
Bone and joint tuberculosis: a continuing problem

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Although tuberculous disease of bones and joints is becoming uncommon, it still occurs and may cause devastating sequelae. It is frequently not diagnosed prior to the onset of permanent damage to the joints or spine; the most important reason for this delay may be the fact that it is not considered in the differential diagnosis of monoarthritis or back pain. Most persons with the disease have other evidence of tuberculosis. Not infrequently an aggressive approach (including synovial biopsy or surgical exploration of the back) is needed to confirm the diagnosis when there are no other clues.

Bien que la tuberculose des os et des articulations devienne rare, elle se voit encore et peut laisser des séquelles dévastatrices. Souvent elle n'est pas diagnostiquée avant que ne se soient installés des dommages permanents aux os ou à la colonne vertébrale; la plus importante raison de ce retard peut être le fait que la tuberculose n'est pas prise en considération dans le diagnostic différentiel de la monoarthrite ou du mal de dos. La plupart des personnes souffrant de cette maladie présentent d'autres signes de tuberculose. Il n'est pas rare qu'une démarche agressive (comprenant une biopsie synoviale ou une exploration chirurgicale du dos) soit nécessaire pour confirmer le diagnostic en l'absence d'autres indices.

Tuberculosis has been a scourge of mankind since earliest times. Archeologic evidence shows that deformity of joints and the spine due to this disease occurred in ancient Egypt.

In the past, tuberculous disease of bones and joints accounted for a very high proportion of admissions to facilities for the physically handicapped; this situation still prevails in areas of the world where tuberculosis is common. Fortunately in our society this disease is much less common than it was a century ago.

With this condition there have been two modes of infection: air-borne and by ingestion. The latter was more common for the bovine tubercle bacillus, *Mycobacterium bovis*, which used to cause about 20% of all cases of bone and joint tuberculosis, particularly in children.¹ This source of infection has been almost entirely eradicated from our society. However, *M. tuberculosis*, the bacillus pathogenic for humans, continues to cause disease of bones and joints. We recently encountered several patients in whom the complications of this disease had devastating effects. It seemed that the main reason for these sequelae was a delay between the time symptoms first appeared and the time the diagnosis was made. This prompted us to review the subject of bone and joint tuberculosis to identify factors that might aid in the diagnosis of this condition before complications ensue.

Methods

Through the kindness of Statistics Canada and with the permission of the provincial directors of tuberculosis control, we obtained for review the notification records of all cases of active tuberculosis notified in Canada from 1970 through 1974. From these we identified 555 cases of bone and joint tuberculosis.

Included in the records were place of residence and of birth, year of arrival in Canada if foreign-born, ethnic origin (specifically, whether the individual was a registered Indian or Inuit) and site and type of disease. However, much of the information was insufficient for detailed analysis, and the period under consideration was too short to clearly show trends in the incidence of the disease.

To obtain a clearer picture of the disease, particularly the method of diagnosis, symptoms, exact site of disease, treatment and outcome, we reviewed all notifications of active tuberculosis in British Columbia from 1967 through 1976. Of the 100 cases of active bone and joint tuberculosis identified, 1 was excluded from the study because the causative agent was *M. xenopi*; records of the other 99 cases were studied thoroughly.

Results

Incidence

From 1970 through 1974 in Canada 21 483 active cases of tubercu-

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Table I—Incidence (per 100 000 population) of various forms of tuberculosis, British Columbia, 1967 through 1976

| Year | Form of tuberculosis | | | | | |
|--------------|----------------------|-----------|---------------|------------------------|-----------|---------------|
| | Bone and joint | | | Pulmonary (adult-type) | | |
| | No. of cases | Incidence | Log incidence | No. of cases | Incidence | Log incidence |
| 1967 | 13 | 0.60 | -0.51 | 400 | 20.57 | 3.02 |
| 1968 | 12 | 0.59 | -0.53 | 390 | 19.43 | 2.97 |
| 1969 | 10 | 0.48 | -0.73 | 402 | 19.43 | 2.97 |
| 1970 | 13 | 0.60 | -0.51 | 361 | 16.87 | 2.82 |
| 1971 | 9 | 0.41 | -0.89 | 351 | 16.07 | 2.78 |
| 1972 | 13 | 0.58 | -0.54 | 409 | 18.35 | 2.91 |
| 1973 | 7 | 0.30 | -1.20 | 352 | 15.48 | 2.74 |
| 1974 | 11 | 0.47 | -0.76 | 336 | 14.50 | 2.67 |
| 1975 | 8 | 0.33 | -1.11 | 310 | 13.13 | 2.57 |
| 1976 | 3 | 0.12 | -2.12 | 261 | 10.85 | 2.38 |
| Total | 99 | | | 3572 | | |

losis were notified. The 555 cases of bone and joint tuberculosis, the fourth most common form of extrapulmonary tuberculosis, constituted 2.6% of the total. There were 1516 cases of genitourinary tuberculosis, 1083 cases of tuberculous lymphadenitis and 934 cases of tuberculous pleurisy.

