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Management and outcome of pulmonary tuberculosis in adults notified in England and Wales in 1983

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ABSTRACT The management and outcome of treatment were studied, two years or more after notification, in previously untreated adult patients of white and Indian subcontinent (Indian, Pakistani, and Bangladeshi) ethnic origin with pulmonary tuberculosis notified in England and Wales in the first six months of 1983. Of the 1068 patients, 10% had died, 3% defaulted, and 1% left the UK before completing chemotherapy. Of the 917 patients who completed chemotherapy, 90% were prescribed rifampicin and isoniazid throughout, most having ethambutol in addition either in the initial phase only (72%) or throughout (3%); 18% had pyrazinamide. The outcome of chemotherapy at the time the patient was last seen was reported by the clinician. Of those completing treatment, most were classified as cured after the primary course of chemotherapy (86%) or after modification of chemotherapy because of toxicity (10%) or therapeutic failure (2%). Altogether, 28 patients were classified as therapeutic failures because of a slow response, deterioration, or failure during chemotherapy (12) or relapse after stopping chemotherapy (16). A further 151 patients, however, failed to complete chemotherapy, some for reasons attributable to a failure of the routine clinical services. This should prompt continued efforts to maximise the efficiency of the services for tuberculosis. The main differences between the findings of this survey and those of the previous Medical Research Council survey (of patients starting chemotherapy in 1978–9) were an increased use of pyrazinamide and a reduction in the duration of the chemotherapy prescribed.

Introduction

The efficacy of short course regimens of six to nine months' duration based on isoniazid and rifampicin has been established by controlled clinical trials in many countries[1] and such regimens have been recommended for routine treatment in both technically advanced[2–5] and developing countries.[6,7] A survey of treatment of adult patients with pulmonary tuberculosis notified in England and Wales in 1978–9,[8] however, showed that, although the drug combination recommended for routine use in Britain by the British Thoracic Association[2] in 1976 and reiterated in 1980[9] was often prescribed (for about two thirds of patients), many patients were still being treated for substantially longer than the recommended nine months. Unnecessary prolongation of treatment exposes the patients to greater risk of toxicity, increases the cost of treatment, and has social and psychological disadvantages for the patient and family. In addition, most patients (79%) were admitted to hospital initially,[8] adding unnecessarily to costs and wasting resources, as ambulatory outpatient chemotherapy has been shown to be effective.[10]

We now report the results of a second survey of the management and outcome of adults with pulmonary tuberculosis notified in the first six months of 1983 in England and Wales, nearly five years after the first survey. Additional information on outcome has been collected to assess the efficacy of short course chemotherapy regimens in the routine treatment services of England and Wales.

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Methods

The population was drawn from the 1827 adult patients (aged 15 years or more) with tuberculosis notified from 1 January to 30 June 1983 who had respiratory disease only.[11] The survey was confined to patients who had a pulmonary lesion on a pretreatment chest radiograph, confirmed at independent assessment, and also had at least one pretreatment culture result available (in most cases from sputum), and who were of either white or Indian subcontinent (Indian, Pakistani, or Bangladeshi) ethnic origin (92% of all patients notified). Patients were not included if they had had previous treatment for tuberculosis, if they had extrapulmonary tuberculosis or died before treatment could be started, or if their organisms were initially resistant to one or more antituberculosis drugs.

A total of 1164 patients fulfilled the inclusion criteria and were followed up two years after the last patient was notified. A form was sent to the clinician in charge of each patient to obtain information on (1) the antituberculosis drugs prescribed in the initial and continuation phases and the duration for which they were prescribed; (2) for patients prescribed ethambutol, the dose and the patient's weight; (3) whether or not corticosteroids were prescribed; (4) whether or not chemotherapy had been completed as planned; (5) whether the patient had any adverse reactions necessitating modification of the chemotherapy; (6) whether the patient had been admitted to hospital initially and, if so, why and for how long; and (7) the condition of the patient when last seen and the date. If the patient was reported to have been transferred or was lost from follow up attempts were made to obtain further information from the relevant clinic or from the patient's general practitioner.

A survey form was returned for 1160 (99·7%) of the 1164 patients. Of these, 92 were excluded from the analyses. Sixty eight were found to be ineligible by the original criteria, one had started treatment abroad, and for 23 the information required was not available because the notes had been lost or destroyed. Results are therefore presented for 1068 patients (of whom one defaulted before starting chemotherapy and two had incomplete information on chemotherapy).

Stepwise multiple regression analyses were used to examine possible associations between pretreatment factors and the management of the patient.

