

## Tuberculosis of Bone and Joints Indonesia Experience

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**Abstract :** Tuberculosis is one of the most ancient medical problems and still a threat for global mankind. One to seven percent of patients with tuberculosis will have skeletal involvement, with the spine, hip and knee as the most frequently involved site. Tuberculosis is not only a disease but also a public health problem. Diagnosis can be established by positive clinical features, laboratory results, imaging, histopathology, and culture and the polymerase chain reaction. The treatment principles for bone and joint tuberculosis are to eradicate or arrest the disease ; correct the deformities ; prevent complications ; treat the pain ; and rehabilitation.

### Introduction

Tuberculosis (TB) has plagued humankind since ancient times : there are reports of tuberculosis in mummies in Egypt dating from 3400 BC and notes written in Sanskrit at sometime between 1500 and 700 BC. TB is still a threat for global mankind and affects one third of the world's population<sup>13)</sup>. Indonesia ranks as the 3<sup>rd</sup> most affected country in the world, with 583000 new cases every year, with most of these occurring during the productive ages (15-54 years old)<sup>15)</sup>. One to seven percent of children with tuberculosis will have skeletal involvement<sup>5)</sup> ; in order of decreasing frequency involving the spine, hip, knee, foot, elbow, hand, and shoulder. The first 30 years of life are the most involved<sup>7)</sup>.

In the most recent few decades, some developed countries have also recorded a resurgence in skeletal tuberculosis associated with the acquired immunodeficiency syndrome and the recent increase in cross-country transportation. The development of the active disease in persons

with latent infection is a continual threat for tuberculosis transmission and outbreak. Lack in expertise in identification and management have shaped osteoarticular tuberculosis into a significant challenge in developed countries.

Tuberculosis is not only a disease but also a public health problem. Malnutrition, poor sanitation, overcrowded population, drug resistance, immunosuppressed status, and health care availability must be taken into account, if we want to eliminate tuberculosis. The objective of this paper is to present the management of osteoarticular tuberculosis infection in Ciptomangunkusumo General Hospital, Faculty of Medicine, University of Indonesia.

### Pathogenesis<sup>5)7)9)11)13)</sup>

Osteoarticular tuberculosis is the secondary focus of infection with hematogenous spread from the viscera (lungs, kidney and lymph node) as the primary focus. The cellular immune systems will phagocyte the organism once it is deposited. The monocytes will coalesce into the epiteloid cells with the lymphocytes to form a ring around those

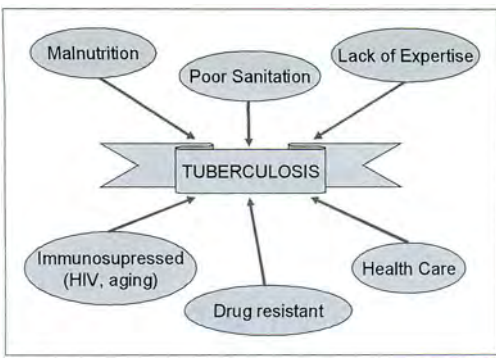


Fig. 1.

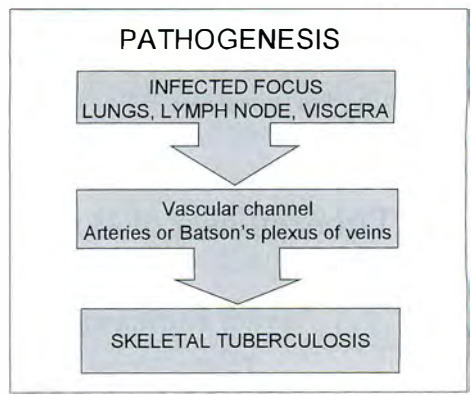


Fig. 2.

