# INITIAL RESULTS OF A TRIAL OF CIBA 1906 IN DDS-INTOLERANT AND REACTION-PRONE LEPROSY CASES IN KOREA

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## Patients

Heretofore unused in this institution, Ciba 1906 (diphenylthiourea) was administered to a selected group of 33 inpatients who had proved particularly difficult treatment problems, either because of reaction or DDS intolerance. These patients would fall into the category COCHRANE speaks of when he says, "Those who have had long experience in institutional work admit that there is a hard core of cases which seem to reach a certain point on the ladder of improvement, but are unable to make complete recovery".[1] Corticosteroids had been needed in controlling most of these cases during the past 18 months. The median duration since the onset of leprosy was six years. Six of these 33 patients had had the disease more than 10 years. Thirty-two of the 33 patients had the active lepromatous form of the disease.

## Method

A beginning dosage of 0.5 gm. of Ciba 1906 daily was used, no attempt being made to increase this dosage until 4–6 weeks had passed with no evidence of sensitivity or reaction. The maximum dosage used in this study was 1.5 gm. daily though GARROD reports innocuousness with Ciba 1906 dosages as high as 3 and even 8 gms. daily over as long a period as 24 months.[2] Many of these patients were begun on Ciba 1906 while in the mild stage of reaction. Others were in a quiescent stage following reaction or prolonged DDS intolerance. Yet others were still on steroid therapy, usually a maintenance dosage of 5–10 mgm. prednisolone daily. In event of (1) return of reaction, (2) a definite increase in nodules, fever or neuralgia, or (3) requirement of increased dosage of prednisolone to control symptoms of reaction, Ciba 1906 was cut to 0.25 gm. per day or discontinued altogether.

## Results

See Table. Each patient's response to Ciba 1906 was judged largely on clinical grounds, this being a fairly objective basis in a group of patients with such an unstable form of the disease. Those 17 who were felt to have poor response were those who had to be discontinued from use of the drug, showing the same quick flare-up

as might be elicited with reinstitution of DDS. Some of these patients had to be taken off Ciba 1906 in less than two weeks after beginning. Eleven patients, or one-third of the group were classified as having good response to Ciba 1906. A patient was considered as having a good result with lessening or disappearance of nodules, fever, neuralgia or other clinical signs of activity. Some of these cases were able to get along comfortably without corticosteroids for the first time in many weeks or months.

**Special Cases**

From this group of 33 patients, five cases will be described to illustrate elements of success and failure in attempted treatment with Ciba 1906.

*Case No. 4:* This 46 year old female with a 18 year history of lepromatous leprosy had had attempted DDS treatment for the past 4 years but was unable to take more than 0–100 mgm. per week. During November and December 1960, she was given 2 short courses of prednisolone to alleviate severe lepra reaction. In January 1961 a week of chloroquine treatment was instituted but with no relief. On January 23rd 1961, she was begun and maintained on prednisolone until July 12th, 1961.

On 28th June, 1961, the patient was begun on Ciba 1906 and two weeks later was successfully taken off corticosteroid. By the end of the fourth week of Ciba therapy, the patient had marked clearance of her nodules which had covered face and extremities and her long-standing peroneal neuralgia. Now having been on the drug for three months, the patient continues to do well. Skin smear dropped from 3+ to 1+ upon institution of Ciba 1906 therapy.

*Case No. 7:* This 31 year old male with a 7 year leprosy history had begun DDS three years ago, but had been unable to take the drug at all since February 1959. He began with ulnar neuralgia and recurrent nodules, especially of the face, in the fall of 1959. During the ensuing year, he received 42 injections of thiamine, approximately 30 intravenous injections of sodium salicylate, a week's course of chloroquine and 4 intraneural injections of corticosteroid. In September 1960, the patient was begun on a regular course of oral prednisolone which continued without reprieve excepting 10 days' lapse in June 1961. Ciba 1906 was begun on 1st June, 1961 and stopped after 8 weeks of 3.5 gm. weekly dosage. The patient continues to have leproma over the entire body and ulnar neuralgia unless maintained on the high dosage of 10–15 mgm. prednisolone daily. Skin smear was 3+ in January 1961, and 2+ in September 1961.

