CHEMOTHERAPY OF ECZEMA—DERMATITIS*

I. ORAL ADMINISTRATION OF SULFAPYRIDINE: ANALYSIS OF 301 CASES


Although considerable advances have been made in the understanding and management of eczematous eruptions, there remains the need for a non-specific remedy with an effect comparable to that of the anti-histaminics in urticaria. This series of papers is submitted in the hope that drugs may be found for the alleviation and suppression of symptoms in eczema and atopic dermatitis; such a discovery would not take the place of rational investigation and treatment any more than does the use of anti-histaminics in cases of urticaria. These have, of course, been tried extensively in eczema, first on the assumption that what is "anti-allergic" must also be "anti-eczematous", and later because they were found to exert an anti-pruritic effect in some patients. Thus Baer and Sulzberger (1) first had promising results in a small series of cases of atopic and eczematous dermatitis; soon, however, Sulzberger (2) was to remark that he had found the anti-histaminic drugs not at all effective in eczematous contact dermatitis and only slightly beneficial in reducing itching in isolated and few cases of atopic dermatitis. Later Bettley and Spence (3) obtained rather better results, using Anthissan and Antistine, more recently synthesized antihistaminic drugs: 13 of 22 cases showed subjective or objective improvement, and 10 showed both. Encouraging as these figures are, they do not approach the success obtained in similar treatment of urticaria.

The use of sulfapyridine followed on the observation that it was beneficial in most cases of dermatitis herpetiformis (Swartz & Lever, 4). Gordon and Loewenthal (5), believing that many cases of chronic eczema were variants of this disease, obtained satisfactory results in suppressing symptoms and signs with the use of sulfapyridine. The next step was the realization that the clinical and histologic pictures of such cases of "endogenous eczema" differed in no way from those of cases of auto-sensitization or of the generalized eczematous states which may follow contact dermatitis. Such cases can, in fact, be differentiated only by careful history-taking and, occasionally patch-testing. In these cases, too, sulfapyridine appeared to alleviate signs and symptoms.† Finally, the drug was tried in other forms of eczema and in atopic dermatitis, and the results prompted me to communicate with Messrs. May & Baker, in the hope that some other closely related substance could be found, which would prove superior to sulfapyridine. The preliminary results which I mentioned have apparently gained recognition and one may find in a recent publication (6) that sulfapyridine "has been used successfully in cases of eczema and other sensitization skin reactions."

EXPERIMENTAL

The average daily dose of sulfapyridine was 3 tablets (1.5 grams), proportionately reduced for children. A few severe cases were given 3 or 4 grams daily for a short time and the dose reduced as improvement occurred. In some instances 3 tablets daily could not be tolerated, but 2 could be taken. If there was sufficient improvement the dose was normally reduced from 3 to 2 tablets daily at the end of a week, and then to 1 tablet at the end of the second week. There were naturally

* This compound title has been chosen in order to include those conditions, such as atopic dermatitis, which cannot strictly be classified as eczemas.
† The drug was obviously not used when sensitization to sulfonamides was suspected.

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slight deviations from this plan in some cases, but the figures given above repre-
sent both the average and the mode of variations. The great majority of patients
were ambulant during treatment; a few were advised to rest for the first few
days.

Side effects were remarkably rare. 2 cases of drug eruption, one of them an
acquired light-sensitivity, were encountered. Both cleared promptly when sul-
fapyridine was withheld. About 25% of patients complained of depression, head-
ache, nausea or vomiting; in all but 3 a temporary reduction of dosage enabled
them to continue until their progress justified taking only 1 tablet on retiring.
This dose is usually well tolerated. Leukocyte counts were done in many patients
during the early stage of this investigation; persistent absence of significant
changes then persuaded me that this precaution was not necessary as a routine.
The large number of infants and children in this series was singularly free from
any of the disagreeable side effects observed in adults.

Many patients had previous sulfonamide medication for minor ailments such
as coryza, sore throat and influenza; the small number of untoward effects sug-
gests that the population has not become sensitized to an appreciable extent.

When arsenic was given in addition to sulfapyridine it was either as 3 minims
(0.2 c.c.) of Fowler's solution or as a 3 1/2 grain (0.25 gram) tablet of carbarsone
3 times daily. Prolonged courses were never given in view of the dangers of late
sequelae, and the average period of administration was 2 weeks; arsenic was not
usually repeated in the treatment of relapses. Anti-histaminics were not given.

