

## SIX YEARS AQUEOUS SULPHETRONE THERAPY IN A RURAL AREA

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### **Introduction**

The sulphones have become firmly established as an effective method of treatment of leprosy and any more literature on this subject may appear superfluous but the apology for this paper is that it deals with the results of aqueous sulphetrone therapy in outpatient clinics in a rural area where the patients differ from those in the urban areas and institutions.

This centre is one of the Pilot Projects for Leprosy Control established in 1955 in a predominantly rural area. Prior to the opening of this centre, there was another Leprosy Unit, which was working here and which was converted and expanded into the present one. As the present centre has taken over the working of the same area, there has been uninterrupted observations of the effects of the therapy. (See map of the area of this centre.)

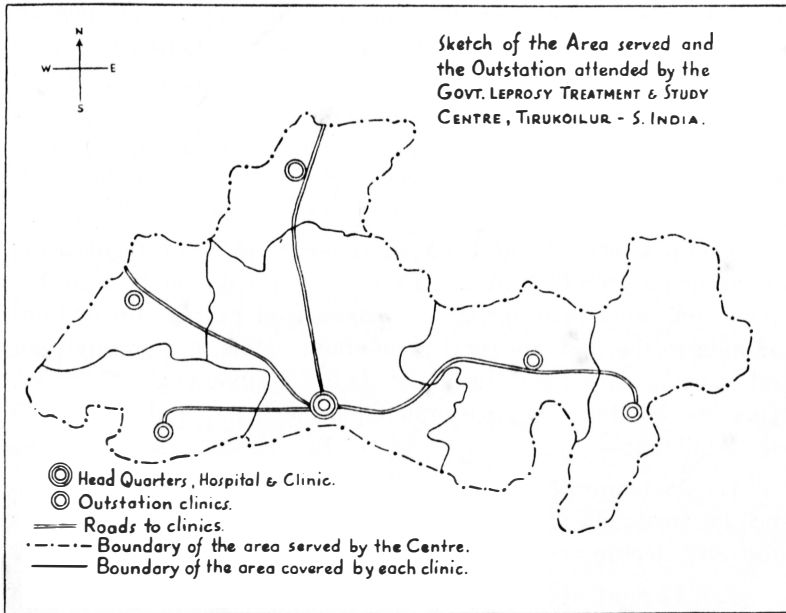
This centre is unique of its kind in this country as it consists of the Medical and Public Health wings working in co-ordination for the control of leprosy. The Medical Unit undertakes the curative part of the work and the Public Health section does intensive survey on the incidence of leprosy in the area chosen for the intensive work, as well as the study of the healthy contacts, follow-up of absentee patients, and health education about the nature and prevention of leprosy.

The treatment given in this unit is mostly oral DDS but a few cases which had been started on parenteral therapy by aqueous sulphetrone were continued and the present paper is a study of the results of the same.

The work of this centre is arranged as follows:—

The headquarters of the centre is at Tirukoilur (South Arcot District of Madras State) and 5 outstation clinics have been established in the various zones of the Pilot Project area, where patients get treatment once a week.

Each clinic is worked once a week at each of these zones so that the treatment is taken to the nearest possible point to the patients' homes. The patients are examined and treated and their progress noted in the case sheets with records of bacteriological examinations. This being a rural area, the clinics are held under the shade of trees, as buildings are not available except at two places. Also, no facilities are available for biopsy or any other



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Work begun: 28.4.55.

No. of villages served by the Centre: 54.

Total population of these villages: 65,290.

Total No. of out-station clinics: 6.

| Ser. No. | Name of Clinic     | Day open  | Distance from Headquarters | No. of villages served |
|----------|--------------------|-----------|----------------------------|------------------------|
| 1.       | Tirukoilur         | Saturday  | —                          | 18                     |
| 2.       | Velandai & Sangiam | Monday    | 8 miles                    | 7                      |
| 3.       | Veerapandi         | Wednesday | 6 miles                    | 7                      |
| 4.       | Attipakkam         | Thursday  | 6 miles                    | 4                      |
| 5.       | Mugaiyur           | Tuesday   | 9 miles                    | 13                     |
| 6.       | Ayandur            | Friday    | 11 miles                   | 5                      |

All these clinics operate once a day on one day of the week at each place.