Results

PATIENTS

Of the 1068 patients, 821 (77%) were of white (71% male) and 247 (23%) of Indian subcontinent (ISC) (43% male) ethnic origin (table 1). White patients of both sexes were on average older than the Indian subcontinent patients and more likely to have bacteriologically confirmed disease, and according to the chest radiograph the disease was more severe and showed cavitation more often.[12] These differences are due in part at least to the younger age distribution of the Indian subcontinent population in England and Wales from which the patients were drawn (Office of Population Censuses and Surveys, unpublished findings).

Table 1 *Pretreatment characteristics of the 1068 patients*

Pretreatment characteristic	*Ethnic origin*			
	White		*Indian subcontinent*	
	No	*%*	*No*	*%*
Males: age (y)				
15–34	113	*19*	53	*50*
35–54	151	*26*	34	*32*
⩾55	321	*55*	19	*18*
Total	585	*100*	106	*100*
Females: age (y)				
15–34	78	*33*	90	*64*
35–54	59	*25*	28	*20*
⩾55	99	*42*	23	*16*
Total	236	*100*	141	*100*
Bacteriological results from sputum specimens				
Culture positive				
Smear positive	497		121	
Smear negative	161	*82*	41	*69*
No smear result	13		8	
Culture negative	150	*18*	77	*31*
Radiographic characteristics at independent assessment				
Total area affected:				
More than 1 lung (3 zones)	138	*17*	13	*5*
More than 1/3 lung (1 zone)	392	*48*	114	*46*
Up to 1/3 lung (1 zone)	291	*35*	120	*49*
Cavitation:*				
Extensive	62	*8*	6	*2*
Moderate	137	*17*	33	*13*
Slight	91	*11*	26	*11*
Nil	529	*64*	182	*74*
Total patients assessed	821	*100*	247	*100*

*For two patients (both white) cavitation could not be assessed.

CHEMOTHERAPY

Of the 1068 patients, 64% completed chemotherapy as planned by the clinician in charge (table 2). Chemotherapy was not completed in 151 (14%) patients, the main reasons being that they had died (10%), defaulted (3%), or left the United Kingdom (1%, all of Indian subcontinent ethnic origin). The major difference between the ethnic groups was the higher proportion of white patients who died.

Chemotherapy was completed but not as planned initially in 22% of the patients. The most common reasons for change in treatment were drug toxicity (9%), poor compliance (6%), and prescribing error

Table 2 *Completion of chemotherapy*

Chemotherapy	White No	%		Indian subcontinent* No	%		Total No	%	
Not completed									
Died	103	13		2	1		105	10	
Defaulted	22	3	16	5	2	9	27	3	14
Left the UK	0	0		14	6		14	1	
Other reasons	5	1		0	0		5	<1	
Completed									
Not as planned									
Toxicity	72	9		24	10		96	9	
Poor compliance	49	6	21	14	6	23	63	6	22
Error	21	3		5	2		26	2	
Other reasons	31	4		14	6		45	4	
As planned	516	63		169	68		685	64	
Total patients assessed	821†	100		247	100		1068†	100	

*Ethnic origin.
†For two patients (both white) the information was not available.

(2%). Other reasons included slow response or failure of treatment, pregnancy, transfer, or change of doctor. The findings were similar for the two ethnic groups.

REGIMENS PRESCRIBED AND DURATION OF CHEMOTHERAPY

Regimens based on isoniazid plus rifampicin throughout were prescribed for 821 (90%) of the 917 patients (table 3) and for 660 (96%) of the 685 in whom chemotherapy was completed as planned. Of the latter group, 67% received ethambutol initially, 12% ethambutol plus pyrazinamide initially, and 7% pyrazinamide initially; 4% did not receive a third drug (table 3). Ethambutol was continued throughout in 3%.