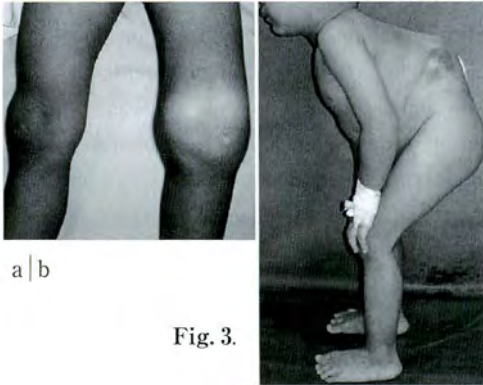


Fig. 3.

cells and to form a tubercle. The center of the tubercle progresses into caseation. The local inflammatory response answers the challenge by producing exudation, liquefaction, swelling, and abscess. It also induces the synthesis of chemical mediators which act as a potent bone resorption agent that eventually leads to bone destruction,

### Diagnosis

**Clinical Findings :** The infection occurs mostly during the 1st three decades of life with its typical insidious onset. It is usually monoarticular or single bone involvement, although a few cases may have multiple lesions. The constitutional symptoms are low-grade fever, anorexia, loss in weight, anemia, and night perspiration. Local symptoms include pain and tenderness, sinuses, enlargement in regional lymph nodes, swelling/effusion, restriction in joint motion, and the possibility of some neurological deficit in cases of spinal tuberculosis.

**Laboratory Findings :** The usual features of tuberculosis infection are anemia and lymphocytosis. As a chronic inflammation, tuberculous patient will have an increase in the C-reactive level and in the erythrocyte sedimentation rate ; however, we can not rely on this measurement only. Al-Marri<sup>2)</sup> reported 144 children with tuberculosis, of whom 33% presented a normal erythrocyte sedimentation rate. The increase in C-reactive protein level is believed to be associated with abscess formation.

Intracutaneous injection of tuberculin will produce a delayed antigen-antibody reaction which may be used to detect tuberculosis infection, judging from the size of the inflammatory response. Interpretation of such antigen-antibody reaction depends on the immune status of the patient, history of BCG vaccination, and any exposure to any tuberculosis organism.

Serologic measurement using ELISA to detect specific antibody within blood is reported to have 60-80% sensitivity<sup>13)</sup>. In a tuberculous-endemic population however, almost everybody is exposed to tuberculosis, so this examination may give a false-positive result and it can not determine which patients still have an active disease.

Identification using polymerase chain reaction (PCR) is still under intense development. The procedure includes denaturation, amplification and identification of *Mycobacterium tbc* DNA.

The test yields a result quickly with a high level of specificity. Development is continuing to reduce the cost and to enable the test to be more widely adopted in screening to identify which patient is in the active stage of the disease.

**Histopathology** : Tuberculosis infection will incite granulomatous inflammation which is quite specific so that it can be used to help establish diagnosis. The presence of tubercle formed by epithelioid cells and lymphocyte with central caseation provide the highest diagnostic value<sup>(6)(8)</sup>.

**Microscopic Examination** : Stains for acid-fast bacilli are rapid and inexpensive, so these tests may be used for screening ; however they may produce false-negative results in inexperienced hands. Acid-fast bacilli stain requires  $10^4$  bacilli per milliliter of specimen to produce an accurate result whereas a culture of *Mycobacterium tuberculosis* only requires  $10^3$  bacilli per milliliter of specimen to produce a colony of *Mycobacterium tuberculosis*<sup>(3)</sup>.

**Culture** : *Mycobacterium tuberculosis* grows only in enriched medium containing serum (albumin) base with the colonies firstly seen in the 2<sup>nd</sup> or 4<sup>th</sup> week. Culture is the gold standard of establishing diagnosis of tuberculous infection. However, due to the prolonged-time required to get the result and the frequent false-negative result, this test is often not performed on orthopaedic patients.

**Imaging** : Even in this sophisticated, modern era of medical technology the role of plain X-ray is still undebatable in establishing the diagnosis of osteoarticular tuberculosis. Even though there is no specific radiographic features that are pathognomonic for bone and joints tuberculosis, the combination of clinical, laboratory and radiographic findings is adequate to establish the diagnosis of tuberculosis in most cases. Only in special cases, further findings are required.

