# The management of lymph node tuberculosis notified in England and Wales in 1993

**ABSTRACT – We have compared the management of 219 cases of lymph node tuberculosis reported to the 1993 national notification survey with the recommended standards of treatment. The diagnosis was supported by positive histology and bacteriology in 81 cases (37%), positive histology in 70 (32%), positive bacteriology in 26 (12%), and on only clinical grounds in 40 (18%). Most patients (88%) were under the care of thoracic physicians. Almost all (97%) were commenced on a recommended drug combination, but only 81% continued to receive it, with thoracic physicians more likely than other physicians to use a recommended combination. Non-standard durations of the initial and/or continuation phases of treatment were used in 83 patients, but in only 49 cases was a satisfactory reason given for the modification. Definite or suspected drug toxicity was reported in 22 cases (10%), and was significantly more likely with non-standard regimens. There were no deaths. Of the 209 patients observed to treatment completion, 129 (62%) were then discharged. There were adequate reasons for follow-up after the end of treatment in all but 32 (15%) of those so managed. Further education is required to increase the percentage of patients treated with evidence-based regimens and durations of chemotherapy.**

No systematic study has been undertaken of the regimens used in the treatment of non-pulmonary tuberculosis. In 1990, the Joint Tuberculosis Committee (JTC) of the British Thoracic Society (BTC) published guidelines covering both pulmonary and non-pulmonary disease[1]. The regimen recommended for superficial lymph node disease was six months' treatment with isoniazid (H) and rifampicin (R), supplemented by either pyrazinamide (Z) for the first two months where there was a low risk of isoniazid resistance (2HRZ/4HR), or an initial two months of pyrazinamide and ethambutol (E) where there was a higher risk of isoniazid resistance (2HRZE/4HR). The JTC guidelines also recommended that uncomplicated cases with good compliance could be discharged on completion of treatment[1].

Superficial lymph node tuberculosis accounts for approximately 50% of all non-pulmonary tuberculosis notified in the 1993 notification survey[2]. The survey presented here reports for the first time the management of this condition in routine practice in England and Wales, covering treatment and its outcome, including unwanted effects and morbidity.

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## Methods

The survey was conducted as described in the preceding paper (pages 662–5). The following additional information was recorded:

- diagnostic criteria, histological and/or microbiological, or clinical
- the site of lymph node disease
- sensitivity tests on positive bacterial cultures.

Tuberculosis at any other site was classified as respiratory, non-respiratory or both. Starting and stopping dates were noted for each drug, and whether treatment was given daily or intermittently.

## Results

### *Exclusions*

Sixty-eight cases were excluded from analysis: 18 had no clinical form returned, the diagnosis was changed in 14, and 36 because of late or unanswered questionnaires.

### *Patient characteristics and clinician supervising treatment*

Of the 219 patients studied, 85 were men and 134 women; 38 were white, 138 from the Indian subcontinent (ISC), 21 Black-African, 3 Black-Caribbean and 19 from other ethnic groups. Thoracic physicians treated 193 cases (88%), infectious disease physicians treated 9 (4.5%), 6 each (3%) were treated by general physicians and paediatricians, 2 (1%) by surgeons, 1 (0.5%) by a genitourinary physician and 2 (1%) by other clinicians.

### *Site of disease and method of diagnosis*

The sites of lymphadenopathy were cervical (196), axillary (18), inguinal (2), with 1 at another site and multiple sites in 2. The diagnosis was made by positive histology and bacteriology (81), positive histology (70), and positive bacteriology (26). The diagnosis was solely clinical in 40 cases. Tuberculosis was present at another site in 43 cases: 31 were respiratory (usually mediastinal lymphadenopathy), 8 non-respiratory and 4 both.

*Bacteriology*

Positive cultures were obtained in 107 cases, 99 (92.5%) being fully sensitive and 8 (7.5%) showing drug resistance; 2 cases were resistant to isoniazid, 1 to cycloserine and 1 to pyrazinamide, while 4 cases had combined streptomycin and isoniazid resistance. Seven of the 8 drug resistant patients were from the ISC ethnic group, the other was Black-African.

*Treatment*

One patient left the country before starting treatment. Rifampicin and isoniazid were given to all 218 patients treated, pyrazinamide to 211 (97%), and ethambutol to 57 (26%). A standard drug regimen was used in 176 (81%) patients (Table 1). Treatment modification was necessary in 49 of these patients: for drug reaction (11), drug resistance (1), and prescription error (5). Five patients failed to attend, with the result that treatment continued for longer than scheduled. The clinician deliberately prolonged treatment in 27 because of concern over progress.