Over half (513, 56%) of the patients had treatment for nine months or less (table 4); 128 (14%) had treatment for more than 12 months. For the two regimens most commonly prescribed (HRZE/HR and HRE/HR—see footnote to table 3) 76 (89%) and 276

Table 3 *Regimens prescribed for the patients who completed chemotherapy*

Regimen†	1983 survey Total No	%		Completed as planned No	%		1978–9 survey Completed as planned No	%	
HR throughout									
HRZE/HR	101	11		80	12		9	1	
HRZS/HR	9	1		5	1		6	1	
HRZ/HR	53	6		48	7		26	3	
HRS/HR	5	1	90	5	1	96	33	4	86
HRE/HR	555	61		458	67		468	57	
HRE	31	3		22	3		93	11	
HR	28	3		24	4		60	7	
Other HR based	39	4		18	3		11	1	
HE throughout									
RHE/HE	20	2		8	1		68	8	
SHE/HE	3	<1	4	2	<1	2	9	1	12
HE	0	0		0	0		17	2	
Other HE based	16	2		3	<1		1	<1	
Miscellaneous	57	6		12	2		19	2	
Total patients assessed	917*	100		685	100		820	100	

*Excluding 105 patients who died, 27 who defaulted, 14 who left the UK, and five who did not complete chemotherapy.
†H, isoniazid; R, rifampicin; E, ethambutol; Z, pyrazinamide. Letters before the oblique indicate initial drug treatment and letters after it drugs given in the continuation phase.

Table 4 *Total duration of chemotherapy*

Duration (months)*	1983 survey All patients† No	%	Completed as planned HREZ/HR No	%	HRE/HR No	%	Total No	%	1978/9 survey Completed as planned No	%
6 or less	69	8	39	46	7	2	54	8	7	1
7 or 8	51	6	4	5	11	2	30	4	38	5
9	393	43	33	39	258	56	346	51	228	28
10 or 11	156	17	3	4	91	20	117	17	143	17
12	116	13	3	4	53	12	80	12	174	21
13–15	79	9	2	2	25	5	39	6	132	16
16–18	29	3	0	0	8	2	13	2	58	7
≥19	20	2	1	1	5	1	6	1	39	5
Total patients assessed	913	100	85‡	100	458	100	685	100	819	100
Median	9·1		8·0		9·0		9·0		11·1	

*The duration of chemotherapy has been calculated so that, for example, seven months represents from 6·5 to 7·5 months.
†Excluding patients who died, defaulted, or left the UK and four for whom the duration was not known.
‡Includes five patients who had HRES/HR.
Abbreviations as in table 3.

(60%) of patients were treated for nine months or less. The duration of the initial phase (data not tabulated) was two months or less for 69 (81%) and 274 (60%) of the patients having the HRZE/HR and the HRE/HR regimens, and more than three months for 2 (2%) and 60 (13%).

Intermittent chemotherapy was used for only 39 patients (4%), all except one in the continuation phase only, and for only 22 of the 685 (3%) who completed chemotherapy as planned. All of these notifications came from five doctors.

ANTITUBERCULOSIS DRUGS PRESCRIBED

All except five of the 1067 patients who started chemotherapy had isoniazid and all except 15 had rifampicin. Ethambutol was prescribed for 88%, pyrazinamide for 26%, and streptomycin for only 6%.

Ethambutol was prescribed to 938 patients at some time during their course of chemotherapy. Of the 851 patients for whom details of dosage and duration of treatment were available, 513 (60%) had it for two months or less, 195 (23%) for three months, 143 (17%) for four or more months, and 46 (5%) for more than six months. The daily dosage was less than 13 mg/kg for 52 (6%), 13–17 mg/kg for 641 (75%), 18–22 mg/kg for 83 (10%), and 23–27 mg/kg for 75 (9%). Forty two patients (5%) received more than 17 mg/kg for more than two months (16 of them more than 22 mg/kg).

ADVERSE REACTIONS

Adverse reactions requiring modification of the drug regimen were reported for 139 (13%) of the 1067 patients who started chemotherapy (table 5). The drug or drugs causing individual reactions were often not clearly established.

In the opinion of the clinician in charge, hepatitis occurred in 41 patients, 28 with jaundice. Of the 219 patients who received isoniazid plus rifampicin with pyrazinamide initially (with or without ethambutol), 11 (5%) had hepatitis, nine with jaundice, whereas for the 795 who received isoniazid plus rifampicin without pyrazinamide the corresponding figures were 24 (3%) and 16 (2%) ($p > 0.3$ for both comparisons). Eight patients, all having ethambutol, were suspected of having ocular toxic reactions, but in none was this confirmed at ophthalmological assessment. Four of the 32 patients with cutaneous reactions had a generalised hypersensitivity reaction; only two of the four patients with musculoskeletal reactions were receiving pyrazinamide.

USE OF CORTICOSTEROIDS

Corticosteroids were prescribed to 72 (7%) of the 1068 patients (60 (7%) white, 12 (5%) Indian subcontinent patients). Steroids were prescribed because of the severity of the illness in 32 patients, a slow response or deterioration in 19, pleural effusion in nine, and adverse drug reactions in eight. Prednisolone was usually prescribed (69 patients), the most frequent initial dose being 30 or 20 mg (33 patients) (range 10–60 mg). The mean duration of treatment for the 59 patients who completed the course of corticosteroids (excluding those who died) was 17 weeks (range 14 days to 87 weeks).

