



## The Treatment of Bone and Joint Tuberculosis

**W. PERRY**

*Royal National Orthopaedic Hospital,  
Stanmore, Middlesex, England*

Spinal tuberculosis is by far the commonest and most serious form of bone and joint tuberculosis in Britain, followed some way behind by tuberculosis of the hip. The chemotherapy of the spinal disease can be broadly taken to apply to other forms of skeletal tuberculosis. However, the role of surgery in the concurrent management of the disease is more difficult to assess than the minor role surgery plays elsewhere in the skeleton. About 1% of all tuberculous cases involve the skeleton, but it has particular importance in the spine because the diagnosis is often delayed and such delay can have very serious consequences.

The data contained in this paper are based on the treatment schedule of the National Orthopaedic Hospital, where patients come largely under the care of the surgeon, Mr Hugh Kemp. As this is a specialized hospital, referral is mainly from other hospitals, where there has been difficulty in diagnosis or in management of the patient, and direct referral from GPs is small. The data to be presented are based on 148 patients seen over a period of 16 years, i.e. since 1962.

### **Differential Diagnosis of Spinal Tuberculosis**

The diagnosis is suggested by the clinical history and the X-ray findings in the spine; this will have already been commented on by the radiologist as likely to be an infective spondylitis although malignant disease can never be excluded. It is obvious that if tuberculosis is found elsewhere (e.g. chest or kidneys) then the diagnosis is quite simple. Of the 148 cases covered by this report 5% had active disease in the chest, so it is considerably less than it used to be in this country and certainly so compared to developing countries, whereas in the MRC Pusan, Korea study (1973) the figure was 35%. Only about 4-5% of our patients had genito-urinary TB as well as tuberculosis in the spine, in the Pusan study there were about 10% of patients with concurrent genito-urinary tuberculosis and skeletal tuberculosis.

*Rifampicin in Extra-pulmonary Tuberculosis: Royal Society of Medicine International Congress and Symposium Series No. 11, published jointly by Academic Press Inc. (London) Ltd., and the Royal Society of Medicine.*

If there is no evidence of tuberculosis elsewhere a needle biopsy of an affected vertebra is carried out by the radiologists. This can be done in the first day or two of the patient's admission and is carried out using a special C arm under X-ray control. The usefulness of this technique has not yet been fully evaluated and some would argue that a large amount of tissue may be needed to make the diagnosis requiring an exploratory operation. However, in disc infections Armstrong *et al.* (1978) have reported that 68% of organisms which included tuberculous organisms amongst others, were isolated on a needle biopsy. Most of the others were malignancies, but there were about 10% which later proved to have an infection which was not isolated on needle biopsy. Thus needle biopsy may have a role but probably a distinction has to be drawn between tuberculosis and other infections of the spine, for in tuberculosis a great deal more tissue may be needed. Other possible infections include in particular Staphylococci which accounts for 20% in our series of infective spondylitis and a variety of rarer ones, such as *E. coli*, Proteus, Brucella and Salmonella, (3% altogether).

If a diagnosis cannot be made, then tissue, whether it be from needle biopsy, aspiration of the abscess or exploratory operation, is examined by all possible methods of culturing and isolating the tubercle bacillus—histology, Ziehl-Nielsen staining, Lowenstein-Jensen media and guinea-pig inoculation. When this is done the percentage diagnostic success rate increases to about 85% of suspected tuberculous lesions, Kemp *et al.* (1973). The Mantoux was immensely valuable and no patient who was found to have spinal tuberculosis had a negative Mantoux. This is not to say that some patients do not have negative Mantoux when tested at concentrations of 1 in 10,000 or 1 in 5,000 but at 1 in 500 or 1 in 100 there was no case in which the patient was not sensitive. It is obvious, however, that some patients who have a positive Mantoux will have other infections of the spine.

Finally, a technetium polyphosphate bone scan is valuable as a focus of infection outside the spine and show up, which may provide a more readily accessible bone from which to obtain a biopsy specimen to verify the diagnosis.

## Patient Data

The racial distribution of the 148 patients is shown in Table 1. Of the 85 Europeans treated between 1962 and 1973, 51 were British born and 31 were either Irish or Continental. From 1974 to 1978 there has been a much higher preponderance of Indian patients. While there has been an increase in the Indian population these data may also reflect a change in the referral pattern.