Of the 176 treated with a recommended combination, 83 received inappropriate durations of initial and/or continuation phase treatment (Table 2); this was due to treatment modification in 49, and no explanation was given in 34 cases. Recommended combinations were used in 160/192 treated by thoracic physicians, 7/9 treated by infectious disease physicians, 4/6 treated by general physicians, 2/6 treated by paediatricians, 1/2 treated by surgeons, 1/2 by other doctors, and in the 1 case treated by a genitourinary physician. Thoracic physicians treated a significantly higher percentage of patients with a recommended combination than did other physicians ($\chi^2 = 6.99$; 1df; $p = 0.008$).

**Table 1. Drug treatment regimens.**

| Drug combination | | | |
|---|---|---|---|
| Regimen | No. | % | Treatment modified |
| HRZ/HR | 135 | 62 | 26 |
| HRZE/HR | 40 | 18 | 23 |
| EHR/HR | 1 | 0.5 | 0 |
| Other | 42 | 19 | 24 |

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

**Table 2. Patients on standard regimens meeting treatment duration criteria.**

| | Drug combination | | |
|---|---|---|---|
| | HRZE/HR | HRZ/HR | EHR/HR |
| Criteria met | 14 | 79 | – |
| Criteria not met | 26 | 56 | 1 |

| | Initial phase | | |
|---|---|---|---|
| Total duration | Within range | Too short | Too long |
| Within range | 93 | 2 | 10 |
| Too short | 6 | – | – |
| Too long | 45 | 2 | 18 |

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

*Drug toxicity*

Drug(s) were stopped because of definite or suspected adverse drug reactions on 26 occasions in 22 patients. The drugs suspected were pyrazinamide (12), rifampicin (6), isoniazid (5), ethambutol (2) and not recorded (1). Reactions were reported in 12/176 patients on standard combinations, compared with 10/42 on non-standard combinations – a highly significant difference ($\chi^2 = 14.85$; 1df; $p < 0.001$).

*Outcome*

There were no deaths, and 10 patients left the country. Of the remaining 209 patients, 129 were discharged to the care of their general practitioner on completion of treatment. Forty-one of the remaining 80 were not discharged because they had received prolonged treatment. The other reported reasons for non-discharge were continuing tuberculosis related problems (9), other medical problems (21), doubts about compliance (12), and other reasons (32) (most of these 32 were followed up as part of 'standard policy'). Most patients had more than one reported reason.

## Discussion

Lymph node disease accounts for approximately 50% of non-respiratory tuberculous disease in England and Wales[4]. This study reports the management of 80% of the patients notified in the 1993 national notification survey[2], with thoracic physicians responsible for 88% of the cases. Compared with other clinician groups, thoracic physicians were significantly more likely to treat patients with a recommended combination.

The management of lymphatic tuberculosis recommended by the JTC in 1990[1] was rifampicin and isoniazid for six months, with either pyrazinamide alone or pyrazinamide and ethambutol for the initial two months, depending on the risk of primary isoniazid resistance. This was later supported by the

third BTS lymph node study, both during treatment[5] and in follow-up to 30 months[6].

Of the 218 patients treated, nearly all (211) started on a recommended drug combination, but only 176 continued to receive this, and in 28% treatment modification became necessary later. In 83 who continued on recommended combinations, the duration of the initial and/or continuation phase fell outside the acceptable ranges. Whilst 53% of the variations were made for valid reasons, in 41% no justification was offered.

Definite or suspected drug reactions were significantly more common in those on non-standard combinations. No deaths were reported, and 129/209 patients remaining in the country at the completion of treatment were discharged from follow-up, in line with recommendations for uncomplicated cases[1]. Satisfactory reasons for follow-up were given in 48 patients, and 'other reasons' for 32 more. The main 'other reason' was that it was unit policy to follow up irrespective of clinical status. When this was the only reported reason, it would appear that these patients were unjustifiably followed-up.

## Conclusion

Overall, the treatment of lymph node tuberculosis was satisfactory, with all patients receiving rifampicin and isoniazid, and over 95% pyrazinamide. The majority (81%) were treated with a recommended combination, even if some had extended treatment duration, with thoracic physicians performing better than other clinical groups. Approximately 20% of patients were treated for longer than required in either the initial or continuation phase. Most patients were discharged at the completion of therapy, but up to 15% were followed up unnecessarily. Education which encouraged adherence to current evidence-based treatment guidelines[1] would prevent unnecessary prolongation of therapy or follow-up and save resources.

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## References

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