Local treatment was kept to a minimum. Potentially harmful applications were
discontinued in the few cases who confessed to using them; in many others the
application of bland substances such as calamine lotion was allowed to continue.
Where a placebo was indicated a shake lotion containing 3% of Burow's solu-
tion or 1% of liquor picis carbonis was prescribed. It is not my belief that such
applications alone could have produced more than transient and incomplete
relief. When there was secondary infection, or when an eczematous eruption had
its origin from an infected cutaneous focus, such as impetigo, local treatment of
the infected areas was given in addition to sulfapyridine medication. Vioform was
the usual remedy as 2% or 3% in a shake lotion or cream.

Classification of Cases

No classification of eczema-dermatitis can please everyone, and in a series of
this size there must be cases assigned to incorrect groups. Thus, an unreliable
history or unwillingness to cooperate in investigation may result in examples of
eczematous contact dermatitis being overlooked and classified with endogenous
eczema. Again, certain group distinctions are almost impossible to delimit:
should all cases of infantile eczema be regarded as manifestations of atopy?
If so, must they be grouped with adults who have suffered from atopic dermatitis
since infancy? Should these again be combined with flexural dermatitis appear-
ing for the first time in adults? In order to evade rather than answer these and
similar questions I have placed the cases in categories which are at least homo-
geneous; the relationships of the various categories are ignored, but they have been arranged so as to bring related groups together.

*Results*

The results are those of partial or complete suppression of symptoms and signs over a period of from 1 month to 4 years. A skin which has once reacted by manifesting eczema or dermatitis must always be under suspicion of reacting again when adverse conditions, specific or non-specific, are encountered. Many patients who have had a complete remission communicate from time to time, personally or through their physician, to say that they remain well; others have been lost sight of. Still others have repeated attacks which they themselves control with sulfapyridine; these have been designated as "Relapse/Response". A fair number belong to certain medical benefit organizations, thus ensuring that they would have to be seen personally by me in the event of a relapse.

"Improvement" is here taken to mean an appreciable degree of symptomatic relief along with objective improvement. In chronic cases such relief is considered significant only when it exceeds the temporary spontaneous improvements that are often experienced.

Maintenance doses have been required in many cases, as they are in dermatitis herpetiformis, and recrudescences often have to be checked by temporarily increasing the dose. Patients whose dermatoses have recurred over many years are to be regarded as improved if a given attack is controlled more quickly with treatment, and in some instances when further attacks are prevented by maintenance doses of sulfapyridine.

The tables represent 301 consecutive cases who took sulfapyridine and reported back at least once. They were attended in private practice, and include many seen and treated by Dr. S. Gordon. 297 were whites, 2 Indian and 2 Chinese. The sexes are represented about equally. Results in a further series of cases, treated at the Johannesburg General Hospital over the same period, are comparable; their records are, however, difficult of access and hence are not included.

*Group I—Infantile Eczema.*

These cases manifested the disease in the first year of life. The majority began with a rash of the face and milk crust and after a varying interval developed eczematos lesions of the trunk and/or limbs; this agrees closely with Hall's (7) findings. Such cases are often called "dermatitis seborrhoeica of infants" and are suggestive of a primary impetigo with secondary bacterid or auto-sensitization (Gordon, 8). Hence local treatment to the scalp and face was usually instituted at the same time as sulfapyridine therapy.

*Comment:* Most of these cases have been followed for periods varying from 1 month to 1½ years and 11 remain well. In some infants the original (?) impetigi-

* (i) The cases in this series have been indexed separately, and records are available for scrutiny.
(ii) The figure "693" is used throughout the tables in place of "sulfapyridine".

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nous) area remained troublesome for a few weeks after the generalized eruption cleared, and eventually responded to local treatment.

Group II—Atopic Dermatitis (Besnier's Prurigo, Flexural Eczema).

The patients in this group showed their first manifestation in early childhood, 27 of them before the age of 2 years. The eldest (No. 257) had the disease continuously for 27 years, since early infancy.