Table 1  
Racial distribution of spinal tuberculosis  
in 148 patients

	1962-73	1974-78
European	85	11
African	10	2
Indian	22	17
Chinese	0	1
	117	31

The age incidence shows clearly that there is a much smaller number of children and adolescents compared to patients over the age of 20; this is in marked contrast to the findings in developing countries where in a number of the MRC trials half the patients have been children. Of our patients 62% were males.

Looking at the vertebral involvement by TB (Fig. 1) it can immediately be seen that it is quite a rare disease in the cervical spine. In the thoraco-lumbar region the disease is common in most of these vertebrae, and this experience is similar to that reported from other countries.

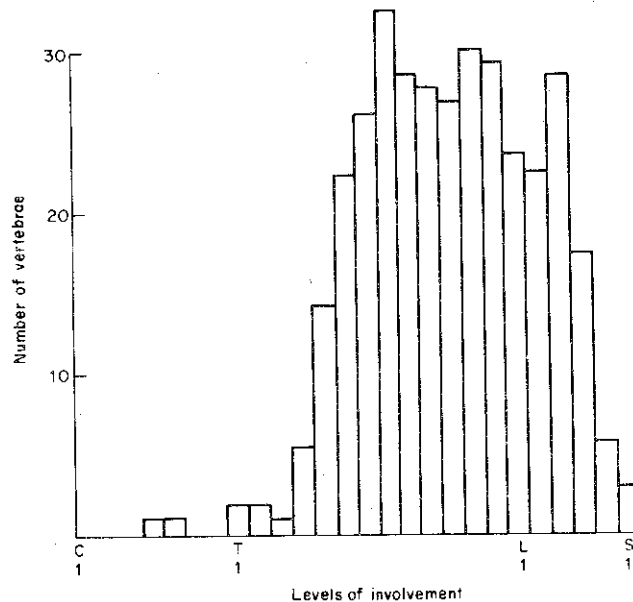


Fig. 1. Tuberculous vertebral involvement ( $n = 148$ ).

## Treatment

One of the most important studies undertaken has been the MRC working party reports on the treatment of spinal tuberculosis of which there are now seven. Five-year follow-ups from their centres in Korea, Hong Kong, Rhodesia and South Africa have been reported. It is quite clear from these reports that the great majority of cases are cured by a combination of PAS and isoniazid for 18 months. Neither the addition of prolonged bed rest, plaster jackets nor surgical debridement of the tuberculous lesion improved the rate of cure compared to ambulant patients receiving chemotherapy. This confirmed the point that Konstam had made as far back as 1958 when he found an excellent response among Nigerians who were treated as ambulant patients with thoraco-lumbar disease because there were neither the hospital or the surgical facilities, nor personnel to look after patients on long-term stay in hospital. This is a very good example of economic and other conditions in a developing country forcing a certain

method of treatment and, as a result, discovering that this is also probably the best form of treatment in the developed countries. The vast majority of patients were cured by PAS and isoniazid, with or without streptomycin, which does not seem to offer any advantage in most of the developing countries.

There are now two principal areas of difficulty that remain to be solved in the treatment of this disease, (a) the place of radical surgery and (b) the use of shorter regimes of chemotherapy usually incorporating rifampicin as a first line drug.

## Surgery

Most cases of spinal tuberculosis present to the orthopaedic surgeon and the physician is asked to manage the chemotherapy. However, the place of surgery in the treatment of the spinal disease remains, in spite of chemotherapy, an important one. Griffiths (1975) has divided the indications for surgery into absolute and relative. The two absolute indications are (a) to establish the diagnosis if in doubt, and (b) paraplegia during active disease. It has been shown that patients with early neurological signs of paraparesis or with acute paraplegia can make a complete recovery on chemotherapy alone. However, there are a number of patients who have permanent neurological deficit at the end of treatment, and in this country at any rate, the general feeling will be that any patient suffering paraplegia during active disease must have pressure on the cord, and that pressure should be relieved at the earliest possible moment.

The surgical approach is invariably anterior with excision and clearance of all the affected vertebral and disc tissue down to the dura. The next problem is bone grafting of the tissue. Hodgson and Stock (1956) in their classic and original paper on anterior fusion of the spine, advocated rib or banked bone for the grafting of the excised vertebral tissue, however Kemp *et al.* (1973) found that iliac crest grafting was much superior as shown in Series 2 (Table 2). He removed the diseased tissue with a coronal diameter wedge and into this was slotted an iliac crest graft. He found an excellent response in terms of early bony union and the degree of subsequent kyphosis. In his hands this technique was superior to the Hodgson and Stock method using autologous ribs, and the average fusion time was significantly reduced. Autologous rib also carried a much greater incidence of increased kyphosis which can be a particularly disfiguring aspect of spinal tuberculosis.