The mean annual incidence of bone and joint tuberculosis in Canada during this period was 0.5 cases per 100 000 population. There was a steady downward trend in incidence during this period, as there was between 1967 and 1976 in British Columbia (Table I). This trend was not significantly different from that for adult-type pulmonary tuberculosis in British Columbia (Fig. 1).

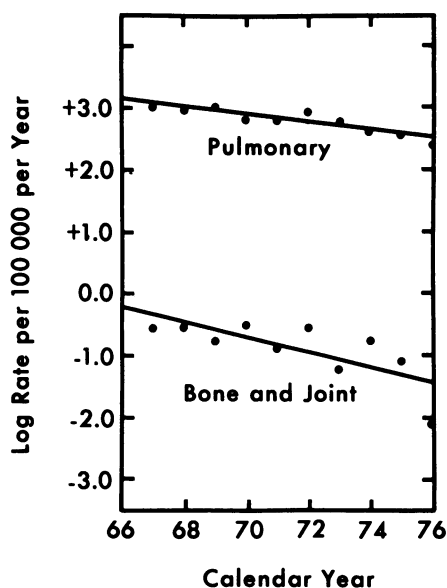


FIG. 1—Incidence of pulmonary and bone and joint tuberculosis, British Columbia, 1967 through 1976.

Further analysis of Canadian data

Most (457; 82.3%) of the cases of bone and joint tuberculosis in Canada were notified as instances of new active disease; the remainder (98; 17.7%) were reported as cases of reactivated disease. In contrast to most other forms of tuberculosis, disease of bones and joints was almost as common among females as among males in Canada: 256 of the 555 cases from 1970 to 1974 were in females and 299 in males. The mean

Table II—Mean annual incidence (per 100 000 population) of bone and joint tuberculosis according to age and sex, Canada, 1970 through 1974

| Age (yr) | Sex | |
|----------|------|--------|
| | Male | Female |
| 0-14 | 0.14 | 0.12 |
| 15-24 | 0.18 | 0.20 |
| 25-34 | 0.25 | 0.43 |
| 35-44 | 0.63 | 0.43 |
| 45-54 | 1.00 | 0.75 |
| 55-64 | 1.30 | 1.02 |
| 65 + | 1.60 | 1.40 |

age of the patients was 48 years (range less than 1 year to 92 years, with a symmetric distribution). The variation of incidence with age was striking (Table II).

Table III shows that, whereas the incidence of bone and joint tuberculosis varied 15-fold (from 0.4 to 5.8 per 100 000) among various population groups in Canada, the proportion of cases of this disease among all forms of active tuberculosis varied less (1.8% to 3.6%). The higher incidence of bone and joint tuberculosis in certain groups reflected the higher incidence of all forms of tuberculosis in these people (particularly the Asian-born) rather than a racial predisposition to this form of disease. Indians and Inuit had the lowest proportion of bone and joint disease.

Further analysis of British Columbia data

In British Columbia, among the 99 cases of bone and joint tuberculosis the proportion notified as instances of reactivated disease (34.3%) was higher than that for all of Canada. In seven cases in which tuberculosis had not previously been diagnosed, apical scarring was noted on chest roentgenograms and recorded as evidence of "presumed pulmonary tuberculosis, inactive" or as a "fibrotic lesion". In only 38 cases was there no evidence of tuberculosis (previous or concurrent) at other sites (Table IV).

