lepers. They certainly threatened to do so with a regularity that
never became monotonous. Indeed I cannot recall a week during
which they did not threaten to bomb-out or machine gun the
whole settlement. The reason why the Japanese confined them­
selves to threats is simply told. The leper settlement contained
patients from all over the Federated Malay States. Under the
British regime these various states paid so much per head per
day for their lepers maintained at Sungei Buloh. This payment
was continued under the occupation for the Japanese, terrified
of infectious disease, would rather levy money than risk the return
of lepers to their various districts. Except for a token payment
for the maintenance of Sungei Buloh this money was retained
by the local Japanese Governor for his own use. It will be
realised that if he retained one shilling per head per day (which
is about correct) for a thousand patients, he was making a profit
of fifteen hundred pounds per month. And so the lepers were
spared—they were profitable.

When the end came the hospital wards were empty, for
no-one was left able to care for the sick. Like wraiths over the
untended paths, the patients came out of their houses with un-
certain eyes and wavering gait, to welcome their liberators.

* TREATMENT OF LEPROSY WITH
Diasone—A PRELIMINARY REPORT

By G. H. Faget, M.D. and R. C. Pogge, M.D., Carville, La.

Recently a number of new derivatives of diamino diphenyl
sulfone have been tried in the chemotherapy of experimental
animal tuberculosis and more recently of human tuberculosis.
One of these agents is diasone, the disodium formaldehyde
sulfoxylate derivative of diamino diphenyl sulfone. Callomon
has reported that diasone inhibited the progress of experimen­tal
tuberculosis in the guinea-pig and that it was less toxic than
promin. Feldman and associates have corroborated the therapeu­
tic

*Reprinted from New Orleans Medical and Surgical Journal (1945), 99, 145,
effect of diasonne in experimental tuberculosis and found it less toxic than the parent drug diamino diphenyl sulfone. Diasonne has been used in human tuberculosis with promising results by Petter and Prenzlau, but their report has not been generally confirmed and the status of diasonne therapy of tuberculosis is still under clinical investigation.

In the chemotherapy of leprosy, promin is still being used intravenously at the National Leprosarium with encouraging results. Promin, however, has been found to be too toxic when medication is advantageous in such a chronic disease as leprosy, the low toxicity of diasonne when given by mouth had a special appeal to the writers.

Petter and Prenzlau advocated 1 gram of diasonne a day as an adequate dose in treating human tuberculosis. They found blood levels ranged between 1.5 mg. and 2 mg. per 100 c.c. with this dose. Upon increasing the dose they found that the blood concentration levels did not increase proportionately, and expressed the opinion that a dose greater than 2 grams a day was not indicated in the treatment of clinical tuberculosis.

Technic of medication.

In the writers' preliminary study a small group of leprosy patients were started on 1 gram of diasonne daily (one 5 grain capsule three times a day). Careful clinical and laboratory examinations were conducted. Urinalyses and hemograms on every patient were done twice a week at first and later at intervals of at least two weeks, and other laboratory tests were carried out when indicated. Within a few days of the inception of treatment, several patients experienced hematuria, so that treatment was necessarily discontinued. Indeed the frequency of hematuria was the chief indication for changing the technic of administration of diasonne. It was found that by starting with smaller doses of diasonne, 1/3 gram daily, the development of hematuria could be avoided. After the patient had acquired a tolerance for the drug, that is after one or two weeks, it was found to be safe to increase the dose to 2/3 gram daily. Several weeks later, if no toxic symptoms had developed, the full dose of 1 gram could be administered.

At present, the maximum dose is 1 gram daily, and this dose is administered only to patients exhibiting no evidence of intolerance after one month or more of clinical and laboratory observation.

Toxic manifestation and reasons for discontinuing treatment.

Although diasonne was administered to 70 patients altogether,
TREATMENT OF LEPROSY WITH DIAISONE

TREATMENT OF LEPROSY WITH DIAISONE

Treatment had to be discontinued in 23 of them. Table 1 lists the causes for discontinuance of treatment.

<table>
<thead>
<tr>
<th>Causes for discontinuance of daisone treatment.</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematuria</td>
<td>6</td>
</tr>
<tr>
<td>Gastritis</td>
<td>4</td>
</tr>
<tr>
<td>Anemia</td>
<td>3</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>1</td>
</tr>
<tr>
<td>Iridocyclitis</td>
<td>2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Deserting absconding patients</td>
<td>2</td>
</tr>
</tbody>
</table>

Renal damage. Renal irritation resulting in gross or microscopic hematuria was the cause for interrupting therapy in six patients. This condition developed exclusively during the early stage of the investigation, when the drug was given in initial doses of 1 gram. Since the adoption of new technic of starting all patients on 1/3 gram of daisone daily and increasing to 2/3 gram only after one or two weeks of treatment, no further evidence of renal dysfunction has occurred.