Comment: 7 patients remain symptom-free more than a year later, 3 of them on small maintenance doses of sulfapyridine. Duration of the disease appeared to make no difference to the speed of initial response, though the presence of pronounced lichenification entailed a longer course of treatment, and delay in

<table>
<thead>
<tr>
<th>TABLE I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile eczema</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>AVERAGE AGE AT ONSET IN WEEKS</th>
<th>AVERAGE DURATION OF DISEASE IN WEEKS</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td>693</td>
<td>16</td>
<td>13</td>
<td>43</td>
<td>6 8 2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>3</td>
<td>5</td>
<td>171</td>
<td>1* 2</td>
<td>---</td>
<td>1*</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>11.7</td>
<td>63</td>
<td>7 10 2</td>
<td>3</td>
<td>1</td>
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</table>

* This child subsequently had a relapse which could not be satisfactorily controlled with further medication.

<table>
<thead>
<tr>
<th>TABLE II</th>
</tr>
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<tbody>
<tr>
<td>Atopic dermatitis</td>
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<table>
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<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>AVERAGE DURATION OF DISEASE IN WEEKS</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td>693</td>
<td>18</td>
<td>4.5</td>
<td>4 9 5</td>
<td>3</td>
<td>---</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>10</td>
<td>12.8</td>
<td>4 1 1</td>
<td>3 4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>7.5</td>
<td>8 10 6</td>
<td>6 4</td>
<td></td>
</tr>
</tbody>
</table>

reducing the dosage. In 2 cases there had been previous, temporary response to arsenic.

Group III—Chronic Disseminated Neurodermatitis (Atopic Dermatitis).

This group is distinguished from the previous one only by the age of onset being at or after puberty. It is not suggested that the etiology of these cases is necessarily different from that of Group II, and it will be seen that the results of treatment are comparable.

Comment: The greater proportion of those given arsenic as well as sulfapyridine, as compared with Group II, is due to the fact that this group consisted of adults exclusively. Again the course of arsenic was a short one, and it was not given a
second time; hence responses after relapse took place while the patients were on sulfapyridine only.

**Group IV—Acute Endogenous Eczema.**

These cases were of a duration of less than 2 months before treatment was begun. Origin from contact dermatitis or auto-sensitization had been excluded as far as possible by the history and clinical appearances. One of the patients developed the eczematous eruption 2 days after an injection of procaine-penicillin; it had proved unresponsive to various anti-histaminic drugs.

*Comment:* The high incidence of improvement in the first week should no doubt be correlated with the fact that the disease had been evident for less than 2 months. Actually those who improved in the first week averaged a previous duration of only 2.7 weeks' illness, the others 3.9 weeks.

**Table III**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>AVERAGE DURATION OF DISEASE IN YEARS</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td>693</td>
<td>7</td>
<td>2.4</td>
<td>5 1 1 1</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>17</td>
<td>7.3</td>
<td>5 5 2 1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>6.0</td>
<td>10 6 2 1</td>
<td>4</td>
<td>5</td>
</tr>
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</table>

**Table IV**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td>693</td>
<td>24</td>
<td>19 4 1</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>23</td>
<td>20 1 1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>39 4 1 1</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>
(2). 8 patients showed improvement on sulfapyridine only, after showing no response to 2 weeks' arsenic therapy.

(3). The series includes 3 patients whose eczematous eruptions were located on sun-exposed areas. However, the margins always extended on to unexposed areas; thus in men who wore open-neck shirts the rash on the chest was U-shaped, not V-shaped. These patients became almost well in the first 2 weeks and had no residual sun-sensitivity, even while on sulfapyridine treatment.

(4). 4 patients were given daily doses of 6 tablets (3 grams) of sulfapyridine because of the severity of their condition (Nos. 1, 142, 170, 219). Only one was given arsenic in addition. All showed considerable improvement in the first week.

**TABLE V**

*Chronic endogenous eczema*

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td>693</td>
<td>39</td>
<td>20 12 2 1 —</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>59</td>
<td>37 12 2 3 1</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
<td>57 24 4 1 13</td>
<td>13</td>
<td>8</td>
</tr>
</tbody>
</table>

**TABLE VI**

*Pregnancy cases*

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td>693</td>
<td>5</td>
<td>3 2</td>
<td>2</td>
<td>—</td>
</tr>
</tbody>
</table>

*Group VI—Pregnancy Cases.*

Five patients, who would otherwise be classified as endogenous eczema, had their eruption only since becoming pregnant. They are listed separately here.

*Comment:* (1). Arsenic was not given to these patients.