As Table V shows, the mean interval from the diagnosis of pulmonary tuberculosis to the diagnosis of bone and joint tuberculosis for cases in which this was known was

Table III—Rates of bone and joint tuberculosis in various groups, Canada, 1970 through 1974

| Birthplace | Form of tuberculosis | | | |
|-------------------|-------------------------|----------------|------------|--|
| | All forms, no. of cases | Bone and joint | | |
| | | No. of cases | % of total | Mean annual incidence per 100 000 population |
| Canada | | | | |
| Indians and Inuit | 2 433 | 43 | 1.8 | 3.1 |
| Others | 14 233 | 368 | 2.6 | 0.4 |
| Europe | 2 996 | 80 | 2.7 | 0.6 |
| Asia | 1 334 | 48 | 3.6 | 5.8 |
| Other | 487 | 16 | 3.3 | 0.6 |
| Total | 21 483 | 555 | 2.6 | 0.5 |

17 years (range 1 to 42 years), the mean interval from the diagnosis of pleurisy to the diagnosis of bone and joint disease was 10 years (range 2 to 20 years) and the mean interval from the first diagnosis to the diagnosis of reactivation of bone and joint disease at the same site was 35 years (range 14 to 76 years).

Reactivation of bone and joint tuberculosis at the same site was most frequent in those with hip disease, who accounted for 7 of the 14 such cases of reactivation, and reactivation was very common at the hip, occurring in 7 of 16 cases of hip tuberculosis.

The site of bone and joint disease is shown in Table VI. Of the 99 cases 59 were of arthritis, 37 of spondylitis and 9 of osteomyelitis; in 6 cases there was disease at two sites. In tuberculous arthritis the larger joints of the legs were most frequently involved: there were 16 cases of tuberculosis of the hip and 12 of the knee, whereas the wrist was affected in 8 cases, the elbow in

7 and the shoulder in 5. Of the 37 persons with spondylitis 17 had disease in one disc space, 10 in two spaces, 5 in three spaces, 2 in four spaces and 1 in five spaces. Most persons (32) had disease in contiguous disc spaces, but a few (5) had disease in two areas of the spine separated by normal disc spaces. The second, third and fourth lumbar discs were the most commonly affected (in eight cases each). The pelvis was the most common site of osteomyelitis; there were four such cases.

The presenting symptoms and signs of bone and joint tuberculosis varied (Table VII). Persons with arthritis usually complained of pain (in 40 cases), which was often accompanied by swelling (in 27 cases) and a draining sinus (in 10 cases). Pain was also the most frequent presenting complaint of patients with spondylitis (it was the only complaint in 20), and was often associated with radiation along the distribution of a nerve root. Five individuals complained of weakness of the legs in

association with pain at the time of presentation. A small group presented with other forms of tuberculosis (three with lymphadenitis and one with genitourinary disease) and were found to have involvement of bone and joints as well. In five of the nine women of child-bearing age who had spondylitis the first symptoms developed during pregnancy.

In 30 of the 99 cases there was a history of trauma to the affected area prior to the onset of symptoms, and seven individuals had been treated with intra-articular injections of corticosteroids prior to the diagnosis of tuberculosis.

Symptoms were present, on the average, for 16 months prior to diagnosis; there was little variation in this

Table IV—Activity of disease at time of notification of cases of bone and joint tuberculosis, British Columbia, 1967 through 1976

| Status of disease | Form of tuberculosis; no. of cases of active disease | | |
|------------------------------|--|-------------------|------------------------------|
| | Bone and joint | Pulmonary as well | Other extrapulmonary as well |
| New active | 58 | 15 | 5 |
| Reactivated from | | | |
| Pulmonary disease | 10 | 1 | 1 |
| Pleurisy | 10 | 5 | 0 |
| Disease at same site | 10 | 2 | 0 |
| Adenitis | 2 | 1 | 0 |
| Other bone and joint disease | 2 | 0 | 0 |
| Subtotal | 34 | 9 | 1 |
| Apical pulmonary fibrosis* | 7 | 0 | 0 |
| Total | 99 | 24 | 6 |

*Termed "presumed pulmonary tuberculosis, inactive" or "fibrotic lesion".

Table VI—Sites of tuberculous involvement of bones and joints in 99 cases,* British Columbia, 1967 through 1976

| Site | No. of cases | Site | No. of cases† |
|------------------|--------------|--------------|---------------|
| Joint | 59 | Spine | 37 |
| Wrist | 8 | C4-5 | 1 |
| Elbow | 7 | C5-6 | 3 |
| Shoulder | 5 | C6-7 | 1 |
| Costosternal | 1 | T5-6 | 1 |
| Sternoclavicular | 1 | T6-7 | 2 |
| Sacroiliac | 4 | T7-8 | 2 |
| Hip | 16 | T8-9 | 4 |
| Knee | 12 | T9-10 | 3 |
| Ankle | 2 | T10-11 | 5 |
| Foot | 3 | T11-12 | 4 |
| Bone | 9 | | |
| (osteomyelitis) | | T12-L1 | 3 |
| Finger | 1 | L1-2 | 6 |
| Sternum | 1 | L2-3 | 8 |
| Rib | 1 | L3-4 | 8 |
| Pelvis | 4 | L4-5 | 5 |
| Fibula | 1 | L5-S1 | 6 |
| Calcaneus | 1 | Unknown | 2 |

*In six cases there was tuberculous disease at two sites.