More controversial is the place of radical resection and anterior fusion in preventing deterioration of the kyphosis which can be considered a relative indication for surgery. In the MRC controlled trial of patients in Hong Kong (1974) half of whom were children or adolescents the radical operation was definitely superior to all other forms of treatment in preventing any increase in kyphosis. However, in the MRC South African trial (1978) in which the population was mainly adult, the radical operation was, of course, done by expert surgeons were not the originators of the operation, as in Hong Kong, and no improvement in kyphosis occurred. The follow-up of the children in Hong Kong into adulthood will confirm or deny whether the operation is justified in the long term for its effect on the kyphosis.

The one operation which must not be done is laminectomy as the diseased bone is nearly always anterior to the cord. However, the occasional additional involvement of the posterior vertebral facets can result in gross mechanical instability.

Table 2  
Analysis of results in relation to type of graft

Type of graft	Number	No follow-up	Non-union or incomplete fusion	Bony fusion	Average time to fusion (months)	Final kyphosis		
						Decreased	Static	Increased (and average)
Autologous rib	63	8	21	34 (62%)	24	1	30	24 (13 degrees)
Autologous ilium Series I	23	—	6	17 (74%)	14	1	21	1 (nil)
Autologous ilium Series II	18	—	1	17 (94.5%)	10	2	11	5 (7 degrees)
Homologous rib	1	—	—	1	24	—	1	—
Homologous tibia	7	—	2	5 (71%)	28	—	5	2
Heterologous Kiel bone, 4 Kiel bone + ilium, 1	5	—	1	4 (80%)	18.5	—	3	2

Autologous ilium: Series I denotes full thickness ilium used as an inlay graft. Series II denotes full thickness ilium crossing the coronal diameters of the affected vertebrae. The difference between the rate of fusion for autologous rib and autologous ilium was statistically significant ( $P < 0.001$ ).

## Chemotherapy

Up to 1973 all patients at the National Orthopaedic Hospital were receiving PAS and isoniazid for 18 months and, for the first 3 months, streptomycin, on this regime there is a dramatic change in the distribution of ESR. The vast majority of patients return to a level below 20 Westgren units after 18 months, although some patients are still left with elevated ESRs (Fig. 2). A few of those do have another intercurrent illness, but the majority will have no evidence of active tuberculosis and still seem to have mildly raised ESRs for which there is no obvious reason.

It is known that rifampicin is very effective in the treatment of bony tuberculosis and there have been five or six reports showing this. Also nearly all tubercle bacilli isolated from bone have been sensitive to rifampicin, whereas occasional organisms were resistant to PAS and streptomycin in the past. Rifampicin can penetrate into bone at bactericidal levels as shown by the work of Furesz (1970). (Table 3). These data were from different individual patients and the samples were looked at at different times. Although some levels are at the borderline of bactericidal activity, all are bactericidal using liquid media culture, and are probably adequate.

Twelve patients have been followed who have not had surgery and who have completed or are still receiving a combination of rifampicin, isoniazid and ethambutol (the latter for the first 3 months) which is the main regime at the NOH (Table 4). By 6 months the ESR had fallen as far as it is going to fall, except in one patient (SH) where there was a further significant fall. There was a large number of patients who had doubtful activity radiologically at 6 months. At 12 months, using the MRC criteria of radiological activity of tuberculosis, only one patient had doubtful activity on lateral X-rays of the spine, and at 18 months they were all fully healed, which confirmed the efficacy of rifampicin as a drug for spinal tuberculosis.

The MRC are currently conducting a short regime trial with rifampicin in spinal tuberculosis but one major problem, unlike pulmonary TB, will be a satisfactory test