(2). At least one patient has required maintenance doses of sulfapyridine since her pregnancy terminated.

*Group VII—Nummular Eczema.*

This ill-defined group is based purely on clinical grounds. The disease is presumably a manifestation of a number of causes, differing between cases, and inability to incriminate dietary, bacterial or other factors does not necessarily absolve them from suspicion in these cases. But as this is an attempt to assess the value of sulfapyridine in cases of eczema and atopic dermatitis, *irrespective of their etiology*, these cases are presented as a group without apology.
Comment: 3 cases responded to sulfapyridine only, having previously responded to arsenic. 2 responded to sulfapyridine who had previously been given arsenic without benefit.

**Group VIII—Residual Eczema after Contact Dermatitis.**

This type of case commonly follows over-treatment, and many patients listed here originally developed local eczema from the application of acriflavine to minor injuries of the skin. Subsequently a generalized eczematous outbreak occurred, with exacerbation on re-exposure to acriflavine. Where patch-testing is considered safe the result is constantly positive. A similar train of events can follow sensitization to any other contact allergen—cosmetics, wood dusts and so on. This group comprises those whose eczema was caused this way, but who continue to exhibit its manifestations even when not exposed to the allergen.

Pirilä and Kilpio (9) have recently drawn attention to instances of residual dermatitis after bichromate rashes persisting up to a year after ceasing contact with the allergen.

**Comment:** "Duration" is not tabulated as it was found impossible in many cases to distinguish the residual eczema period from the period of exposure to the allergen.

**Group IX—Auto-sensitization Eczema.**

It will be recalled that one of the clinical varieties of auto-sensitization originally described by Whitfield (10) consisted of widely-distributed papulo-vesicular

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**TABLE VII**

*Nummular eczema*

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>DURATION IN YEARS</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td>693</td>
<td>14</td>
<td>9.0</td>
<td>7 5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>6</td>
<td>4.3</td>
<td>3 —</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>6.5</td>
<td>10 5</td>
<td>1 3</td>
<td>4</td>
</tr>
</tbody>
</table>

**TABLE VIII**

*Residual eczema after eczematous contact dermatitis*

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>693</td>
<td>19</td>
<td>14</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>21</td>
<td>9</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>23</td>
<td>11</td>
<td>6</td>
</tr>
</tbody>
</table>
patches occurring after an exacerbation of chronic lichenified eczema. The clinical picture is well known to dermatologists; it need not follow exclusively on chronic eczema. Engman (11) has stated that it occurs in about one fourth of the cases in which there is an acute dermatitis in some part of the body—and it is treated as distinct from the general sensitivity developing after contact dermatitis (Group VIII). Cormia (12) has made important investigations which suggest that the antigen in these cases is a water-soluble fraction of epidermal cells.

*Comment:* The figures do not necessarily reflect improvement in the original lesion, merely in the secondary eczematous eruption.

### TABLE IX

*Auto-sensitization eczema*

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>DURATION</th>
<th>IMPROVED IN WEEKS</th>
<th>RELAPSE/RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>months</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>693</td>
<td>7</td>
<td>42</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>9</td>
<td>11.7</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>25</td>
<td>11</td>
<td>3</td>
</tr>
</tbody>
</table>

### TABLE X

*Infectious eczematoso dermatitis*

<table>
<thead>
<tr>
<th>DRUG</th>
<th>NUMBER OF CASES</th>
<th>DURATION IN YEARS</th>
<th>IMPROVED IN WEEKS</th>
<th>FAILED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td>1</td>
<td>2</td>
</tr>
<tr>
<td>693</td>
<td>3</td>
<td>0.8</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>693 + arsenic</td>
<td>1</td>
<td>2.5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>1.25</td>
<td>2</td>
<td>—</td>
</tr>
</tbody>
</table>

*Group X—Infectious Eczematoid Dermatitis.*

This is taken to mean an eczematous reaction in an area contaminated with infectious discharges, e.g., around persistent axillary boils, or the pinna in a case of chronic discharging otitis media.

*Statistical Note*

No significant difference is found in responses in Groups I to X. The figures suggest that improvement takes place more quickly in cases where the disease is of recent origin, and this is in accordance with expectation, for diseases of short duration should provide a greater proportion of spontaneous recoveries.