†The numbers in the left-hand column indicate the frequency of involvement of an individual site; the solitary number to the right is the total no. of cases.

Table V—Interval from previous diagnosis to current diagnosis in cases of bone and joint tuberculosis, British Columbia, 1967 through 1976

| Previous diagnosis | Mean (yr) | Actual values (yr) | | | | | | | | | |
|--|-----------|--------------------|----|----|----|----|----|----|----|----|----|
| | | | | | | | | | | | |
| Pulmonary disease | | | | | | | | | | | |
| Age at time of previous diagnosis | 23.1 | 40 | 32 | 35 | 10 | 7 | 15 | 7 | 29 | 41 | 15 |
| Age at time of current diagnosis | 46.3 | 48 | 51 | 52 | 30 | 29 | 37 | 32 | 55 | 72 | 57 |
| Interval | 23.2 | 8 | 19 | 17 | 20 | 22 | 22 | 25 | 26 | 31 | 42 |
| Pleurisy | | | | | | | | | | | |
| Age at time of previous diagnosis | 30.3 | 66 | 48 | 47 | 33 | 19 | 29 | 21 | 14 | 17 | 9 |
| Age at time of current diagnosis | 52.4 | 68 | 53 | 58 | 52 | 39 | 59 | 51 | 47 | 50 | 47 |
| Interval | 22.1 | 2 | 5 | 11 | 19 | 20 | 30 | 30 | 33 | 33 | 38 |
| Bone and joint disease at same site | | | | | | | | | | | |
| Age at time of previous diagnosis | 12.8 | 15 | 28 | 11 | 17 | 13 | 22 | 2 | 6 | 5 | 9 |
| Age at time of current diagnosis | 54.6 | 34 | 51 | 37 | 56 | 54 | 64 | 46 | 56 | 63 | 85 |
| Interval | 41.8 | 19 | 23 | 26 | 39 | 41 | 42 | 44 | 50 | 58 | 76 |

Table VII—Presenting problems in the 99 cases of bone and joint tuberculosis

| Problem | Type of tuberculous disease; no. of cases | | |
|--------------------------------------|---|-------------|---------------|
| | Arthritis | Spondylitis | Osteomyelitis |
| Pain alone | 11 | 20 | 2 |
| Pain and swelling | 17 | 3 | 2 |
| Pain, swelling and draining sinus | 10 | 1 | 0 |
| Swelling only | 3 | 0 | 2 |
| Swelling and draining sinus | 1 | 0 | 0 |
| Draining sinus only | 3 | 0 | 1 |
| Pain and draining sinus | 2 | 1 | 0 |
| Pain and paralysis | 0 | 5 | 0 |
| None (disease diagnosed post mortem) | 0 | 1 | 0 |
| Tuberculous arthritis | — | 5 | 0 |
| Tuberculous lymphadenitis | 2 | 1 | 0 |
| Genitourinary tuberculosis | 1 | 0 | 0 |
| Unknown | 9 | 0 | 2 |
| Total | 59 | 37 | 9 |

Table VIII—Duration of symptoms prior to diagnosis of bone and joint tuberculosis in the 99 cases

| Duration (mo) | Type of tuberculous disease; no. of cases | | | | |
|---------------|---|-------------|-------------|-------------|---------------|
| | Arthritis | | Spondylitis | | Osteomyelitis |
| | New active | Reactivated | New active | Reactivated | |
| 0-6 | 7 | 1 | 5 | 6 | 3 |
| 7-12 | 10 | 5 | 8 | 4 | 4 |
| 13-18 | 1 | 0 | 0 | 0 | 1 |
| 19-24 | 6 | 2 | 0 | 2 | 0 |
| 25-36 | 2 | 2 | 1 | 1 | 0 |
| 37-72 | 0 | 0 | 1 | 1 | 0 |
| 73-84 | 0 | 0 | 1 | 0 | 0 |
| Unknown | 16 | 7 | 5 | 2 | 1 |
| Total | 42 | 17 | 21 | 16 | 9 |
| Mean | 14.4 | 18.2 | 18.9 | 15.8 | 8.6 |



FIG. 2—Advanced tuberculosis of wrist, with destruction of joint and osteoporosis of surrounding bone.

period between the diagnostic groups (Table VIII).