*Case No. 20:* This 24 year old male has not been able to take DDS since admission to our institution three years ago. In December

## TABLE OF RESULTS

| Case No. | Age | Sex | Type L=Lepromatous T=Tuberculoid | Years Duration | D.D.S. Duration | D.D.S. MGM Weekly Dosage | Past Lepra Reaction | Oral Cortico-Steroid Treatment | CIBA 1906 Total Dosage in grams | CIBA 1906 Stopped because of Reaction | Result |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 22 | F | L | 5 | 18 mos. | 200 | Mod. | 3 mos. | 175 | | Good |
| 2 | 70 | F | L | 30 | 10 yrs. | 4–500 | Severe | 1 mo. | 91 | | Fair |
| 3 | 21 | F | L | 5 | 4 yrs. | 2–300 | Mod. | 6 wks. | 145 | | Good |
| 4 | 46 | F | L | 13 | 4 yrs. | 100–0 | Mod. | 2 mos. | 129.5 | | Good |
| 5 | 34 | F | L | 11 | 10 yrs. | 4–500 | Mild | | 14 | | Good |
| 6 | 32 | M | L | 7 | 2 yrs. | 4–600 | Mod. | 1 wk. | ,63 | | Poor |
| 7 | 31 | M | L | 7 | 3 yrs. | 0–200 | Severe | 10 mos. | 47.25 | X | Poor |
| 8 | 24 | M | L | 4 | 6 mos. | 0–700 | Severe | 10 mos. | 14 | X | Poor |
| 9 | 37 | M | L | 8 | 15 mos. | 0–600 | Mild | | 66.5 | X | Poor |
| 10 | 30 | M | L | 7 | 12 mos. | 0–600 | Severe | 3 mos. | 24 | | Fair |
| 11 | 24 | M | L | 3 | 3 yrs. | 0 | Severe | 2 mos. | 35 | | Fair |
| 12 | 37 | M | L | 8 | 2½ yrs. | 0–600 | Severe | 4 mos. | 66.5 | | Good |
| 13 | 14 | M | L | 4 | 2 yrs. | 0 | Mild | 1 mo. | 16.5 | | Fair |
| 14 | 21 | M | L | 7 | 2¼ yrs. | 300/600 | Mod. | 4 mos. | 34 | | Good |
| 15 | 19 | M | L | 5 | 3½ yrs. | 0–300 | Mod. | 6 mos. | 44 | | Poor |
| 16 | 33 | M | L | 5 | 2½ yrs. | 0–600 | Severe | 3 mos. | 24.5 | X | Poor |
| 17 | 30 | M | L | 6 | 1 yr. | 0–300 | Mod. | 3 mos. | 14 | X | Poor |
| 18 | 25 | M | L | 16 | 4 yrs. | 300 | Severe | 3 mos. | 70 | | Good |
| 19 | 37 | M | L | 8 | 1½ yrs. | 0–300 | Mod. | | 35 | X | Poor |
| 20 | 24 | M | L | 4 | 3 yrs. | 0 | Mod. | 3 mos. | 49 | | Good |
| 21 | 25 | M | L | 10 | 1½ yrs. | 0–600 | Mod. | 6 mos. | 3.5 | X | Poor |
| 22 | 22 | M | L | 8 | 2 yrs. | 0–600 | Severe | 12 mos. | 3.5 | X | Poor |
| 23 | 23 | M | L | 7 | 1 yr. | 0–300 | Mod. | 8 mos. | 42 | | Poor |
| 24 | 24 | M | L | 4 | 1½ yrs. | 0–600 | Mod. | 3 mos. | 7 | X | Poor |
| 25 | 22 | M | L | 4 | 2½ yrs. | 0–600 | Severe | 6 mos. | 7 | X | Poor |
| 26 | 24 | F | L | 5 | 5 yrs. | 0–400 | Severe | 2 mos. | 19 | X | Poor |
| 27 | 22 | F | L | 3.5 | 2 yrs. | 0–600 | Mod. | 2 mos. | 7 | X | Poor |
| 28 | 65 | M | L | 30.9 | 7 yrs. | 0 | Severe | 4 mos. | 98 | | Good |
| 29 | 18 | F | L | 6 | 5 yrs. | 400/600 | Mild | | 7 | X | Poor |
| 30 | 37 | M | T | 12 | 10 yrs. | 0–50 | | | 59.5 | X | Poor |
| 31 | 20 | F | L | 3 | 3 yrs. | 0–50 | Mod. | | 105 | | Good |
| 32 | 21 | F | L | 3 | 15 mos. | 300/600 | Mod. | | 21 | | Fair |
| 33 | 26 | F | L | 3 | 3 yrs. | 0–600 | Mod. | | 94.5 | | Good |