Table XI shows that while improvement took place equally in the first week, whether sulfapyridine was given alone or with arsenic, in the second week sulfapyridine alone produced more improvements. Testing these figures with the Loewenthal-Wilson (13) table, we find that the observed difference (46 against
is statistically significant at \( P = 0.05 \). This means that the odds are 19 to 1 against such a difference occurring by chance. A similar significance attaches to the higher rate of failures on sulfapyridine + arsenic, in the last column. The rational explanation is that the sulfapyridine + arsenic "population" tends to include the more chronic and serious cases, to whom one would naturally give the more intensive treatment.

**Patch Tests**

Serial patch-tests were done in 5 cases of contact dermatitis with generalized sensitization, i.e. an eczematous eruption appearing spontaneously on parts not in contact with the allergen. The sites of application were on unaffected areas of skin.

No. 33. White male, age 61, carpenter. Has had recurrent attacks of an itching rash on face, neck and forearms for 10 years. Noticed that working with Imbuya wood produced attacks. Present attack 1 month. Is still working with Imbuya. 12 Jan. 1950. Severe vesicular, squamous and partly lichenified eczema affecting face, neck, hands and forearms. Taken off work. Given sulfapyridine, 1 tablet (0.5 gram) thrice daily. Lead-in-milk lotion. Progress as below:

<table>
<thead>
<tr>
<th>Date</th>
<th>At work</th>
<th>Eczema</th>
<th>Imbuya patch-test (24 hours)</th>
<th>693</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 Jan.</td>
<td>Stops</td>
<td>++</td>
<td>++</td>
<td>begun</td>
</tr>
<tr>
<td>26 Jan.</td>
<td>off</td>
<td>±</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2 Feb.</td>
<td>off</td>
<td>±</td>
<td>±</td>
<td>+</td>
</tr>
<tr>
<td>3 Feb.</td>
<td>Resumes work</td>
<td>±</td>
<td>±</td>
<td>+</td>
</tr>
<tr>
<td>8 Feb.</td>
<td>working</td>
<td>+</td>
<td>++</td>
<td>stops</td>
</tr>
<tr>
<td>13 Feb.</td>
<td>working</td>
<td>±</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>20 Feb.</td>
<td>working</td>
<td>+</td>
<td>±</td>
<td>+</td>
</tr>
<tr>
<td>24 Feb.</td>
<td>working</td>
<td>+</td>
<td>neg</td>
<td>+</td>
</tr>
</tbody>
</table>

This patient subsequently had 2 relapses, took sulfapyridine irregularly, and by August was clear. Since May he had not worked with Imbuya wood.

No. 56. White female, age 43. Housewife. 5 years' recurrent summer eruption where metal articles are in contact with the skin. This summer also in antecubital fossae, where there is no metal contact.
In this case there was no recurrence of the generalized eczema but contact with metal invariably produced a local reaction, whether she was taking sulfapyridine or not.

No. 171. White male, age 48. Office executive. Recurring, almost constant rash of hands and feet from age of 6 until 44, when contact dermatitis from leather discovered. Remained well, when not in contact with leather, except for areas of papular eczema on back of neck and shoulders, where no contact with leather occurred. Temporary or no benefit from local applications and from roentgen therapy. Patch-tests with leather (not chrome) always positive since first done in 1945.

This patient had no recurrence in a year and has taken no more sulfapyridine. Unwilling to have more patch-tests.

No. 182. White female, age 51. Housewife. Eczema in area of shoe and garter contact for 6 months. Recently affecting parts not in contact with leather.

Discussion

(i). Action of Sulfonamides in various dermatoses: The reason for the selection of sulfapyridine has been discussed. When several sulfonamides are active in varying degrees in apparently non-bacterial dermatoses, it is usually found that sulfapyridine is the most effective. Thus, in discussing the treatment of dermatitis herpetiformis, Lever (14) placed sulfapyridine first, sulfathiazole second, sulfanilamide third and sulfadiazine a poor fourth. Similarly Sulzberger (15) gave sulfapyridine as the drug of choice in dermatitis herpetiformis, acrodermatitis continua, dermatitis repens, impetigo herpetiformis and relapsing, non-suppurative, nodular panniculitis. He stressed the point that the drug must be given for a long time, a dictum which applies also to many of the cases under review here. Careful study of the literature, and especially of society meetings, shows that these views have been generally adopted. Nevertheless, earlier reports show that sulfonamides other than sulfapyridine have been credited with clearing up eczematous eruptions. Combes and Canizares (16), for instance, quote Sutton and Sutton as obtaining good results in “eczema of the legs” from the use of sulfanilamide, and Cornbleet similarly in “chronic exudative dermatitis with
edema of the ears." Lindsay (17) also claimed to have cleared up a case of chronic eczema of 10 years' standing with small doses of sulfanilamide, and Shoch (18) is reported as observing improvement with sulfanilamide in nummular eczema. Larger doses were recommended by Fox (19) for the same condition. Both Andrews (20) and Costello (21) have seen good results from sulfapyridine in the Sulzberger-Garbe disease.