M. tuberculosis was isolated from the skeletal lesions in 59 of the 99 cases. In 11 cases the diagnosis was made after the organism was discovered at another site. The diagnosis in 17 cases was made on the basis of histologic findings only, and in another 8 cases was made because of reactivation of previously diagnosed disease. In two cases characteristic changes in spine roentgenograms were accompanied by resolution of symptoms with chemotherapy. In the remaining two cases the records were insufficient for the means of diagnosis to be determined.

Skin tests with 5 tuberculin units of purified protein derivative of tuberculin were negative in 3 of 66 cases. Bacteriologic examination of material from the skeletal lesions in 65 of these cases failed to demonstrate *M. tuberculosis* in 6.

Roentgenograms of the affected area were available for review in 75 cases. The abnormalities in the 42 cases of tuberculous arthritis included destruction of periarticular bone (in 29 cases), narrowing of the joint space (in 23 cases) and osteoporosis (in 23 cases), as in Fig. 2. In the 31 cases of spondylitis, narrowing of the disc spaces (in 29 cases), vertebral destruction adjacent to the space (in 27 cases) and evidence of paravertebral abscess (in 8 cases) was noted, as in Figs. 3 and 4.

Myelograms done in six cases showed extradural defects due to abscess formation. At subsequent operation the abscesses were drained.

Chest roentgenograms made at the time of presentation were abnormal in 47 cases, showing changes consistent with pulmonary tuberculosis in 45 and pleural changes alone in 2.

Chemotherapy was used in 97 cases. In one other case the diagnosis was made only after death, and one patient refused treatment. Records were inadequate for assessment in nine cases. In the remaining 88 cases triple drug therapy was given initially for 2 months in 79; the daily dose of isoniazid was 300 mg. Therapy

was continued with two drugs (including isoniazid) for at least 18 months in 69 cases. It was terminated by death in two cases and by emigration in one.

Arthrodesis was performed in 15 of the 59 cases of tuberculous arthritis, and spinal fusion in 16 of the 37 cases of tuberculous spondylitis.

Eight of the persons with spondylitis suffered traumatic myelopathy, in five instances before the diagnosis was made. Four of the eight had paraparesis, three paraplegia and one quadriplegia. Six patients died — four of unrelated problems, one prior to diagnosis of tuberculosis and one after pleurectomy.

Case reports

The following case reports illustrate some of our observations.

Case 1

A 68-year-old Chinese woman was admitted to hospital with pleuritic chest pain. A chest roentgenogram showed a small right-sided pleural effusion, and a diagnosis of carcinoma of the lung was considered. The effusion spontaneously resolved and she was discharged a week after admission.

She was readmitted to hospital 11 days later with back pain and weight loss. A chest roentgenogram was normal but a roentgenogram of the spine revealed a destructive lesion at the 11th dorsal interspace, with surrounding soft tissue swelling. This was thought to represent carcinomatous metastases. A month later, when signs of myelopathy developed, needle aspiration of the lesion yielded pus that was positive on smear and culture for *M. tuberculosis*. Therapy

with streptomycin, isoniazid and ethambutol in standard dosage was begun immediately. After spinal fusion 4 months later, the myelopathy gradually resolved, and chemotherapy was completed after 2 years.

Comment: The failure to consider tuberculosis as the cause of the pleural effusion and spondylitis with paravertebral abscess in this elderly Asian woman permitted traumatic myelopathy to develop.

Case 2

A 41-year-old Caucasian woman presented to her doctor with complaints of pain and stiffness of the right shoulder of 1 year's duration. Although a roentgenogram of the joint revealed narrowing of the joint space with some destruction of both humerus and scapula, she was treated with an intra-articular injection of cortisone. When she returned 2