Table 5 *Adverse reactions requiring modification of chemotherapy in 1067 patients who started chemotherapy*

Type of reaction	*No*		*%*
Hepatic			
Hepatitis	41	55	*5*
Abnormal liver function tests	14		
Gastrointestinal			
Nausea	14		
Vomiting	13	31	*3*
Other	4		
Cutaneous	32		*3*
Neurological	9		*1*
Ocular	8		*1*
Vestibular	6		*1*
Musculoskeletal	4*		*< 1*
Miscellaneous or non-specific	6		*1*
Total with one or more reactions†	139		*13*
Action taken			
One or more drugs stopped	64		*6*
Regimen changed	33		*3*
Regimen interrupted	38		*4*
Dosage reduced	4		*< 1*

*One patient had pyrazinamide discontinued because of an asymptomatic raised serum urate concentration.
†Twelve patients had two, one had three, and one had four different reactions.

HOSPITAL ADMISSION

Of the 1068 patients, 790 (74%) were admitted to hospital initially, the main reasons being for investigation (379, 48%), severity of disease (98, 12%), coexisting disease (67, 8%), and social factors (45, 6%). For 539 patients whose hospital admission was solely for tuberculosis and for whom details are available the median duration of stay was 21 days, but 182 (34%) were in hospital for more than four weeks and 67 (12%) for more than eight weeks.

Hospital stay was prolonged for reasons other than tuberculosis in 207 patients, the most common reasons being other diseases (125, 16%) and social factors (67, 5%). In the 180 patients for whom data were available in this group, the median duration of stay was longer—46 days, 116 (64%) of these being in hospital for more than four weeks and 71 (39%) for more than eight weeks.

FACTORS AFFECTING MANAGEMENT

The independent variables studied in the multiple regression analyses were age, sex, ethnic origin, the

results of smear examination and of culture of sputum, radiographic extent of disease and cavitation, and the enlargement of intrathoracic lymph nodes at independent assessment.

In the 660 patients who completed as planned chemotherapy based on isoniazid and rifampicin the most significant independent variable affecting duration of treatment was whether or not the patient received pyrazinamide initially, patients receiving pyrazinamide being treated for a shorter time. Other significant factors were the extent of disease (the more extensive the disease the longer the treatment) and the presence of enlarged intrathoracic lymph nodes (associated with a longer duration).

The duration of hospital stay in the 539 patients whose stay was solely for tuberculosis was significantly associated with three variables: radiographic extent of disease, pretreatment culture result, and extent of cavitation (in order of significance). Patients with a positive culture and more extensive radiographic disease and cavitation stayed in hospital longer.

The independent variables, however, accounted for no more than 12% of the total variation for duration of chemotherapy or hospital stay.

OTHER DISEASES

Coexisting diseases were reported for 513 (48%) of the 1068 patients (53% of white and 33% of Indian subcontinent patients). The most common concomitant diseases among the 821 white patients were chronic bronchitis and emphysema (127, 15%), alcoholism (64, 8%), diabetes (36, 4%), ischaemic heart disease (28, 3%), and carcinoma of the lung (24, 3%). A further 40 patients had other cardiovascular disease (including 11 with hypertension); 19 had asthma, 16 pneumoconiosis, and 16 rheumatoid arthritis. Among the 247 Indian subcontinent patients the most common diseases were diabetes (31, 13%) and anaemia (8, 3%); no other disease was reported in more than four patients.

OUTCOME

Duration of follow up at last attendance

The duration of follow up after completion of chemotherapy is known for 886 patients; of these, 119 (13%) were not seen after completing chemotherapy (12 reported as lost from follow up). A further 20% were last seen within six months of stopping chemotherapy, 24% from six to 12 months, 27% from 12 to 18 months, and the remaining 15% after more than 18 months. In all 39 patients were considered to be lost from follow up, eight of whom had been seen a year or more after completing chemotherapy. In addition, 56 patients had died after completing chemotherapy, 12 had been transferred, and eight had left the UK.

