

## ISONIAZID ALONE AND IN COMBINATION WITH OTHER DRUGS IN THE TREATMENT OF LEPROSY

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The known efficacy of modern drugs with prolonged treatment in leprosy limits the opportunity for experiment with new drugs which also require considerable time to give a true indication of their usefulness. Experiments are generally limited to a few individual cases. Unfortunately, in a disease of remission and relapses, a true picture cannot be obtained from a few cases. This report does not therefore presume to present the whole picture regarding the effects of isoniazid but merely to give an indication of its effect on two small series of cases so that the results may be added to those of other workers and thereby contribute in some small measure to the final judgment.

Series I consists of 10 cases (6 new cases and 4 cases previously given sulphetrone, etc.) under trial with isoniazid for 17 months. Intramuscular sulphetrone was introduced during the course of this treatment.

Series II consists of 6 cases, all old cases previously treated unsuccessfully with sulphetrone.

Isoniazid was under trial in this series for 12 months and neustab was introduced for the last three months.

Progress was recorded by the group marking system for clinical appearance and smear count explained in a previous report in this Journal<sup>(1)</sup>.

### SERIES I:

1st—6th month:	Treatment: INH 200 mg. daily. Progress: No improvement was evident until after 3 months, whereupon progress was rapid. Progress index at end of 6 months: 1.425.
7th—9th month:	Treatment: INH 250 mg. daily. Progress: Slower but maintained. Index: .4
10th—14th month:	Treatment: INH 350 mg. daily plus intramuscular sulphetrone increasing to 4 ccs. 50% sol. twice weekly. Progress: Little improvement noted in any case and several cases deteriorated Index: —.075.

The general deterioration of progress was so marked throughout this five month period that the possibility of interference or biological incompatibility of the drugs had to be considered. To test this possibility, the ten cases were divided into two groups of five as nearly similar as possible. To Group A for the next three months only isoniazid was given, and to Group B only intramuscular sulphetrone.

#### GROUP A OF SERIES I

15th—17th month: Treatment: INH 350 mg. daily.

Progress: Good.

Index: .6

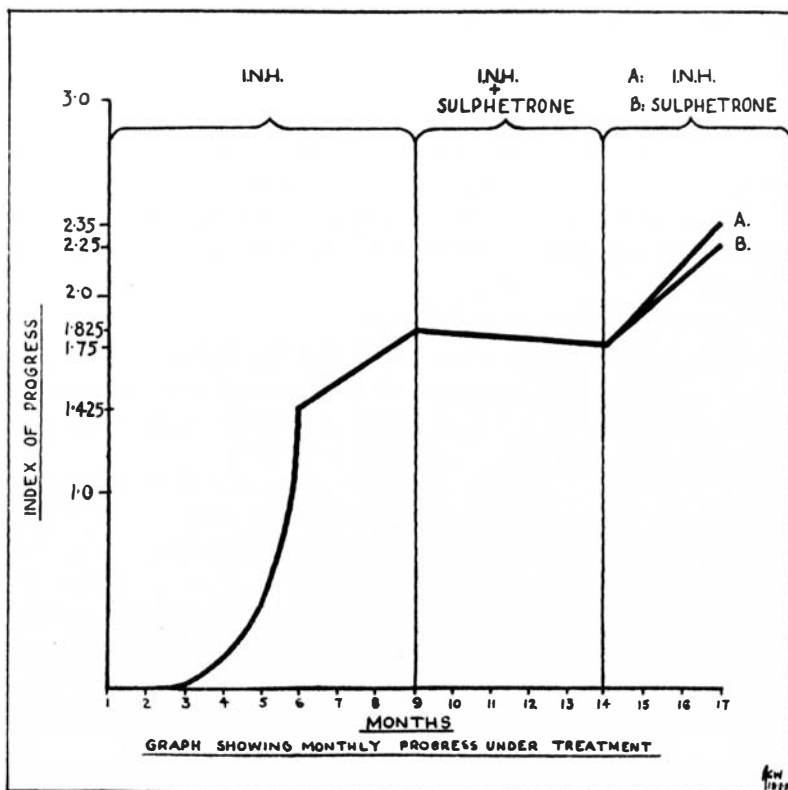
#### GROUP B OF SERIES I

15th—17th month: Treatment: 4 ccs. 50% sol. Sulphetrone intramuscularly twice weekly.