Total number of cases under treatment on 31.12.57:

|                 |     |     |     |       |
|-----------------|-----|-----|-----|-------|
| Lepromatous     | ... | ... | ... | 536   |
| Non-lepromatous | ... | ... | ... | 1,352 |
| TOTAL           |     |     |     | 1,888 |

complicated laboratory investigations, and the only routine investigations that are performed are the smear examinations for leprosy bacilli as well as the ordinary haematological examinations. Every patient is given treatment as an outpatient and attends the clinic once a week (in the case of aqueous sulphetrone therapy once at the outstation clinic in the respective zone and once at the headquarters clinic).

The patients are all from rural areas, most of them being agriculturists and illiterates. They are normal members of the village following their usual occupations and having superstitions common to the illiterate rural population. Most of them are poor and have to earn their livelihood daily as labourers. There are many special difficulties encountered in such a population which are as follows:—

1. As many of them are agriculturists, regularity of attendance for treatment is seasonal, depending on the agricultural work; most absenteeism occurs during the agricultural season.

2. As most of them are illiterate, they have to be instructed repeatedly about the necessity for regularity in treatment and to report complications at the earliest moment.

3. Superstitions and religious obligations cause absenteeism for many.

4. They are usually hired labourers and so it is difficult to get them to be regular every week for treatment.

5. There is a well equipped hospital in this centre for the hospitalization of any intercurrent complications, but because of illiteracy, poverty, and superstitions, it is difficult to get them to come to hospital for the treatment of any complication.

Aqueous sulphetrone therapy for 6 years in this centre is assessed as follows:—

#### **The Number and Types of Cases Chosen and Previous Treatment**

All the 34 cases chosen for this therapy were lepromatous, and except for 6 cases have had hydnocarpus oil treatment for varying periods as shown in Table 1. These were started on the sulphetrone therapy because they did not derive much benefit from hydnocarpus oil. It happens that this was the first sulphone to be used in this centre.

Initially 22 cases began treatment in July 1951 and 12 cases were added up to the end of the year 1951. The present report is based on the findings made in the 15 patients who have been on continuous treatment since 1951 to date from among the 34 initial cases. Reasons for the stoppage of treatment in the other 19 cases are given below.

| No. of cases | Reasons for stopping treatment  |
|--------------|---|
| 3            | Died due to intercurrent illness not connected with leprosy.                                |
| 8            | Migrated to other areas.  |
| 5            | Changed to oral DDS therapy as they could not come twice a week for sulphetrone injections. |
| 3            | Discontinued treatment for any reason.  |
| 19           | Total.  |

The types of cases who have been on continuous treatment are as follows:—

| No. of cases | Types of cases                         |
|--------------|--|
| 6            | Macular lepromatous (L <sub>1</sub> ). |
| 6            | Diffuse lepromatous (L <sub>2</sub> ). |
| 3            | Nodular lepromatous (L <sub>3</sub> ). |
| 15           | Total.                                 |

As regards the previous treatment of these cases, all of them except one case have had treatment with hydnocarpus oil for varying periods as shown in Table II.

#### **Initial Examination**

This comprised examination of the leprotic lesions and general physical examination; also bacteriological examination using the "slit-scrape" method. At least 6 smears were taken of each patient and the bacterial index calculated, taking the maximum positivity as 6, as described in Practical Textbook of Leprosy by R. G. Cochrane, page 71. Also there were routine haematological examinations, i.e. haemoglobin percentage and RBC count were done for the first year as a routine every three months but these were given up later as unnecessary, except in cases where there was clinically recognised anaemia.