Common radiograph findings are regional

osteopenia, soft tissue swelling with minimum periosteal reaction, narrowing in the joint space, bone cysts adjacent to the joint, and subchondral erosion.

Magnetic resonance imaging is especially useful in spinal tuberculosis because it can reveal any subligamentous spread in inflammation, discriminate abscess from granulation tissue and delineate the soft tissue mass from bony destruction. MRI gives features of heterogenous signal intensity and a rim enhancement pattern.

### Treatment

The principles of the management for osteoarticular tuberculosis are

- 1 . eradicate or arrest the disease
- 2 . prevent or correct deformities
- 3 . prevent complications
- 4 . treat the pain
- 5 . rehabilitation

Musculoskeletal tuberculosis is a medical problem ; surgery is an adjunct to chemotherapy. This kind of infection requires a long-term multi-drug regimen of chemotherapy to which the organism is susceptible and at least one of the drugs must be bactericidal. Beware of drug side-effects due to long-term administration. In the first 4 months four drugs are administered, followed then by Rifampicin and INH until 9-12 months. The fourth drug may be ethambutol or streptomycin.

The numbers in parentheses are maximal daily dosages. The Isoniazide dosage must not exceed 10 mg/kg body-weight/day if it is combined with rifampicin.

**Classification** : The classification suggested by Tuli correlates the clinical and radiographic findings with both the recommended treatment and the expected outcome in patients with



**Fig. 4.**

Coxitis tuberculosa with regional osteopenia, soft tissue swelling



**Fig. 5.**

Gonitis tuberculosa with regional osteopenia, joint destruction



**Fig. 6.**

Tuberculous arthritis of the cuneiforme pedis

Isoniazide	5-15 (300 mg)
Rifampisin	10-20 (600 mg)
Pyrazinamide	15-40 (2 g)
Ethambutol	15-25 (2.5 g)
Streptomisin	15-40 (1 g)

**Table 1.**

Daily dosages in antituberculous chemotherapy<sup>5)</sup> (mg/kg body-weight/day).

articular disease. Chemotherapy is recommended for all patients with active disease. During the early stages of the disease, the goal is to obtain or maintain a normal or near normal range of motion. Rest is important, and the joint should be non-weightbearing. Range of motion exercises (active and active-assisted) are started when symptoms allow. Splinting helps to prevent deformity, and traction or serial casting may be used to restore or improve motion and/or alignment before splinting or bracing.

**Tuberculous spondylitis :** The spine is the most frequently involved site in the musculoskeletal system—involving in 50% of all skeletal tuberculosis<sup>3)9)~11)13)</sup>. The involvement of a vertebral body and neural arch will produce translational instability which allows displacement. Such displacement may compress the cord and eventually produce neurological problems. The clinical

features are truncal rigidity, muscle spasm and pain. Neurological deficit and vertebral deformity may appear. Cold abscess produced by the granulomatous inflammation could migrate in various directions following gravitation, the fascial plane on sheath.

Infection in the vertebra may begin on the paradiscal, central, anterior, posterior appendicular or posterior facet. The X-ray may feature a paravertebral shadow suggesting a cold abscess, loss of disc height, variable degrees of osseous destruction with collapse of bone leading to kyphotic deformity, often multiple bodies are involved.

Chemotherapy is an effective treatment for spinal tuberculosis (Medical Research Council). However, gross kyphosis, neurological deficit and delayed fusion are continuing problems. Multiple vertebral body involvement and a high risk to progressive kyphosis may require surgical intervention.

