

The management of pulmonary tuberculosis notified in England and Wales in 1993

ABSTRACT We have compared the management of 925 cases of pulmonary tuberculosis reported to the 1993 national tuberculosis notification survey with the recommended standards of treatment. Forty-eight per cent of patients were white, 36% came from the Indian subcontinent (ISC) and 15% were of other ethnic origin. Most patients (86%) were under the care of thoracic physicians. Sputum microscopy was positive in 44%, and culture confirmation was obtained in 64% of cases. Drug resistance was reported in 30/582 isolates (5%), ranging from 13% in Black-Africans to 4.5% in ISC ethnic groups and 2% in the whites, with none reported in those of Black-Caribbean origin. Almost all patients (94.5%) were started on a recommended drug combination, but only 74% continued to receive one, with thoracic physicians significantly more likely than other physicians to use a recommended combination. Non-standard durations of either initial and/or continuation phase therapy were used in 303 patients, but in only 167 was a satisfactory reason given for the modification. Definite or suspected drug toxicity was reported in 79 (9%) and was significantly more likely with non-standard regimens. Seventy-two patients died before the survey was carried out one year after their notification, only 15 of them directly due to tuberculosis. Of the 815 cases observed to treatment completion, 430 (53%) were then discharged. There were adequate reasons for follow-up after the end of treatment in all but 98 of those so managed. Although the results were satisfactory overall, continued efforts are required to increase the percentage of patients treated with evidence-based recommended regimens and durations of chemotherapy.

National surveys of tuberculosis notifications in England and Wales in 1983 and 1988 were followed by analyses of the management of the cases of pulmonary tuberculosis^{1,2}. In 1990 the Joint Tuberculosis Committee (JTC) of the British Thoracic Society published national chemotherapy guidelines³ against which treatment could be compared. The regimen recommended for pulmonary tuberculosis was six months' treatment with isoniazid (H) and rifampicin (R), supplemented by either additional pyrazinamide (Z) for the first two months (2HRZ/4HR) where there was a low risk of isoniazid resistance, or with ethambutol (E) as an

additional fourth drug in the first two months (2HRZE/4HR) where there was a higher risk of isoniazid resistance. The JTC guidelines also recommended that uncomplicated cases with good compliance could be discharged on completion of treatment.

The survey reported here covers the treatment given to cases of pulmonary tuberculosis of all ages notified in England and Wales in 1993, the associated problems and morbidity, and the outcome. In addition to demographic patient details and treatment given, measures of disease severity – sputum smear status, the number of lung zones involved, and the presence/absence of cavitation on the chest radiograph – were also recorded, as these are independently related to mortality^{4,5}.

Methods

All patients who had a notification of tuberculosis (all forms) made to the Office of Population Censuses and Surveys between 14 December 1992 and 30 June 1993 inclusive were reported to the national notification survey. The clinician notifying the patient was sent a form by the national survey team to obtain more clinical and epidemiological information. Twelve months after notification, the doctors who had returned these forms on patients notified with pulmonary tuberculosis (excluding pleural effusion and isolated mediastinal lymphadenopathy) were sent a questionnaire on its treatment and sequelae.

Information sought included the age, sex and ethnic group of the patient, and the name of the responsible clinician. The clinician's specialty was obtained from information in the Medical Register or, if not available, direct from the hospital concerned. The bacteriological status at diagnosis was recorded with the results of sputum microscopy and culture, or 'no specimen' if no samples had been taken. The drug sensitivity results of those with positive cultures were also obtained. The X-ray at diagnosis was recorded as having or not having cavitation, and the number (1–6) of lung zones involved. Starting and stopping dates for each drug, and whether treatment was given daily or intermittently, were noted. The clinician reported if recommended treatment as defined³ was started and, if so, the reason for any amendment or interruption, for example drug toxicity (suspected or proven), drug resistance, patient failure to attend, prescription error or deliberate decision.

Status at 12 months after notification was classified as death due to tuberculosis, death not due to tuberculosis, or alive. The clinician was also asked if the

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patient had been discharged to the care of the general practitioner at the completion of treatment and, if not, why not.

The questionnaires were returned to the audit centre where each patient was given a unique patient identifier known only to the authors. Data and clinical information were entered in numerical or coded form on a data sheet. At the completion of the data collection, the sheets were sent to the Medical Statistics Unit, Edinburgh University, for analysis. As in the report on treatment of pulmonary tuberculosis in the 1988 notification survey, fairly wide ranges were allowed as fulfilling the criteria for standard durations of treatment²: 6–12 weeks for the initial phase, and 22–30 weeks for the total duration for the 2HRZ/4HR and 2HRZE/4HR regimens.

Results

Exclusions

Of the 1,238 cases notified, 313 were excluded (Table 1). Forty-three of the 90 with a diagnosis other than tuberculosis had non-tuberculous mycobacterial disease.

Patient characteristics

Of the 925 patients, 526 were men and 399 women; 447 were white, 337 came from the Indian sub-continent (ISC), 46 were Black-African, 26 Black-Caribbean, and 69 from other ethnic groups.