Gastritis. Nausea of a mild nature was reported at first by approximately one-fourth of the patients taking daisone. With continuance of treatment, as the patients acquired a tolerance for the drug, nausea decreased or disappeared. Only a few patients complained of severe nausea with anorexia and loss of weight. Vomiting seldom occurred. It was found that, by giving daisone during meals or in conjunction with alkalies, nausea often could be prevented. Some patients experienced instead of nausea an improvement in appetite, gain in weight, and increase in energy. Gastric irritation with nausea and vomiting was the complaint of six patients, in whom treatment was discontinued at their own request.

Hemolytic anemia. Daisone being an hemolytic agent, anemia developed in the majority of patients early in the course of treatment. The anemia was generally mild and with the development of tolerance was often replaced by an actual increase in erythrocytes and hemoglobin. Even a moderate degree of anemia was usually controllable by the oral administration of iron, liver extract and Vitamin B or by Ventrex as adjuvant therapy. The writers have considered a fall in the red blood cells below the level of 3,000,000 as an indication for temporarily discontinuing daisone. Persistent anemia necessitated permanent discontinuance of treatment in four patients.

Table 2 shows the changes which occurred in the erythrocyte counts of the 47 patients who were able to continue treatment
for more than three months.

Table 2. Changes in erythrocyte counts during treatment.

<table>
<thead>
<tr>
<th>Cases</th>
<th>No change (differences of less than 50,000)</th>
<th>Decreased counts</th>
<th>Increased counts</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>10.7%</td>
<td>53.2%</td>
<td>36.1%</td>
</tr>
</tbody>
</table>

The average decrease in red blood cells counts in individual cases varied from 50,000 to 1,480,000 and the mean of the averages for the patients was 350,000.

The average increase in the red blood cell counts in individual cases varied from 50,000 to 900,000 and the mean of the averages for the 17 patients was 270,000.

Dermatitis. Toxic dermatitis, manifesting itself twice as erythema nodosum and once as erythema multiforme was the reason for discontinuance of treatment in three patients.

One case of iridocyclitis, one case of hypertension, which were merely coincidental, and two patients who deserted account for the other interrupted treatments.

It is interesting to note that all 23 patients in whom treatment was stopped had taken diasone less than three months, too short a period for evaluation of therapeutic results. It is gratifying that, symptoms of intolerance severe enough to demand cessation of treatment, do not develop after the early stage in the course of treatment.

Clinical material.

The above 23 patients eliminated, there were 47 who took treatment for more than three months. These 47 cases form the clinical material upon which this report is based.

Type of disease treated.

Of the 47 patients under study, 42 were of lepromatous or mixed type, 4 were of the maculo-anesthetic or neural type, and 1 was of the tuberculoid type. It is thus evident that patients with the least favourable prognosis formed the bulk of the clinical material under investigation.

Furthermore, of the 42 lepromatous and mixed cases, 25 were far advanced, 14 moderately advanced, 3 minimal in extent of the disease.

Approximately four months of treatment with diasone usually was necessary before clinical evidence of improvement was observed. Thereafter, improvement was usually progressive and increased directly with the length of the period of treatment. This is demonstrated in table 3.
TREATMENT OF LEPROSY WITH DIASONE

Table 3.

Relation of duration of diasone therapy to therapeutic effect.

<table>
<thead>
<tr>
<th>Duration of therapy</th>
<th>No. of cases</th>
<th>Improved</th>
<th>Percentage improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 to 6 mo.</td>
<td>16</td>
<td>11</td>
<td>68.7</td>
</tr>
<tr>
<td>6 to 12 mo.</td>
<td>26</td>
<td>19</td>
<td>73</td>
</tr>
<tr>
<td>12 to 18 mo.</td>
<td>5</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47</strong></td>
<td><strong>35</strong></td>
<td><strong>74.5</strong></td>
</tr>
</tbody>
</table>

Table 3 shows that the percentage of improvement also increased with the size of the daily dose of diasone up to a certain point.

Table 4.

Relation of average daily dose of diasone to therapeutic effect.

<table>
<thead>
<tr>
<th>Gram/day</th>
<th>No. of cases</th>
<th>Improved</th>
<th>Percentage improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1-0.19</td>
<td>...</td>
<td>3</td>
<td>33</td>
</tr>
<tr>
<td>0.2-0.29</td>
<td>...</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0.3-0.39</td>
<td>...</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>0.4-0.49</td>
<td>...</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>0.5-0.59</td>
<td>...</td>
<td>12</td>
<td>100</td>
</tr>
<tr>
<td>0.6-0.69</td>
<td>...</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>0.7-0.79</td>
<td>...</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>0.8-0.89</td>
<td>...</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>0.9-1.00</td>
<td>...</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47</strong></td>
<td><strong>35</strong></td>
<td><strong>74.5</strong></td>
</tr>
</tbody>
</table>

Table 4 shows that the percentage of improvement also increased with the size of the daily dose of diasone up to a certain point.