#### **Periodical Examinations**

These comprised clinical and bacteriological examination once in six months to assess the progress of the cases; and clinical photography of a few cases where there were lepromatous nodules; biopsy or lepromin test could not be done due to lack of facilities.

#### **Records**

Complete and detailed records were maintained, with diagrammatic representations of the lesions and photographs when necessary. Notes were recorded about any serious complication

or intercurrent illness affecting any patient during the course of therapy.

### **The Treatment**

(a) *Basis for Aqueous Sulphetrone Therapy*: As the Madras Leprosy Workers regarded DDS as too toxic for mass treatment (Cochrane and Ramanujam—1945) during this period and as aqueous sulphetrone was considered a cheap, effective and safe therapy, this therapy was introduced here. (Ref. Ramanujam "A cheap, safe and effective sulphone" at the Third All India Leprosy Workers' Conference at Madras in 1950.)

(b) *The Drug*: The drug used for this has been the sulphetrone granules manufactured by Messrs. Burroughs Wellcome and Company Limited.

(c) *Method of preparation*: The solution used is of a 50% strength and is made up as follows:—

50 gm. of sulphetrone granules are dissolved in hot distilled water and the final volume made up to 100 ml. No preservative is used. This solution is then placed for 10 minutes in a boiling water-bath as a substitute for autoclaving, as no facilities exist in this centre for autoclaving. This solution is acid in reaction and gives rise to excessive burning sensation at the site of the injection, hence it is neutralized by the addition of sodium carbonate (about 1.5 gm. of sodium carbonate to 1 litre of the solution). The solution is then transferred to a sterilized transfusion bottle from which it is drawn into a syringe for injections.

To avoid deterioration, only about 8 ozs. (327.44 ml.) of the solution are prepared at a time so that the solution is not used for more than two weeks before a fresh solution is made.

### **Injection Method and Dosage**

The injections are given intramuscularly twice a week. The starting dose is  $\frac{1}{2}$  ml. twice a week increased by  $\frac{1}{2}$  ml. every week till a maximum of 3 ml. twice a week is given (3 gm. of sulphetrone). No abscesses or any other complications have been met with from these injections except at one period, when there was a series of injection abscesses from the injections given during one week. On investigation the defect was found to be due to the carelessness of the injectors, which was immediately rectified. Except for this very brief period the injections have been free of such complication.

### **Duration of Treatment**

The maximum period of treatment of the 15 cases who have been on continuous treatment has been 72 months and the minimum period has been almost the same, but the actual period of treatment of each has been much less due to the irregularity of the patients.

The total duration of treatment in weeks and the actual period of treatment for each patient is given in Table II.

### Complications

The complications during treatment have been very few and not of such a serious nature as to stop treatment permanently. The commonest complication has been the lepra reaction which necessitated temporary hospitalization and temporary cessation of treatment. The details are as follows:—

1. *Lepra reaction*

8 cases—maximum number of days of absence due to this was 30.

2. *Anaemia*

Very few cases have shown any serious degree of anaemia such as to warrant any special attention or hospitalization.

3. *Neuritis*

Nil.

4. *Eye complications*

Only one patient developed iritis of both eyes which later on developed into iridocyclitis. But in a later series of cases started in 1952, there were a few cases of iritis for which I cannot account properly. The patients who manifested such eye complications had an allergic diathesis, as evidenced by eczema in many of them.

There was one patient who showed a peculiar allergic manifestation immediately after the injection which consisted of severe itching and urticarial rashes but which did not occur when the dose of sulphetrone was kept below 2 ml.

### Results of Therapy

Among the fifteen cases treated, six are completely negative, bacteriologically and clinically, five of them for one year and one since July 1957. Of these six cases, three cases are L<sub>2</sub> and three cases L<sub>1</sub>. All of them have been very regular in treatment, the attendance ranging from 75% to 92% of the total treatment days which can be considered extraordinarily good in a rural area in India. It is also noteworthy that none of these patients had any complication except a very minor attack of lepra reaction occasionally so that their treatment has been almost continuous.