It is generally accepted that the foregoing results were not due to any antibacterial action on the part of the drug employed. In the first place the dosage customarily used is too small to raise the sulfonamide blood-level to the necessary concentration. Secondly it has been shown, at least in dermatitis herpetiformis, that the beneficial action of sulfapyridine is not inhibited by giving para-aminobenzoic acid simultaneously, as would undoubtedly be the case if an anti-bacterial action were required (Klaber & Yorke (22); Felscher (23)).

(ii). Role of arsenic: The results, including a consideration of cases responsive to either or both drugs, show that either sulfapyridine or arsenic can produce improvement in some eczema or dermatitis patients, but the former drug appeared to act more constantly. There is no apparent advantage in combining the two.

(iii). It cannot be over-emphasized that the results are to be viewed in terms of suppression, partial or complete. If the disease does not recur when suppressive therapy is stopped it may simply mean that the skin, having been sufficiently rested, loses its altered capacity to react. This is a vague concept, but one that has a parallel in some cases of urticaria on suppressive treatment with anti-histaminics. It may also be that the psychological effect of suppressing a chronic and disfiguring eruption may be enough to neutralize anxiety in cases of neuro-dermatitis.

(iv). The 5 cases in whom patch-test studies were made are of some interest. Nilzén (24) used the same approach with antihistaminics. He found no change in positive patch-test results when anti-histaminics were given orally before and during the period of patch-testing. With the cases on sulfapyridine therapy, on the other hand, there was a tendency for patch-tests to be less positive or even negative under these conditions. In the single case (No. 33) in whom sulfapyridine was mixed with the allergen, the patch-test became more positive. This result agrees with Nilzén's, using a mixture of nickel and antihistaminic. While the general specific epidermal sensitivity was reduced there was no such change in areas previously reacting to contact. Thus, Case No. 33 showed a local flare-up to his allergen on parts affected with eczema, even when his patch-test had become negative.

(v). Caution should be exercised in accepting the numerical results (Table XI) too trustingly. They refer only to improvement, usually in the first few weeks of treatment, and there are undoubtedly many cases who have been lost sight of and in whom the condition has relapsed, to be unresponsive to further sulfapyridine therapy. On the other hand, the immediate results are often so impressive as to gain the patient's confidence and lighten the task of investigation and treatment. Many physicians are now using this treatment without reference to a dermatologist, and it has become routine practice in the Chamber of Mines
Hospital, Johannesburg. This is not necessarily a good thing, for there are real dangers in the indiscriminate use of sulfapyridine, even in small doses. On the other hand other sulfonamides are constantly used in self-medication of minor ailments, and in much larger doses. The effects in this series have not been serious, but this does not dispose of the element of risk.

Summary and Conclusions

1. 301 cases of eczema or atopic dermatitis were treated with small doses of sulfapyridine. 149 of these were also given small doses of arsenic by mouth.
2. 83% showed subjective and objective improvement in the first 2 weeks.
3. The series has been subdivided to compare the response to sulfapyridine with and without arsenic.
4. Further subdivision shows results in clinically different groups of cases.
5. No serious side effects from sulfapyridine were observed in this series.
6. In 5 cases of eczematous contact dermatitis on sulfapyridine, the behavior of reactions to patch-tests was observed. These tended to become less positive while the patient was on sulfapyridine.
7. Results indicate that sulfapyridine may suppress symptoms and signs in many cases. It is, in the writer's experience, the most successful non-specific agent in treating eczema and atopic dermatitis.
8. The indiscriminate use of sulfapyridine for this purpose is not advised, but its action may help in directing research to the discovery of related compounds which are less toxic and more effective. Since this paper was written sodium para-aminobenzoate has given satisfactory results in a few trials.

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