Table 6 *State of the patients who had completed chemotherapy at their last attendance*

	No	*%*	
Cured			
With primary course of chemotherapy	789	*86*	
After modification of chemotherapy			
Toxicity	91	*10*	*12*
Slow response	8	*1*	
Relapse	8	*1*	
Deterioration or failure	4	*<1*	
Not yet cured			
Still on treatment			
Relapse	8	*1*	*2*
Inadequate follow up			
Defaulted	5	*1*	
Died	4	*<1*	
Total patients who completed chemotherapy	917	*100*	
Did not complete chemotherapy	151		
Died	105		
Defaulted	27		
Left the UK	14		
Other reasons	5		

State at last attendance

Of the 917 patients who completed chemotherapy 789 (86%) were considered, by the clinician in charge, to have been cured by the primary course of chemotherapy (table 6). A further 111 (12%) were classified as cured after modification of chemotherapy because of toxicity (91) or slow response (8), deterioration or failure while having chemotherapy (4), or relapse after stopping chemotherapy (8). The definition of "cure" was reported by the clinician to be based on bacteriological evidence (with or without radiographic or clinical evidence) in 425 (47%) of the 900 patients classified as cured, on radiographic evidence in 431 (48%) and on clinical evidence only in 42 (5%). The remaining 17 patients (2%) were classified by the clinician as not yet cured at their last attendance. Eight patients were still having treatment because they had relapsed and nine were considered to have had an inadequate follow up (four having died of non-tuberculous causes and five being lost from follow up). A further 151 patients did not complete chemotherapy for reasons given in table 6.

Therapeutic failures

Only 3% of the 917 patients required modification of their chemotherapy and this was because of slow response (8 patients), deterioration during chemotherapy (4), or relapse (16). Of these, 20 were classified by the clinician as cured at their last attendance and eight as not yet cured. There was doubt about compliance with the primary course of chemotherapy in 15 of the 28, including four in whom the course was considered to be inadequate. A further patient had received inadequate chemotherapy because of a toxic reaction and another because of pregnancy.

Nine of the 16 patients who relapsed had bacteriological confirmation (one with resistance to rifampicin and another with resistance to rifampicin and isoniazid). In the other seven bacteriological confirmation was not reported; one patient developed tuberculosis of the cervical nodes and another a paravertebral abscess (both patients of Indian subcontinent ethnic origin). Relapse occurred within six months of stopping chemotherapy in 10 patients and within 6–15 months in five (time uncertain for one). There were no differences between the white and the Indian subcontinent ethnic groups in the proportion of patients classified as therapeutic failures—3% for both.

COMPARISON WITH THE 1978–9 SURVEY

The proportion of patients who completed chemotherapy as planned by the clinician, 64%, was similar to the proportion in the survey of 1978–9[8] (65%). The main differences in the drug combinations prescribed (table 3) were an increased use of pyrazinamide in the initial phase in 1983 and a smaller proportion having isoniazid plus ethambutol prescribed throughout chemotherapy. The duration of chemotherapy was on average shorter in 1983, both the total duration (table 4) and the duration of the initial phase of the EHR/HR regimen (data not tabulated). Intermittent chemotherapy was used rarely in 1978–9 (2% of patients) as in 1983 (4%).

The proportion of patients admitted to hospital was similar in the two surveys, 79% in 1978–9 and 74% in 1983. The reasons for admission were broadly similar.

Discussion

The previous survey of patients who started chemotherapy in 1978–9[8] showed that although many clinicians were using the drug regimen first recommended by the British Thoracic Society in 1976[2] (and reiterated in 1980[9])—namely, isoniazid plus rifampicin with ethambutol initially (EHR/HR)—they were often treating patients for much longer than the recommended nine months. The present survey of patients who started chemotherapy in 1983 has shown a reduction in the duration of prescribed chemotherapy, the median duration for patients who completed chemotherapy as planned now being 9·0 months compared with 11·1 months in 1978–9. The proportion treated for more than nine months had dropped from 67% to 37% and for more than a year from 28% to 8%.

In 1978–9 there was already good evidence that six month regimens of chemotherapy were highly effective, particularly if pyrazinamide was included,[13] and more evidence has become available since then.[3 14] The proportion of patients receiving pyrazinamide increased from 6% in the first survey to 26% in the current survey. The total duration of chemotherapy was, on average, shorter for those receiving pyrazinamide than for those who did not.

