Discussion.—Wunderly and Wuhrmann (1947) attributed the turbidity of the serum in the cadmium reaction to the dehydrating action of the SO_4 ion. Recently its mechanism has been critically studied by them according to electrophoretic measurements of different protein fractions and they have concluded that the positive reaction is mainly due to the increase of gamma globulin and to a less extent to alpha and beta globulin. Further contribution to this study has been made by Berner (1949) and Adner and Waldenström (1949) who have shown that the degree of positive cadmium reaction depends mainly on the stabilization titre of the albumin and is also related to the ability of albumin to increase the solubility of different globulin fractions. The positive cadmium test in kala-azar may be explained by the hyperglobulinæmia and also hypoalbuminæmia both of which occur in this disease.

Our thanks are due to Dr. P. C. Sen Gupta, for supplying us serum of kala-azar patients with 'aldehyde' and/or 'complement-fixation' test reports.

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A PRELIMINARY REPORT ON THE EFFECT OF THIOSEMICARBAZONE IN PULMONARY TUBERCULOSIS

By B. P. NEOGY, M.B., M.R.C.S., M.R.C.P. (Lond.)

Visiting Physician, Kumud Sankar Ray Tuberculosis Hospital, Jadavpur

Introduction

FROM ancient times, many drugs have been used in the treatment of tuberculosis.

Of the various drugs used recently, the following have received some credit : streptomycin, para-amino-salicylic acid and thiosemicarbazones, especially para-acetylaminobenzaldehyde thiosemicarbazone.

Discovered by Waksman *et al.* (1944), streptomycin was first tried extensively by Feldman and Hinshaw (1945). Synthesized in the year 1889, para-amino-salicylic acid has been studied in detail both in the United States of America and Western Europe (Lehmann, 1946). Similarly, thiosemicarbazone was developed by Professor Domagk (1946) and para-acetyl-aminobenzaldehyde thiosemicarbazone was studied by various workers including Behnisch *et al.* (1950).

The new hopes awakened with the discovery of sulphonamides and sulphones in the treatment of pulmonary tuberculosis were short-lived. These drugs had only a limited activity. The earlier trials of para-acetyl-aminobenzaldehyde thiosemicarbazone were made mostly in conjunction with sulphathiazole. It was soon found that this drug was toxic and its activity lay mainly on the suitably substituted open chain-like arrangement of the nitrogen and sulphur atoms as is present in the thiosemicarbazones.

Of the large number of compounds of thiosemicarbazone, para-acetyl-aminobenzaldehyde thiosemicarbazone is reported to be the most effective preparation.

Recently, a quantity of this drug was made available to the writer from a local firm. As a preliminary measure, it was decided to use this drug on patients suffering from tuberculosis and find out if it was toxic.

Materials for investigation.

As no work had been undertaken with para-acetyl-aminobenzaldehyde thiosemicarbazone (TB1/698) in this country previously, it was thought desirable to administer this drug to a small group of patients. The majority were advanced cases and those who could not afford the other expensive drugs like streptomycin or P.A.S. or those in whom these latter drugs were found totally ineffective.

Eleven cases were chosen for this trial. They may be classified as follows :—

(1) Too poor to afford streptomycin or P.A.S.—4 cases.

(2) Cases where streptomycin was ineffective —4 cases.

(3) Cases where P.A.S. or streptomycin and P.A.S. were ineffective—3 cases.

Lung condition.—Ten of these cases had extensive exudative infiltration with little productive reactions in both lungs. In one case, the lesion was confined to one lung with the history of repeated hæmoptysis.

Temperature.—Almost all the cases were running temperature ranging from 99°F. to 103°F.

It will be seen from the short review of the cases that they were not ideal for thiosemicarbazone therapy. Since this drug was a new introduction in our country, a proper selection could not be made and even during the trial some patients refused to take this drug after a few weeks because of the rumour that thiosemicarbazone was a very toxic drug. This has, of course, prevented a proper assessment to the full extent.