Severity

There were highly significant associations between sputum smear positivity and the presence of cavitation (continuity adjusted $\chi^2 = 111.2$; 5df; $p < 0.0001$) and

with an increased number of lung zones involved on X-ray (Mantel-Haenszel $\chi^2 = 18.7$; 1df; $p < 0.001$). There were also significant associations between sputum culture positivity and the presence of cavitation (continuity adjusted $\chi^2 = 44.8$; 5df; $p < 0.001$) and also with the number of lung zones involved (Mantel-Haenszel $\chi^2 = 14.9$; 1df; $p < 0.001$).

Bacteriology

Sputum microscopy and culture were positive in 411 patients, 180 had negative sputum microscopy but were positive on culture, 218 were negative on both sputum microscopy and culture, 24 were sputum microscopy positive but negative on culture, and 92 had no sputum sample collected. Sensitivity results were available for 582 of the 591 with positive sputum cultures for *Mycobacterium tuberculosis*, of which 552 (95%) were fully sensitive to first-line drugs. Thirty (5%) were resistant to one or more drugs, 15 to isoniazid, 1 each to rifampicin and pyrazinamide alone, 5 were resistant to isoniazid and streptomycin combined, 2 to isoniazid, streptomycin and ethambutol, and 1 to isoniazid and pyrazinamide. Resistance to rifampicin and isoniazid, with or without other drug resistance, was seen in 5 cases. Fifteen of the drug resistant cases were from the ISC ethnic group, 7 were white, 6 Black-African and 2 of other ethnic group.

Treatment

Five patients were not treated: 2 were post-mortem notifications, 2 died from non-tuberculous diseases, and 1 left the country before starting treatment. Rifampicin was given to all but one of the 920 patients who received treatment, isoniazid to all but four,

Table 1. Inclusions and exclusions to the survey.

Consultant	No clinical form returned to national survey	Included	Excluded	
			Altered diagnosis	Form late or not returned
Thoracic physician	58	785	80	91
General physician	12	39	5	5
Infectious disease physician	5	42	—	4
Paediatrician	—	20	1	4
Geriatrician	4	7	—	9
Genitourinary physician	—	2	—	—
Other doctor	7	21	4	—
Not known	15	9	—	9
Total	101	925	90	122

pyrazinamide to 882 (96%), ethambutol to 209 (23%) and streptomycin to 11 (1%). Although 869 (94.5%) of the patients treated were started on a recommended drug combination, only 677 continued to receive one (Table 2), and 167 of those had treatment modification. This was for drug reaction (23), drug resistance (3), both reasons (1), and prescription errors (13). In 30 patients, failure to attend resulted in treatment being prolonged, and the clinician deliberately continued treatment in 97 cases because of concern over progress.

Of the 677 treated with a recommended combination, 303 received inappropriate durations of initial and/or continuation phases treatment (Table 3), in 167 cases because of reasons for treatment modification. No explanation was given for the inappropriate durations of initial and/or continuation treatment in 136 cases. Recommended combinations were used in 600/791 treated by thoracic physicians, 28/42 treated

by infectious disease physicians, 22/38 by general physicians, 13/20 by other clinicians, 9/20 by paediatricians, 3/7 by geriatricians, and in 2/2 by genitourinary physicians. Thoracic physicians treated a significantly higher percentage with a recommended combination than did other physicians ($\chi^2 = 14.9$; 1df; $p < 0.0001$).

Drug toxicity

Drug(s) were stopped because of definite or suspected adverse drug reactions on 98 occasions in 79 patients. The drugs suspected were pyrazinamide (33 cases), rifampicin (28), isoniazid (25), ethambutol (4), and not recorded (8). Reactions were reported in 28/679 on standard combinations, compared with 55/241 patients on non-standard combinations, a highly significant difference (continuity adjusted $\chi^2 = 81.9$; 1df; $p < 0.0001$).

Outcome

Fifteen patients (1.5%) died from their tuberculosis and 57 (6%) of non-tuberculous disease during the study period. In addition, 38 patients left Britain before completion of treatment. Of the remaining 815 patients, 430 were discharged back to the care of their general practitioner on completion of treatment. The reported reasons for non-discharge of the other 385 patients were a continuing tuberculosis related problem (48 cases), other medical problems (112), doubt about compliance (96), other reasons (158) and prolonged treatment (165), with many patients having two or more reasons given. 'Other reasons' were usually unit policy to follow up irrespective of clinical status; 98/385 patients had 'other reason' as the only explanation for follow-up. The reasons given for prolonged treatment were drug reaction (39/165), drug resistance (19), failure to attend (28), deliberate decision (67). In 12 cases none of these reasons was offered.

