

# Drug-Induced Heart Failure in Advanced Pulmonary Tuberculosis

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## SUMMARY

Advanced cases of pulmonary tuberculosis with congestive cardiac failure had been found to carry a high mortality when treated with streptomycin, isoniazid and ethionamide, so a trial was designed to assess the value of using an alternative regimen, consisting of kanamycin and ethambutol. Results showed a highly significant difference between the two regimens in favour of the latter. Rifampicin in place of kanamycin appeared to be rather less effective in reducing mortality of these patients.

*S. Afr. Med. J.*, 48, 2352 (1974).

A problem facing those who treat advanced pulmonary tuberculosis with congestive cardiac failure in the Transkei is to know why so many of these patients die soon after admission to hospital. The problem was outlined to the Transkei and Ciskei Research Society in 1972 by Dr Nigel Stott,<sup>1</sup> who showed that there was an apparent association between the starting of antituberculosis drugs and death,

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but he did not have enough cases to test this statistically. He drew attention to the work of Cohen *et al.*,<sup>2</sup> who showed that streptomycin could cause marked depression of the cardiac output in experimental dogs. Later he urged me to look further into this matter, and a trial was designed.

The main aim was to discover whether antituberculosis drugs could have an adverse effect upon the human heart, and, if it were established that they could, to find the two antituberculosis drugs that appeared to have the least adverse effect, so that they could be used in treating patients with pulmonary tuberculosis and already failing hearts.

## PATIENTS AND METHODS

Cases of advanced pulmonary tuberculosis admitted to the adult tuberculosis wards of St Lucy's Hospital were divided into two categories: group I — cases not in heart failure, and group II — cases in failure.

Cases in group I were put at random on to either the so-called streptomycin starter regimen (streptomycin 1 g daily, isoniazid 600 mg daily and ethionamide 500 mg daily), or the kanamycin starter regimen (kanamycin 500 mg daily and ethambutol 1,2 g daily).

TABLE I. AGE AND SEX DISTRIBUTION

Patients suffering from advanced PTB but not in heart failure on admission

	Males							Females						
	Under 20	21-30	31-40	41-50	51-60	61+	Total	Under 20	21-30	31-40	41-50	51-60	61+	Total
<b>Kanamycin starter regimen</b>														
No heart failure—discharged	1	3	2	7	7	5	25	1	1	6	4	7	5	24
Heart failure—died	—	—	1	—	—	—	1	—	—	—	—	1	2	3
<b>Streptomycin starter regimen</b>														
No heart failure—discharged	—	1	2	1	4	—	8	5	7	3	8	4	3	30
Heart failure—died	—	—	—	3	—	—	3	—	2	—	1	1	3	7
Heart failure discharged	—	—	1	1	1	1	4	1	—	—	4	1	—	6

Patients suffering from advanced PTB in heart failure on admission

	Males							Females						
	Under 20	21-30	31-40	41-50	51-60	61+	Total	Under 20	21-30	31-40	41-50	51-60	61+	Total
<b>Kanamycin starter regimen</b>														
Discharged	—	1	1	4	—	6	12	—	2	4	7	10	6	29
Died of heart failure	—	—	—	2	2	—	4	—	—	1	1	—	—	2
<b>Rifampicin starter regimen</b>														
Discharged	1	1	3	5	3	1	14	2	3	—	4	5	4	18
Died of heart failure	—	2	—	2	—	—	4	—	2	1	1	—	1	5

These figures show no particular pattern for either age or sex distribution in the different groups of results, except that on the whole more women than men were treated, which reflects the ratio of men to women in the Transkei.

TABLE II. PATIENTS SUFFERING FROM ADVANCED PTB BUT NOT IN HEART FAILURE ON ADMISSION

Treatment regimen for 1st month	No. treated	Heart failure within 1 month	No. discharged	No. died of heart failure	No. died of other causes after 1 mo.
Streptomycin starter ... ..	59	20 (34%)	48	10	1
Kanamycin starter ... ..	57	4 (7%)	49	4	4

Cases in group II were put at random on to either the kanamycin starter regimen (as above) or the rifampicin starter regimen (rifampicin 450 mg daily and ethambutol 1,2 g daily).

Patients in heart failure were treated with diuretics and digoxin as indicated, in addition to the above. Those on the streptomycin starter regimen, who went into heart failure after admission, were changed to the kanamycin starter regimen and treated with diuretics and digoxin as indicated.

In addition to age, sex and identification details, the following end-points were recorded subsequent to admission: the onset of heart failure if it was not present on admission; the completion of one month's treatment; discharge from hospital (all patients included in the study were kept in for at least one month), and death and its apparent causation.

## Definitions

**Advanced PTB**—cases where the X-ray films showed bilateral disease, or with the whole of one lung involved, and with positive sputum.

**Heart failure:** LVF—a history of breathlessness, with either fine basal crepitations or the presence of gallop rhythm audible over the left ventricle; RVF—elevated pulsatile jugular vein pressure or right ventricular gallop rhythm associated with either oedema (sacral or ankle) or hepatomegaly.

## Age and Sex Distribution

The age and sex distribution is shown in Table I.

## RESULTS

A total of 200 patients were included in the trial, which lasted for a period of 8 months. Of these, 116 were not in heart failure on admission although in a state of

advanced PTB, and 84 had both PTB and heart failure on admission (Tables II and III).

TABLE III. PATIENTS SUFFERING FROM ADVANCED PTB AND IN HEART FAILURE ON ADMISSION

Treatment regimen for 1st month	No. treated	No. who died	Average death rate = 17%
Kanamycin + ethambutol	47	6 (13%)	
Rifampicin + ethambutol	41	9 (22%)	

There was a 27% difference between those on the streptomycin starter regimen who went into heart failure in the course of the first month and those who were on the kanamycin starter regimen. A chi-square test showed a significant relationship ( $P < 0,0005$ ) for both treatment and survival.

The percentage mortality of those treated with rifampicin was higher than that of those treated with kanamycin. Nevertheless, both regimens showed a lower mortality than that which was experienced at St Lucy's Hospital in 1970, which was as high as 66%.<sup>1</sup> The over-all mortality of all the cases of advanced PTB was 17%, compared with 32,5% in 1970;<sup>1</sup> proving that avoidance of the present standard treatment regimen when heart failure is present pays dividends. It is possible that adherence to kanamycin with ethambutol for those cases with advanced PTB and heart failure will lower the mortality even further.

I wish to thank Dr Nigel Stott, Dr Ken Weir, Dr Peter Balmer, Dr Paul Leichtman, Miss Elizabeth Dowler, Sister Tongata, and Sister Mtirara for their help in connection with this trial, and to Dr S. A. Fellingham for statistical help.

## REFERENCES

1. Stott, N. C. H. (1973): *S. Afr. Med. J.*, **47**, 331.
2. Cohen, L. S., Wechsler, A. S., Mitchell, J. H. and Glick, G. (1970): *Amer. J. Cardiol.*, **26**, 505.