Age.—20 to 30 years—7 cases, 30 to 40 years—3 cases, 40 to 60 years—1 case.

Dose.—The usual recommended dose of thiosemicarbazone is from 25 mg. to 200 mg. a day. The maximum dose should always be

based on the calculation of 2 mg. per kg. of body weight.

In the present investigation, a very cautious approach was made. Each case received 25 mg. a day for 6/7 days in order to find out the tolerance. In the second week, 50 mg. were administered. This was gradually increased to 75 and 100 mg. a day during the succeeding weeks.

From the small supply of drug received, it was not possible to observe the results for more than 5 weeks.

Immediate results.—None of the cases had any intolerance to the drug. A blood count was made every week in order to check up the number of leucocytes. Only in one case there was a diminution of leucocytes from 9,000 to 7,000; no other effect could be seen in the rest of the cases except slight diminution of the white blood cells.

Effect on maximum temperature reached.—

Serial number	Initial	Weight	
		After 15 days	After 1 month
1	Too ill to get up from bed.	..	..
2	91 lb.	Not taken	98 lb.
3	120 lb.	124 lb.	..
4	102 lb.	100 lb.	..
5	..	Too ill for weighing.	..
6	Too ill to get up from bed.	..	..
7	108 lb.	Not taken	114 lb.
8	Too ill to get up from bed.	..	..
9	..	Too ill to get up from bed.	..
10	91 lb.	88 lb.	91 lb.
11	104 lb.	102 lb.	104 lb.

Conclusions

1. A small number of cases of tuberculosis has been treated with thiosemicarbazone.

Serial number	Temperature before thiosemicarbazone, °F.	Temperature after 1 week, °F.	Temperature after 2 weeks, °F.	Temperature after 3 weeks, °F.	Temperature after 4 weeks, °F.	Temperature after 5 weeks, °F.
1	102.4	102.0	103.0	Discontinued. General condition too low.		
2	100.4	99.0	99.0	98.8	98.0	98.6
3	99.4	98.4	98.8	98.2	98.4	98.0
4	101.0	100.0	100.0	99.2	98.8	99.2
5	100.8	102.4	102.2	Discontinued. Patient refused to take the drug.		
6	101.8	101.6	101.0	100.6	101.8	Discontinued due to anorexia and vomiting.
7	99.0	99.0	98.4	99.0	..	..
8	101.8	102.6	101.6	Discontinued. General condition poor.		
9	100.0	99.0	Discontinued. Patient refused to take the drug.			
10	100.0	100.0	99.6	99.6	98.2	99.6
11	101.0	98.6	98.6	98.8	98.4	..

From the above it will be seen that 2 patients refused to take this drug. The effect on temperature was satisfactory in 5 cases. The temperature came down to normal after 3 or 4 weeks from the date of administration of the drug.

Weight.—The weight could be taken in only 6 cases. The other 5 cases were too ill to be taken out of bed. It will be seen from the following table that within a period of one month the weight increased in 3 cases. It was stationary in 2 cases. One patient lost weight.

Toxic symptoms.—In the above series of small number of cases, only one case had anorexia and vomiting. As a precautionary measure, the drug was discontinued, although the vomiting was not serious. There was no rash or giddiness in any of the cases. In one case only the white blood cells were diminished by 2,000.

2. Although this drug was given in very advanced cases, the effect on temperature and weight seems encouraging. There was no appreciable toxicity during five weeks when this drug was administered.

Thanks are due to the Superintendent of the Hospital for permission to report these cases and to Messrs. Albert David Ltd., 15, Chittaranjan Avenue, Calcutta, for the free supply of thiosemicarbazone.

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P.S. (7-9-51).—Since writing, more than 12 cases have been given this therapy for a period ranging from 4 to 6 months without toxic symptoms.—B. P. N.