproved .................................................. 3/6

- Exanthetic (over 2 months)
  - Healed ......................................................... 1/15
  - Improved .................................................... 5/15
  - Unimproved .................................................. 4/15
  - Worse ......................................................... 3/15
  - Relapse ....................................................... 2/15

Other forms of lichen planus treated were:

- Hypertrophic
  - Healed ......................................................... 0/9
  - Improved ..................................................... 5/9

- Buccal
  - Unimproved .................................................. 4/9
  - Unimproved .................................................. 2/2

* Relapse while under treatment.
The results for the entire group of lichen planus were as follows:

Improved or healed.................................................. 14/32 or 44-%
Unimproved.......................................................... 14/32 or 43-%
Worse or relapse..................................................... 4/32 or 12-%

C. Results in a miscellaneous group of dermatoses

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granuloma annulare</td>
<td>3 Improved</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>1 Diffuse-unimproved, 2 Circumscribed-improved</td>
</tr>
<tr>
<td>Mosaic wart</td>
<td>1 Improved</td>
</tr>
<tr>
<td>Lichen nitidus</td>
<td>1 Improved</td>
</tr>
<tr>
<td>Mycosis fungoides</td>
<td>1 Unimproved</td>
</tr>
<tr>
<td>Parapsoriasis</td>
<td>1 Guttate-improved, 1 Lichenoid-unimproved</td>
</tr>
<tr>
<td>Psoriasis arthropathica</td>
<td>3 Unimproved</td>
</tr>
<tr>
<td>Keratoderma blenorrhagica</td>
<td>1 Unimproved</td>
</tr>
</tbody>
</table>

COMMENT

As a rule the cases that responded favorably to Bistrimate showed improvement in approximately four to six weeks after treatment was started. In most cases two to three months were required for the maximum therapeutic effect. In three cases improvement continued during the fourth month of treatment and in one case of circumscribed scleroderma, resolution continued into the fifth month of treatment. The initial dose was one tablet three times a day after meals; and the average dose for adults was four to six tablets daily. Each tablet contains 410 mg. of sodium bismuth triglycollamate. This is equivalent to 75 mg. of metallic bismuth.

A gingival bismuth line appeared in most cases, in some as early as two weeks, in others as late as ten to fourteen weeks after therapy was initiated. Treatment was not interrupted in these patients unless a stomatitis supervened. A urine analysis was done routinely every two to three weeks in the majority of cases. Albuminuria was found on one occasion. In twenty-one cases a complete blood count was done at biweekly intervals to ascertain whether or not this bismuth preparation affects the hemogram. The findings are of interest in view of the sparse reports on the effects of bismuth (parenteral as well as oral) on the hemopoietic tissues. A leukopenia (less than 4,000 white blood cells per cubic millimeter of blood) occurred in four of the 21 cases. In six cases the depression of the white blood cells appeared between the sixth and eighth weeks of treatment. A relative decrease in the percentage of polymorphonuclear cells and a rise in the lymphocyte ratio were also noted. The lowest figure obtained was 2,800 white cells per cubic millimeter of blood. The depression in the granulocytes proved to be transitory, however, since normal levels were obtained two to four weeks later despite continuation of therapy.

4 Remarkable improvement after two months of therapy in a seemingly incurable case.
The response of the early cases of discoid lupus erythematosus (duration six months or less) was uniformly good in the small group studied. The results in the more chronic cases varied as the figures indicate. No case was made worse but two suffered relapse while under treatment. The results in subacute disseminated lupus erythematosus were not satisfactory, although both patients improved to a limited extent. Both patients were under treatment for approximately three months. Some of the lesions healed, others remained unchanged, and in one patient new lesions appeared during the course of treatment.

The results in lichen planus are rather equivocal, since the number of improved and unimproved cases tally. It is interesting to note that the subjective and objective changes in lichen planus were not always parallel. In six instances of the exanthematic type, symptomatic improvement (relief of itching) was striking after a few days. The patients continued to be comfortable while taking Bistrimate even though there was no apparent regression in the lesions after four or more weeks of continuous treatment. In three of these, lapse of therapy was followed by a symptomatic relapse and return of pruritus.

Treatment was discontinued in 9 cases because of the following untoward effects:

1. Marked stomatitis and trigeminal neuralgia in two cases. The same symptoms occurred in one of these patients after the subsequent administration of bismuth subsalicylate intramuscularly.
2. Moderate stomatitis in two cases.
3. Gastro-intestinal upset in three cases. The patients complained of abdominal pain, nausea, vomiting and diarrhea.
4. Peripheral neuritis in one case.
5. Generalized pruritus and toxic erythema after ingestion of five tablets by one patient.

In nineteen cases there was an opportunity to compare the therapeutic efficacy or oral bismuth (Bistrimate) with parenteral bismuth (bismuth subsalicylate in oil intramuscularly). Nine cases failed to respond to either form of bismuth, three cases did equally well with both; in three the dermatosis appeared to undergo involution faster with the oral preparation; and in four cases that had failed to respond to injections of bismuth subsalicylate, oral Bistrimate produced a therapeutic response. Among these four cases, the response in one was fair, in two the response was good, and in one (of discoid lupus erythematosus) healing was complete while under Bistrimate therapy.

CONCLUSIONS

This therapeutic assay indicates that Bistrimate is a valuable therapeutic agent in the treatment of the discoid type of lupus erythematosus. The results in this disease may be rated as good to excellent in 50% of the cases, moderate or fair in 25%, and poor in 25%.

It is more difficult to evaluate the efficacy of the drug in the exanthematic type of lichen planus, particularly because of the variable course of this disease.
Subjective or objective improvement was obtained in 40% of the cases. On the other hand 12% grew worse or suffered relapse while under treatment.

The results are also equivocal in the hypertrophic form of lichen planus.

The results in the limited number of cases of scleroderma and granuloma annulare allow no inferences but appear to justify further therapeutic investigation.

In general the drug is tolerated well. Recovery from the apparently mild toxic effects was complete within a few days to two weeks in all cases in which Bistrimate had to be discontinued because of the untoward reactions herein described.