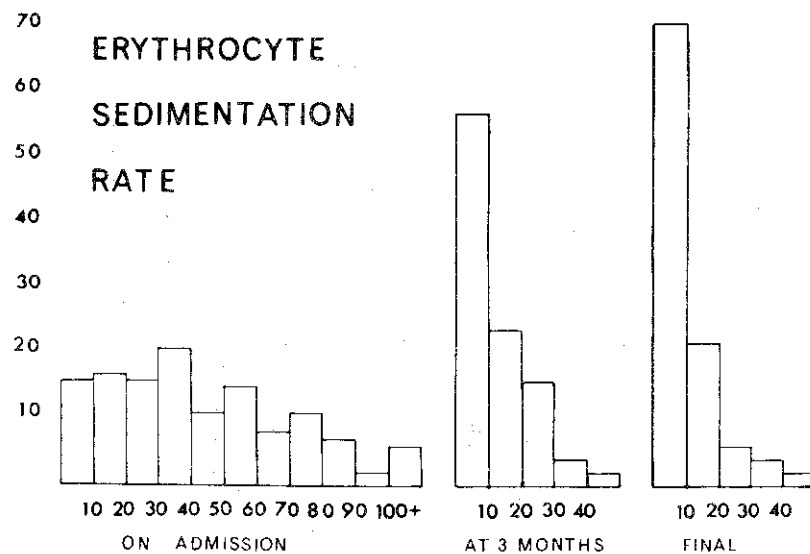


Fig. 2. Changes in ESR on PAS, isoniazid (18 months) and streptomycin (3 months). (Westergren Units.)

Table 3  
Serum and bone levels of rifampicin in man after oral administration  
of a single 450 mg dose (Furesz, 1970)

Case No.	Hours after admin.		Bone $\mu\text{g/g}$	Serum $\mu\text{g/ml}$
1	4	Tooth { crown root	0.14	—
			0.27	—
2	4.25	Femur	0.30	4.15
3	5.30	Phalanx	1.08	7.70
4	7.40	Callus	2.20	6.20
5	11.40	Tibia	— <sup>a</sup>	0.81
6	12	Rib	0.97	2.95
7	12	Tooth	0	—
8	12.15	Vertebral lamina	0.18	0.85

<sup>a</sup> Value not measurable with method used.

Table 4  
Treatment of spinal tuberculosis with rifampicin, isoniazid and ethambutol

Patient	ESR (months)				X-ray of Spine (months)	
	0	6	12	18	12	18
HB	40	20	16	15	NA	NA
JT	29	11	6	7	NA	NA
RA	96	14	7	11	NA	NA
VO	105	40	40	35	NA	NA
TG	57	—	9	13	DA	NA
MW	10	—	—	—	—	—
MK	75	11	—	—	—	—
UM	50	9	9	3	NA	NA
NW	50	8	3	7	NA	NA
MS	65	14	25	10	NA	NA
SH	72	52	35	18	NA	NA
MS	52	38	—	—	—	—

of relapse. Apart from the ESR which could be misleading, one would have to rely on X-ray deterioration and this may subject patients to risk, especially those who have already undergone anterior fusion operations. A possible alternative might be the bone scan, where in cases of doubtful radiological activity, it can be helpful in establishing activity.

## Conclusion

There is every reason to expect that the full radiological healing seen at 12 months in nearly all patients on the rifampicin regime is good evidence of complete eradication of the disease. Confirmation of this in the treatment of spinal tuberculosis will be awaited with interest.

### References

- Armstrong, P., Chalmers, A. H., Green, G. and Irving, J. D. (1978). *British Journal of Radiology* **51**, 333-337.
- Furesz, S. (1970). *Antibiot. et Chemother.* **16**, 316.
- Griffiths, D. L. (1975). *British Journal of Hospital Medicine* **14**, 146-157.
- Hodgson, A. R. and Stock, F. E. (1956). *British Journal of Surgery* **44**, 266-275.
- Kemp, H. B. S., Jackson, J. W., Jeremiah, J. D. and Cook, J. (1973). *Journal of Bone and Joint Surgery* **55-B**, 715-734.
- Konstam, P. G. and Konstam, S. T. (1958). *Journal of Bone and Joint Surgery* **40-B**, 26-32.
- Medical Research Council (1973). *Tubercule* **54**, 261-282.
- Medical Research Council (1974). *British Journal of Surgery* **61**, 853-866.
- Medical Research Council (1978). *Tubercle*, **59**, 79-105.

### Discussion

#### Dr McNicol

The role of surgery is not as important as Dr Perry's paper might suggest. In Brent we see about 20-30 cases per year of bone TB among East African Asians and surgery is only rarely used. Secondly, on the question of surgery you said that laminectomy was inappropriate which may be true where the anterior elements are involved, but with posterior disease, which is frequently the case in immigrants, it may be appropriate. Thirdly, we routinely treat our patients for one year with rifampicin and isoniazid with excellent results. We have stopped draining paravertebral abscesses as these will re-absorb during treatment. I would not quarrel with surgery where neurological compression is present.

