Pyrazinamide and Ethionamide in Resistant Pulmonary Tuberculosis in Africans

AN 18-MONTH FOLLOW-UP OF 32 PATIENTS

BY

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Thirty-two patients in Nyasaland hospitals who were excreting tubercle bacilli resistant to INH and streptomycin were admitted to a trial of pyrazinamide and ethionamide and followed for 18 months. All were adults except one, a girl of 11.

The criteria for admission to the trial were: either the patient had a positive sputum after at least six months' continuous treatment with INH, streptomycin and PAS, or drug-sensitivity tests carried out at the WHO-assisted Tuberculosis Laboratory, Nairobi, had shown that there was resistance to INH and streptomycin.

The dosages of drugs given were:

Pyrazinamide: weight up to 105 lb., 1.5 g. daily; weight 106 lb. and over, 2 g. daily.

Ethionamide: weight up to 119 lb., 0.75 g. daily; weight 120 lb. and over, 1 g. daily.

Three patients included in the analysis were given periods of treatment with pyrazinamide and cycloserine not exceeding 12 days at the start of their treatment.

If a patient died within the first six weeks he was excluded from the analysis, as it was assumed that the drugs had not had time to take effect.

"Failure" of the regime was defined as: death between six weeks and six months, or a persistently positive sputum smear in spite of six months' treatment, or in some cases a positive sputum after at least three months associated with radiological deterioration over the first three months. In these last cases the regime was changed on clinical grounds in the interests of the patient.

RESULTS

I. State of the Patients After 18	Months
Unsatisfactory	27
Absconded before effect of treatment could be determined, and not seen	
again	2
Known dead	13
Treatment failed	12
Satisfactory	5
Having had resection	1
Salvaged with viomycin and cycloserine after trial drugs had failed	2
Regime changed to pyrazinamide with cycloserine after toxic effects from ethionamide	1
Treatment changed by hospital to ethio- namide with cycloserine after three months, for administrative reasons	1
II. Analysis of Results of Treatmet Pyrazinamide and Ethionamide	
Exclusions	17
Different regime given for part	

of the time for administrative

	Incorrect dose of one drug given in error	2	
	Resection done during course	1	
	Died in first month	1	
	Absconded before effect of regime could be determined	4	
For	analysis		15
	Regime unsuccessful	15	
	Stopped after four months due to vomiting caused by ethionamide		
	Failed 14		
	Regime successful	0	

CONCLUSIONS

- (1) The overall results of starting treatment with pyrazinamide and ethionamide in tuberculosis patients with drug-resistant organisms under the conditions prevailing in Nyasaland are very poor. Only five out of 32 in this series were alive and well after 18 months.
- (2) Pyrazinamide with ethionamide is an ineffective combination of drugs. After 18 months it had failed in all of 15 patients. (An exception, however, is the case of patients whose initial radiological extent of disease does not exceed one-third of the total area of the lung fields. A paper on this is in course of preparation.)

SUMMARY

In an analysis at 18 months of 32 patients included in a trial of pyrazinamide with ethionamide in Nyasaland hospitals, it was found that only five were still alive and well.

Fifteen of the patients continued on the combination as long as it was indicated, and in none of these was it successful.

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