Among the remaining nine cases, three cases have improved very greatly, their BI being very small, i.e., less than one. They have also become almost free of clinical signs and their regularity of attendance has been high, ranging from 66% to 90.1%. Of these three cases, one is L<sub>3</sub>, one is L<sub>2</sub>, and one is L<sub>1</sub>. One L<sub>1</sub> case in this group had become bacteriologically negative in 1954

but after a period of absence from treatment he was found to have relapsed into mild positivity on reporting for routine check in July 1957, i. e., three years after the cessation of treatment.

As regards the remaining six cases, one patient who has been very irregular (the regularity of his attendance being only 54% of the total clinic days) and who was treated for iritis by quacks, has shown slight clinical improvement and moderate bacteriological improvement. The remaining five cases have still clinical lesions of a very low intensity, i. e., slight infiltration of skin or slight thickening of ears (some of them are also free of signs and their bacteriological index is 1). Except for the one patient who had an iritis and who had absented himself from treatment, all the other patients have shown very good improvement, clinically and bacteriologically.

### Conclusions

The advantage observed for therapy by intramuscular injection of an aqueous solution of sulphetrone are:—

1. Because of its low toxicity, it can be administered even to anaemic patients and those with low general standard of health. (The general standard health of these patients is poor.)
2. Bacteriological negativity was attained in 40% over the period of five years, which is quite encouraging.
3. Serious complications are uncommon.

### Disadvantages

This therapy is not suitable for mass treatment for the following reasons:—

1. This treatment involves bi-weekly injections which are difficult and cumbersome for the field workers; facilities for injection in field conditions are deficient.
2. Patients in a rural area are not able to attend the clinics regularly even once a week due to their occupations and hence it is very difficult to get them to attend twice a week for this therapy.
3. The period required for bacteriological negativity is rather long (five years being the minimum).
4. The cost of the treatment is definitely higher than that of DDS without the results of the therapy being any better.
5. In an endemic area like this, where a large area has to be covered by this centre under field conditions, a therapy which involves bi-weekly injections and also which costs more without proportionately better results than oral DDS is definitely not suitable for mass treatment.

My thanks are due to Sri. T. R. Krishnamachari, Secretary, Thakkar Baba Kushta Nivaran Sangh, Tirukoilur, for having permitted me to treat the cases in the clinics of the Thakkar Baba Kushta Nivaran Sangh, Tirukoilur.

I also thank Dr. U. Maruthi Rao, B.Sc., M.B.B.S., D.L.O., former District Medical Officer South Arcot District, Cuddalore, for having given me guidance and encouragement in my work.

TABLE I

| Analysis of the Series of Cases on Sulphetrone |   |
|--|---|
| Total No.                                      | 34  |
| Clinical Type                                  | 6 of L <sub>1</sub> , 22 of L <sub>2</sub> , 6 of L <sub>3</sub>  |
| Previous Treatment with Hydnocarpus oil        | 1 for 2—3 years or more<br>nil for 2 years or more<br>27 for $\frac{1}{2}$ —1 year or more<br>6 new cases |
| Stopped treatment                              | 3 died<br>8 migrated<br>5 were transferred to oral DDS<br>3 lapsed from treatment                         |
| Continued treatment for at least 324 weeks     | 15  |