There were changes in the use of ethambutol between the surveys. The proportion of patients receiving isoniazid plus rifampicin with ethambutol throughout the whole period of treatment declined from 11% to 3%. There is no evidence of benefit from prolonging ethambutol for longer than two months and it carries increased risk of severe toxicity. Most patients (81%) were prescribed ethambutol in a dosage of 17 mg/kg or less, although a dose of 25 mg/kg for two months is the recommended dose. Isoniazid and ethambutol throughout the whole period of chemotherapy (with or without other drugs in the initial phase) were prescribed for only 2% of patients compared with 12% in the previous survey. This is an improvement in practice since if patients default early they are more likely to be cured if they are prescribed regimens based on isoniazid with rifampicin throughout treatment rather than ethambutol.

The advantage of short course regimens that are intermittent either from the start[15] or after an initial daily phase[16] is that they can be given under full supervision. They are used routinely in some countries[17] and are acknowledged to have a role in the treatment of certain patients, such as elderly patients living alone, alcoholics, and vagrants, who form an increasing proportion of patients in England and Wales. Perhaps surprisingly, as in the 1978–9 survey, only a small proportion (4%) of patients were treated with intermittent regimens. This is an area where the chemotherapy of difficult and non-compliant patients might be improved.

Controversy about the role of corticosteroids in pulmonary tuberculosis[18] continues. They are occasionally prescribed in addition to antituberculosis chemotherapy particularly for severe, extensive disease and in moribund patients, although there have been few controlled clinical trials. In this survey 7% of patients were prescribed corticosteroids because of tuberculosis. The figure was 23% in the 44 patients who were reported to have died from tuberculosis or in whom tuberculosis contributed to death. The dosage prescribed was on average low, particularly as the pharmacological effect of prednisolone is reduced when it is taken with rifampicin.

Adverse reactions necessitating modification of treatment were reported for 139 (13%) of the patients. The commonest reactions were hepatic, reported in 5%, of whom half had jaundice and about a quarter abnormalities of liver function with no symptoms. The addition of pyrazinamide to isoniazid and rifampicin in the initial phase of treatment did not increase the incidence of hepatotoxicity, confirming in a clinical

setting in England and Wales the findings of the controlled clinical trial conducted by the British Thoracic Association.[19] There has been considerable debate recently about the risk of ocular toxic reactions to ethambutol, which may occur even with the recommended doses.[20] Among the 938 patients prescribed ethambutol in this survey ocular toxicity was suspected in eight but was not confirmed in any. There is no evidence that ethambutol given as the fourth drug in an initial phase of treatment consisting of isoniazid, rifampicin, and pyrazinamide is of benefit to patients with fully sensitive mycobacterial strains[21,22] and ethambutol is not included in the six month regimen recently recommended by the American Thoracic Society.[4] The other common adverse reactions were gastrointestinal (3%) and cutaneous (3%), which were usually mild.

Controlled studies have established that ambulatory chemotherapy for pulmonary tuberculosis is as effective as inpatient treatment for most patients[10] and it carries no additional risk for close contacts of the patient.[23] Unnecessary hospital admissions are expensive. In both surveys most patients were admitted to hospital initially, 79% in 1978–9 and 74% in 1983. In about half the patients in the 1983 survey the main reason was investigation and diagnosis. Hospital stay was prolonged for reasons other than tuberculosis in about a quarter of the patients, but for the patients whose stay was for tuberculosis only the median duration was only 21 days. Although hospital admission was widely used, it was frequently for diagnosis or because of coexisting disease or social reasons and patients admitted because of their tuberculosis were, on average, admitted for relatively short periods of time.

Information on the outcome of chemotherapy was based solely on the clinician's classification and no attempt was made to collect bacteriological specimens for the purposes of the survey or to obtain chest radiographs for independent assessment. The survey form was sent to the clinician at least two years after the case had been notified. Many patients had already been discharged from follow up but for some it was still continuing, so the period of follow up varied considerably. Assessment of the outcome of chemotherapy and also the criteria for changes of chemotherapy for therapeutic failures in a survey of routine practice such as this are inevitably much less consistent than in a controlled clinical trial. Nevertheless, the outcome as reported by the clinician provides an important measure of the results achieved in routine practice.

Most patients (86%) were classified by the clinician as cured by the primary course of chemotherapy and a further 12% after modification of chemotherapy, usually because of drug toxicity. In all, only 28 patients (3%) could be regarded as therapeutic failures and 20 of these were classified as cured when last seen. Thus in routine clinical practice in England and Wales in 1983 a cure was achieved in 98% of the patients who completed chemotherapy. There were, however, a further 151 patients (14% of the 1068 patients) who failed to complete chemotherapy for various reasons, some of which are attributable to a failure of the routine clinical services. This should prompt continued efforts to maximise the efficiency of the services for tuberculosis.

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