### Summary

The treatment schedule for bone and joint tuberculosis employed at the Royal National Orthopaedic Hospital, England, is discussed. Of the 148 cases covered over a period of 16 years, 5% had active disease in the chest and 5% had genito-urinary disease. If no active site is found, needle biopsy is carried out and the material obtained examined by multiple techniques, i.e. histology, staining, culture and guinea-pig inoculation. The final diagnostic technique is technetium polyphosphate bone scan.

The percentage of Indian patients has increased between the years 1962-73 (18.8%) and 1974-78 (54.8%) and there is now a larger proportion of patients over the age of 20. The disease affected mainly the thoraco-lumbar region. Various studies have shown that the majority of cases are cured by a course of 18 months treatment with PAS and isoniazid, with or without streptomycin. The relative merits of various surgical procedures are discussed as is the current trend in chemotherapy. The NOH employ PAS and isoniazid for 18 months, plus streptomycin for the first 3 months, but the main regime is rifampicin and isoniazid with ethambutol (3 months only). The problem of adequately testing rifampicin in spinal tuberculosis is to find a satisfactory test of relapse and a possible alternative to X-ray might in future be bone scan.

### Resumen

Se discute el esquema terapéutico para la tuberculosis ósea y articular empleada en el National Orthopaedic Hospital, Inglaterra. De los 148 casos asistidos durante un



período de 16 años, el 5% presentó un proceso activo torácico y el 5% un proceso genito urinario. En caso de no hallarse focos en actividad, se efectuó una punción biopsia examinándose el material obtenido por múltiples técnicas, es decir, histología, tinción, cultivo e inoculación al cobayo. La técnica más reciente es la escansión ósea mediante polifosfato de tecnecio.

El porcentaje de los pacientes hindues se ha incrementado entre los años 1962 y 1973 (18,8%) y entre 1974 y 1978 (54,8%), y en la actualidad se cuenta con una mayor proporción de pacientes cuya edad rebasa los 20 años. El proceso afectó principalmente la región toracolumbar. Diversos estudios han demostrado que la mayoría de los casos, curaron en el curso de un tratamiento de 18 meses con PAS e isoniacida con o sin estreptomycin. Se discuten los méritos relativos de diversos procedimientos quirúrgicos, así como la tendencia actual en quimioterapia. El NOH emplea PAS e isoniacida durante 18 meses, más estreptomycin durante los 3 primeros meses, aunque el esquema principal es rifampicina e isoniacida con etambutol (sólo tres meses). Existen evidencias de la penetración del compuesto en el hueso, en el riñón, en el LCR y en los ganglios linfáticos. Tiene lugar asimismo un fenómeno competitivo entre la rifampicina y la bilirrubina, resultando en un incremento del nivel de bilirrubina sérica durante el tratamiento que podría interpretarse como signo de hepatotoxicidad, aunque el fenómeno es reversible, no habiéndose podido constatar alteración alguna en la estructura del hepatocito. Se discuten brevemente recientes desarrollos en farmacocinética, incluyendo análisis computorizados.

### Résumé d'article

Le schéma de traitement de la tuberculose ostéo-articulaire pratiqué au National Orthopaedic Hospital, England, est discuté. Sur les 148 cas diagnostiqués sur une période de 16 ans, 5% avaient en outre une tuberculose pulmonaire active et 5% une tuberculose urogénitale. Si aucune autre localisation active n'est retrouvée, on pratique une biopsie à l'aiguille et le matériel recueilli est examiné sur les plans histologique et bactériologique (examen direct, culture et inoculation). En cas de doute, on met en oeuvre une scintigraphie osseuse au polyphosphate de technetium.

Le pourcentage de patients Indiens est passé de 18,8% pour la période 1962-73, à 54,8% pour la période 1974-78 et la proportion de malades de plus de 20 ans a augmenté. La maladie touche essentiellement la colonne thoraco-lombaire. De nombreuses études ont montré que dans la majorité des cas, la guérison peut être obtenue par un traitement de 18 mois associant PAS et isoniazide, avec ou sans streptomycine. Les indications de la chirurgie et les tendances actuelles de la chimiothérapie sont débattues. Le N.O. Hospital utilise le schéma précité (avec streptomycine pendant les trois premiers mois), mais le schéma principal est l'association rifampicine/isoniazide avec éthambutol (les trois premiers mois). Le problème de l'évaluation de la rifampicine dans la tuberculose ostéo-articulaire est de trouver un critère satisfaisant de rechute et sur ce plan, la scintigraphie osseuse pourrait, dans le futur, constituer une alternative à la simple radiographie.