TABLE II

| Analysis of the 15 cases persisting on Sulphetrone |  |
|--|--|
| Case 1.  | Clinical type L <sub>2</sub> N <sub>1</sub> . Treated over 329 weeks with 90% effective attendance, and a total dose of 771 gm. Previous treatment by other methods was for 1 year 3 months. The Bact. Index came down from 4 to greatly improved, and he became symptom free.   |
| Case 2.  | Clinical type L <sub>3</sub> N <sub>1</sub> . Treated over 329 weeks with 90.1% effective attendance, and a total dose of 761 gm. Previous treatment was for 2 months. The Bact. Index came down from 6 to 0.5, or very greatly improved, and he became symptom free.  |
| Case 3.  | Clinical type L <sub>2</sub> N <sub>1</sub> . Treated over 329 weeks with 91% attendance, and a total dose of 709 gm. Previous treatment was for 1 year 4 months. The Bact. Index came down from 4 to negative on 13.6.56, and he became symptom free.   |
| Case 4.  | Clinical type L <sub>2</sub> N <sub>1</sub> . Treated over 329 weeks, with 75% effective attendance, and a total dose of 719 gm. Previous treatment was for 1 year 5 months. The Bact. Index came down from 4 to negative in June 1956, and he became symptom free.  |
| Case 5.  | Clinical type L <sub>1</sub> N <sub>2</sub> . Treated over 329 weeks, with 78% effective attendance, and a total dose of 471 gm. Previous treatment was nil. The Bact. Index came down from 2 to 0.75, or very greatly improved. The ears remained thickened and erythematous. He was negative bacteriologically in 1954, and did not attend for nearly a year after that: he has now returned with relapse. |
| Case 6.  | Clinical type L <sub>1</sub> N <sub>2</sub> . Treated over 329 weeks with 92% effective attendance and a total dose of 604 gm. Previous treatment was for 1 year. The Bact. Index came down from 2 and has been negative since June 1956, and he became symptom free. Operation for gynaecomastia was performed in the Centre.   |
| Case 7.  | Clinical type L <sub>3</sub> . Treated over 329 weeks, with 92% effective attendance and a total dose of 690 gm. Previous treatment was for 1 year. The Bact. Index came down from 6 to 1, and there is very slight infiltration of the skin.  |
| Case 8.  | Clinical type L <sub>1</sub> . Treated over 328 weeks with 89% effective attendance, and a total dose of 440 gm. Previous treatment was for 1 year. The Bact. Index came down from 3, and was negative since June 1956: symptom free.  |
| Case 9.  | Clinical type L <sub>1</sub> . Treated over 329 weeks, with 85% effective attendance, and a total dose of 722 gm. Previous treatment was for 1 year 6 months. The Bact. Index descended from 4 to negative since June 1956: symptom free.  |
| Case 10.   | Clinical type L <sub>3</sub> . Treated over 328 weeks, with 88% effective attendance, and a total dose of 769 gm. Previous treatment was for 6 months. The Bact. Index came down from 5 to 1, which is very good. There remains slight thickening of the ears.   |



- Case 11. Clinical type L<sub>1</sub> N<sub>1</sub>. Treated over 327 weeks, with 54% effective attendance, and a total dose of 345 gm. Previous treatment was for 3 months. The Bact. Index came down from 3 to 1.5. Skin infiltration is still present but nodules have gone. Old age and poor vision have caused his irregularity of attendance.
- Case 12. Clinical type L<sub>1</sub>. Treated over 324 weeks, with 84% effective attendance, and a total dose of 543 gm. Previous treatment was for 1 year 3 months. Bact. Index came down from 4 to 1, and there are no lesions now.
- Case 13. Clinical type L<sub>2</sub>. Treated over 324 weeks, with 84% effective attendance, and a total dose of 627 gm. Previous treatment was for 1 year 3 months. Bact. Index came down from 3 to negative since 1956. Slight thickening of ears remains.
- Case 14. Clinical type L<sub>2</sub>. Treated over 323 weeks, with 81% effective attendance, and a total dose of 472 gm. Previous treatment was for 1 year. Bact. Index came down from 5 to 1. Slight thickening of ears, and slight infiltration of skin remains.
- Case 15. Clinical type L<sub>2</sub>. Treated over 324 weeks, with 66% effective attendance, and a total dose of 409 gm. Previous treatment was for 1 year. Bact. Index came down from 5 to 0.3. Very slight infiltration of skin remains.