From the above tables it is apparent that the percentage of improvement was in direct proportion to the duration of treatment and to the average daily dose of diasone up to 0.8 gram. In estimating the average daily dose, periodic rest intervals of several days, during which no drug was administered, were taken into consideration. Although the optimal dose of diasone for leprosy has not been established, it is felt that 1 gram a day is the maximum dose which should be administered over an extended period of time. A dose of 2/3 gram daily was tolerated by a larger number of patients than the 1 gram dose and was adequate in most cases as can be judged by the improvement shown in table 4. It is doubtful that doses larger than 1 gram daily would be therapeutically more potent than the smaller doses.

Of the 47 patients in this investigation only three have shown any advance of the disease in spite of treatment with diasone. In two of these patients, who had apparently shown some improvement after six months of treatment, a few small nodules appeared at the site of old ones which had temporarily receded. This development can be considered a progression of the disease during treatment, and these two patients can be classified as having become worse. However, upon continuation of diasone, the new
nODULES showed evidence of subsiding. Another patient with far-advanced lepromatous leprosy died of progressive leprous laryngitis. She had taken very inadequate treatment because of repeated and prolonged periods of interruption due to a secondary anemia. Two blood transfusions were necessary when the red blood cells reached the low level of 2,500,000. Altogether this patient was able to tolerate only 47 grams of diasone scattered over nine months of treatment—an average of only 0.21 gram daily. The above three cases, 6.5 per cent of those under study, are the only ones in which the disease advanced.

Previous experience in the National Leprosarium indicates that with the type and stage of leprosy under investigation the frequency and the degree of improvement shown are much greater than might be expected in the absence of treatment with diasone.

Tuberculosis is a frequent and serious complication of leprosy at the National Leprosarium. The development of tuberculosis may be regarded as an additional indication for the institution of promin or diasone therapy. Thus far ten tuberculosis patients have been placed on promin or diasone treatment in the hope that both diseases might be favourably influenced by the same drug. In two of them the tuberculous disease advanced during the course of treatment but in the majority of the others an improvement was shown by serial roentgenograms.

Two brief case histories, representative of a large group, will serve to demonstrate further the effects of diasone in leprosy.

Case Reports.

Case 1.—Coloured female, 30 years of age, had far advanced lepromatous leprosy at onset of diasone treatment. The disease was of five years' duration. Clinical findings were large confluent nodules and infiltration of the face with generalised nodular eruption on arms, forearms, buttocks, thighs and legs, smaller discrete nodules over the chest and evidence of leprous rhinitis. Nasal and skin smears were positive of M. leprae. There was some advance in the disease following chaulmoogra oil treatment. Diasone was administered in doses of 2/3 gram daily, totalling 130 grams. In 7 months objective improvement was observed, although skin and nasal smears remained positive.

Case 2.—Coloured male child, 6 years of age, with moderately advanced lepromatous leprosy of two years' duration. Clinical manifestations were multiple nodules scattered over the face, plaques on the right side of the forehead and the left cheek, infiltration and scattered nodules on the forearms, hands, buttocks,
TREATMENT OF LEPROSY WITH DIASONE

Thighs, legs and feet, and evidence of leprous rhinitis. No improvement was noted with oral administration of chaulmoogra oil. Skin and nasal smears were always positive for *M. leprae*. Diasone was given in 1/3 gram doses daily and totalled 60 grams.

Definite improvement after 8 months is shown in the illustration.* Skin smears still positive.

**Conclusion.**

Diasone is a sulphone drug which can be given orally in the treatment of leprosy with relatively mild toxic reactions in most cases.

The average tolerated dose is 2/3 to 1 gram daily, given in 5 gr. capsules during meals.

Oral medication is preferable in leprosy; hence diasone has an advantage over promin which was found to be too toxic for oral administration in leprosy, and is used intravenously at the National Leprosarium.

The objective improvement observed during the diasone treatment of leprosy is encouraging but further clinical evaluation is necessary before it may be regarded as a leprostatic agent.

* Omitted here.

NOTES ON LEPROSY SETTLEMENTS

TANGANYIKA TERRITORY

A. G. MACKAY.

**The Role of Settlements.**

1. To segregate infective lepers with a view to reducing the incidence of leprosy in the area served by the settlement.

2. To provide a centre for training in leprosy work.

3. To set a standard for treatment which would be generally adopted throughout the Province in which the settlement is situated.

The opening of a leprosy settlement makes the surrounding community leprosy-conscious, and is a valuable step in propaganda towards diminution of the spread of infection.

As regards training this does not only mean the tuition of