Progress: Good.

Index: .5

To illustrate better the meaning of these indices against the background of time involved in their production, reference may



be made to the graph which clearly indicates the steady progress under INH or sulphetrone alone and the marked decline in progress when the drugs were exhibited concurrently. Though statistically insignificant, it is interesting to note that Group A (the INH group) made a slightly better recovery than Group B (the sulphetrone group).

In general, it can be said that in spite of the setback during the combined treatment, the index of progress in INH treatment was 2.3 over a 17-months period. This compares favourably with the index of 2.16 for 12-months' treatment with intramuscular sulphetrone, and the index of 2.58 for 24-months' treatment with oral sulphetrone previously reported by me<sup>(1)</sup>.

How much of the decline in progress during the combined treatment was actually due to the treatment and how much was a normal vagary of the disease, is difficult to determine, but the following observations must be borne in mind.

The decline in progress was general throughout the series, and the low index is not the result of severe relapse in one or two cases. The decline was noted at an examination after 3 months of the combined treatment, and is not solely dependent on the one examination at the end of 5 months. When the treatments were separated (Groups A and B) the normal progress was again immediately resumed. There are therefore indications that the combined treatment may be the cause of the decline, and it is interesting in this connection to note the work of Grunberg and Schnitzer<sup>(2)</sup> in experimental tuberculosis of mice and Szybalski and Bryson<sup>(3)</sup> with various saprophytic organisms in vitro.

These workers report the apparent inhibitory effect that streptomycin and isoniazid have on one another when exhibited in sub-therapeutic dosage.

#### SERIES II:

There were 6 old cases resistant to sulphetrone and other drugs.

They were treated for the first 9 months on INH 350 mg. daily. One case showed improvement and two deteriorated.

For the following three months the INH treatment was combined with neustab (TB1) commencing with 50 mg. daily and increasing gradually to 20 mg. daily. During this period, two further cases showed improvement. The total result of the 12 months' treatment was therefore improvement in three cases, deterioration in two, and no change in one. This experiment in treatment continues and is not therefore reported in greater detail. The point of interest is that the combination INH with neustab appears to be beneficial and

not detrimental as in the combination INH and sulphetrone. This will require further trial but, again, it is of interest to refer to Szybalski and Bryson who, in their experiments, found no antagonism between isoniazid and nicotinaldehyde thiosemicarbazone.

#### TOXIC EFFECTS :

In the 16 patients under treatment there were only two instances of toxic manifestations, one case of headache and cramps and one case of rash. Both recovered quickly with a period of reduced dosage.

Haemoglobin levels increased and remained high, and only fell on the introduction of sulphetrone or neustab as an addition to the treatment.

#### GENERAL CONDITION :

An improvement in general condition was noticeable, and weights markedly increased. Weight increase was not only apparent in new cases where improved diet and institutional care induce such results; it was also noted in the old cases after years in the leprosarium. The average weight increase in new cases was 16 lbs. and in old cases 11 lbs.

#### CONCLUSION :

As far as it is permissible to draw conclusions from such a short exhibition of the drug in a small series, there is an indication that isoniazid has a position in the treatment of leprosy not necessarily inferior to sulphetrone and further work is necessary to establish its true position.

There is little evidence of improvement before the fourth month of treatment.

There are indications that its concurrent exhibition with sulphetrone is detrimental to cure, possibly as a result of a biological incompatibility. This incompatibility has not been evident when INH has been combined with neustab in the treatment.

Hæmoglobin remains high and toxic effects are few, and the general condition of patients under treatment markedly improves; this drug would be invaluable in the treatment of leprosy if the results in the above series were sustained in extensive trial.

#### SUMMARY :

Ten cases for 17 months and 6 cases for 12 months were treated with INH. The results compare favourably with results obtained with sulphetrone.

There are indications against its use in conjunction with sulphetrone, but in conjunction with neustab results improved.

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3. W. SZYBALSKI and V. BRYSON: "Conditional Antagonism between Isoniazid and other Antibacterial Agents." *Ibid.*, 280.