Discussion

This study reports the management of 925 patients with pulmonary tuberculosis, representing 80% of those notified with pulmonary tuberculosis in the 1993 national notification survey⁶. The ethnic composition of the cases reported here is similar, as are the percentages of patients with sputum smear positive and culture positive disease. Of the 794 patients treated by thoracic physicians, 229 (29%) were excluded from the analysis, as were 60 (45%) of the 131 under non-thoracic specialist care. Non-thoracic specialists were therefore over-represented in the excluded group. If the management of the excluded cases was similar to that of those included, this would in fact act in favour of the non-thoracic physician treated group by reducing the significance of the differences between

Table 2. Drug treatment regimens.

Regimen	Drug combination		Treatment modified
	No.	%	
HRZ/HR	569	62	127
HRZE/HR	101	11	37
EHR/HR	7	1	3
EHR/EHR	2	0.2	-
Other	241	26	130

E = ethambutol R = rifampicin
H = isoniazid Z = pyrazinamide

Table 3. Patients on standard regimens meeting treatment duration criteria.

	Drug combination		
	HRZE/HR	HRZ/HR	EHR/HR
Criteria met	44	329	1
Criteria not met	57	240	6

Total duration	Initial phase		
	Within range	Too short	Too long
Within range	374	16	31
Too short	20	2	3
Too long	168	14	49

E = ethambutol R = rifampicin
H = isoniazid Z = pyrazinamide

the two groups. Compared with other clinician groups, thoracic physicians were significantly more likely to treat patients with a recommended combination.

Rifampicin and isoniazid were given to nearly all patients, and 96% received pyrazinamide. This represents a substantial increase from the 79% treated with pyrazinamide in 1988¹, which itself was much higher than the 19% so treated in 1983². Although 869/920 (94.5%) of patients were commenced on a recommended combination, only 677 (74%) of them continued to receive one³, which had to be modified in 167 (25%) patients. In nearly half who continued on a standard combination, the duration of initial and/or continuation phase fell outside the acceptable range. Valid reasons were provided for 167 cases, but no justification was offered in 136 (43%) of these deviations.

As in previous national surveys^{7,8}, drug resistance varied substantially between ethnic groups: Black-Africans (13%), ISC ethnic group (4.5%), whites (2%), and none in Black-Caribbeans. Definite or suspected drug reactions were significantly more common in those on non-standard combinations. The level of side-effects (9%) was slightly less than in 1983¹ (10%) and substantially lower than the 14% reported in 1988², despite the increased use of pyrazinamide. Seventy-two patients died before completion of the one year audit period, 15 (1.5%) from their tuberculosis and 57 (6%) of non-tuberculous disease. The 1.5% dying from their tuberculosis is lower than the 5.5% reported in the 1978-9 survey⁴, and overall mortality was less than in 1983¹ (10%) and 1978-9⁴ (12%). Deaths were not analysed in 1988².

Of the 815 patients remaining in the country at the end of treatment, 430 (53%) were discharged from follow-up in line with JTC recommendations for uncomplicated cases with good compliance³. In 98/385 (25.5%) who were followed up, only unit policy was given as a reason – which would suggest that these patients were followed up unnecessarily.

Conclusion

Overall, the treatment of pulmonary tuberculosis was satisfactory, with nearly 96% commencing on a recommended drug combination; but in only 677 (74%) was such a regimen continued, with thoracic physicians

performing better than other clinician groups. Approximately 20% of patients were treated for longer than required in either the initial or continuation phase. Slightly over half the patients who completed treatment were discharged on completion of treatment, with probably one-quarter of those given follow-up receiving it unnecessarily. Adherence to current evidence-based treatment guidelines³ would prevent unnecessary prolongation of treatment or follow-up and save resources.

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References

- 1 Medical Research Council Tuberculosis and Chest Diseases Unit. Management and outcome of pulmonary tuberculosis in adults notified in England and Wales in 1983. *Thorax* 1988;**43**:591–8.
- 2 The British Thoracic Society Research Committee and the Medical Research Council Cardiothoracic Epidemiology Group. The management of pulmonary tuberculosis in adults notified in England and Wales in 1988. *Respir Med* 1991;**85**:319–23.
- 3 Joint Tuberculosis Committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations of the Joint Tuberculosis Committee of the British Thoracic Society. *Thorax* 1990;**45**:403–8.
- 4 Humphries MJ, Byfield SP, Darbyshire JH, Davies PDO, *et al.* Deaths occurring in the newly notified patients with pulmonary tuberculosis in England and Wales. *Br J Dis Chest* 1984;**78**: 149–56.
- 5 Cullinan P, Meredith SK. Deaths in adults with notified pulmonary tuberculosis 1983-85. *Thorax* 1991;**46**:347–50.
- 6 Watson JM, on behalf of a Public Health Laboratory Service/British Thoracic Society/ Department of Health Collaborative Group. Results of a national survey of tuberculosis notifications in England and Wales in 1993. *Thorax* 1994;**49**:442P.
- 7 Medical Research Council Tuberculosis and Chest Diseases Unit. National survey of tuberculosis notifications in England and Wales in 1983. *Br Med J* 1985;**291**:658–61.
- 8 Medical Research Council Cardiothoracic Epidemiology Group. National survey of notifications of tuberculosis in England and Wales in 1988. *Thorax* 1992;**47**:770–5.

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