Subroto<sup>3)4)12)</sup> from the University of Indonesia has developed a total treatment approach to overcome the problems in tuberculous spondylitis. Treatment is based on the problems found in tuberculous spondylitis patients. The aim is to attain healed infection, a stable painless spine, without any unacceptable neurological deficit, and no deformity—which enable the patient to

**Table 2. Tuli Classification**  
The Natural History of Tuberculous Arthritis Progresses Through 5 Stages

	Clinical findings	Radiological findings	Treatment	Anticipated outcome
Stage I (synovitis)	1. Soft tissue swelling 2. 75% motion preserved	1. Soft tissue swelling 2. Osteopenia	1. Chemotherapy 2. Rest 3. ROM exercise 4. Splinting	Normal or minimal residua
Stage II (early arthritis)	1. Soft tissue swelling 2. 25-50% loss in motion	1. Soft tissue swelling 2. Marginal joint erosion 3. Narrowing joint space	1. Chemotherapy 2. Rest 3. ROM exercise 4. Splinting 5. Synovectomy	50-70% mobility
Stage III (advanced arthritis)	1. 75% loss in motion	1. Marginal erosion 2. Cyst 3. Significant loss in joint space 4. Joint destruction	1. Chemotherapy 2. Osteotomy 3. Arthrodesis 4. Arthroplasty	Stable, painless joint after salvage with or without motion
Stage IV (advanced arthritis)	1. 75% loss in motion 2. Subluxation or dislocation	Joint destruction	1. Chemotherapy 2. Osteotomy 3. Arthrodesis 4. Arthroplasty	Stable painless joint after salvage
Stage V (ankylosis)	Ankylosis	Ankylosis	1. Chemotherapy 2. Osteotomy 3. Arthrodesis 4. Arthroplasty	Stable, painless joint

return to daily social life. In 1989–2000 there were 253 spinal tuberculous patients with one or more of the following ; pain, infection, deformity, pathologic fracture, instability, and neurological deficit. Treatments include anti-tuberculous drugs, supportive treatment, bed rest, a body jacket, abscess drainage, prevention and correction of deformity.

**Tuberculous Coxitis :** Musculoskeletal tuberculosis can occur in either synovial form or osseous form (intra and extra articular). The symptoms, signs and radiologic features of the synovial forms mimic other intra-articular diseases such as transient synovitis, rheumatoid arthritis, osteoarthritis and osteonecrosis.

Prognosis depends on how soon anti-tuberculous drugs are instituted. In the first phase, early chemotherapy and traction are performed to ensure complete, uninterrupted rest to the affected hip and to avoid pelvic obliquity. Treatment in the second phase includes pain

relief, muscle spasm reduction, hip deformity reduction or completely corrected. In the third phase, the functional outcome is usually poor and does not respond well to conservative treatment. It usually requires bone and/or joint clearance surgery.

Surgical intervention includes synovectomy and debridement with excision of the hypertrophied synovium, removal of loose bodies, and excision of the hypertrophied capsule, while the articular cartilage should be retained as much as possible. The salvage procedure includes proximal femoral osteotomy and excision arthroplasty. Joint replacement is only performed after tuberculosis has healed for at least 2 years.

### Tuberculous Gonitis

The majority of patients present synovial involvement with or without bony erosion. Prognosis depends on the extent of the disease and on the adequacy of chemotherapy in the

early stage. Operative intervention aims to drain any abscess and to obtain synovial tissue for biopsy. Synovectomy is rarely indicated at the early stage. If the destruction is so severe, the first aim of treatment is to control the infection. The function of the joint will be addressed afterwards by performing total knee arthroplasty after chemotherapeutic sterilization.

### Conclusion

1) Osteoarticular tuberculosis is still a problem in developing countries and is predicted to become a problem for developed countries.

2) Establishing diagnosis of osteoarticular tuberculosis is a challenge. One should use any available diagnostic measurement with meticulous attention.

3) The diagnostic value of each tool differs region by region based on the epidemiological status of the tuberculous infection in the area.

4) The treatment and final outcome depend on the stage of infection at the time treatment commences.

5) Medical and surgical intervention should be used to get optimal results.

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