1959, and again in February 1961, the patient was given intraneural cortisone for peroneal neuralgia with only partial relief. In April the patient flared up in reaction with widespread nodules and fever. Prednisolone was begun April 1961 and continued until 13th June, 1961. On 1st July, 1961, Ciba was begun and, aside from one week of neuralgia in mid-July, has been taken without adverse effect for the past three months.

*Case No. 28:* This 65 year old male with a 30 year history of leprosy had been treated for about 20 years in this institution with injections of chalmoogra oil and was found completely intolerant to DDS during the past seven years. Skin smears were negative in 1955 and 1956, 1+ in 1958 and 4+ in 1960.

The patient began with lepra reaction in June 1960, manifested by induration, erythema, fever and painful nodules. Corticosteroids begun in September 1960 brought dramatic relief and were continued for $8\frac{1}{2}$ months. Three weeks after discontinuing steroids, the patient still had some neuralgia and nodules but was begun on Ciba 1906 on 19th June, 1961. Three and one-half months later, he was continuing on Ciba 1906 with no sign of reaction.

*Case No. 31:* This 20 year old female with lepromatous leprosy of $3\frac{1}{2}$ years duration has responded to very small doses of DDS with leproma, headache, fever and easy onset of fatigue. On 5th July, 1961, she was begun on Ciba 1906 and has now been on the drug for over three months with no adverse effects.

## Discussion

For those who showed good response to Ciba 1906 it will be necessary again to assess the efficacy of the drug after a full year of treatment. We feel that some of these will prove sensitive to the diphenylthiourea after some length of time, just as many of our diamino-diphenyl sulfone-sensitive cases do not manifest their sensitivity until after a year or more of treatment. Of course, it is often difficult to differentiate between "drug sensitivity" and the reactive phase of lepromatous leprosy unless the patient's reaction is of the erythema nodosum type. Cases No. 8, 10 and 11 had no nodules as the manifestation of their reaction, but marked neuralgia. Skin smear results following further treatment of these cases will also serve to judge the efficacy of diphenylthiourea in this DDS intolerant, reaction-prone group. A follow-up study of this same group with skin smears and the use of "Etisul" in the Ciba 1906 sensitive cases is in our plans.

## Summary

Results of an initial trial of Ciba 1906 in 33 lepromatous leprosy cases either DDS-intolerant, or in a state of chronic reaction, are

reported and discussed. One-third of these patients had good response having definite clearing of signs and symptoms, thus again pointing up the important role that this drug can play in the management of a very difficult and critical problem of medical management in lepromatous leprosy.

**Acknowledgment**

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**References**

1. COCHRANE, R. G. (1959) *Leprosy in Theory and Practice*, p. 221, JOHN WRIGHT and SONS,.
2. GARROD, J. (1959) *Leprosy Review*, **30**, 4.