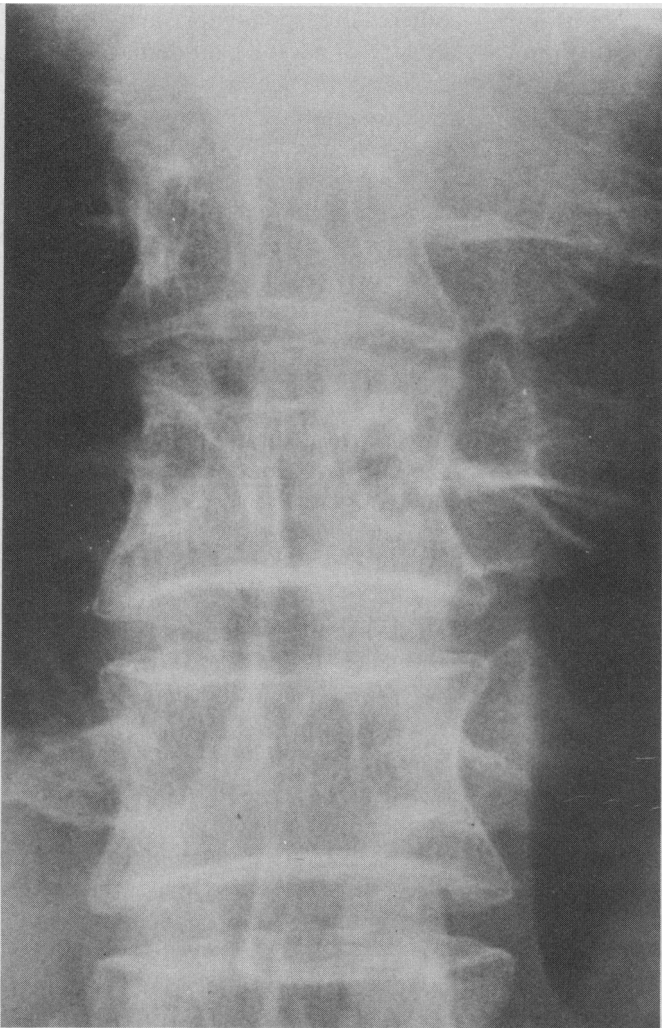


FIG. 3—Disc space narrowing at ninth dorsal interspace due to tuberculous spondylitis.

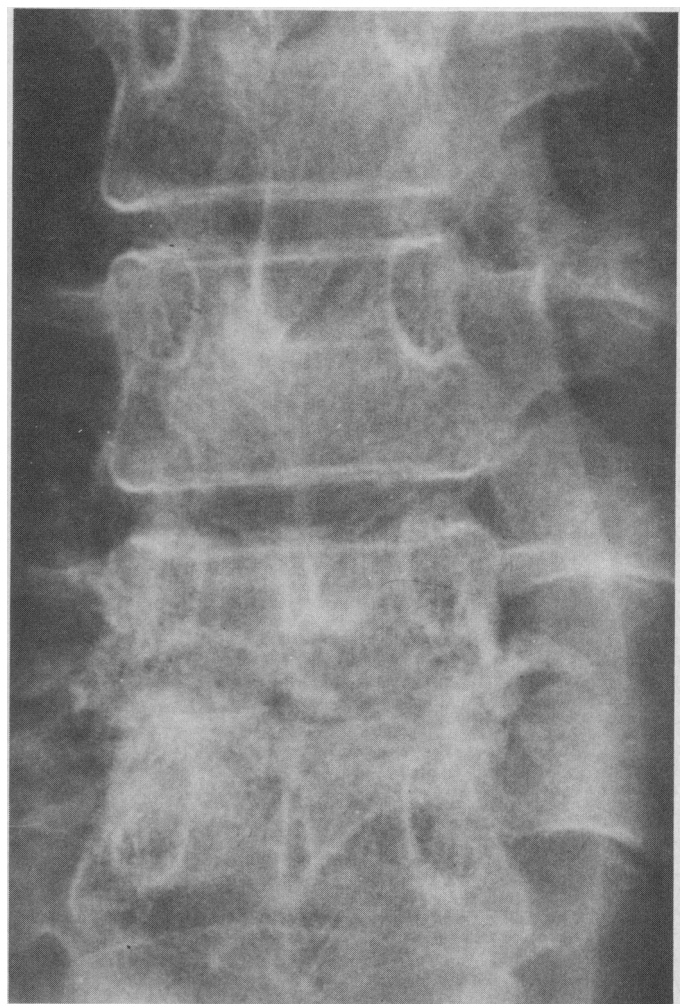


FIG. 4—Extensive destruction of first lumbar interspace and adjacent bone due to tuberculous spondylitis, and paravertebral abscess.

Motrin

(ibuprofen)

Action: Ibuprofen has demonstrated anti-inflammatory, analgesic, and antipyretic activity in special animal studies designed to specifically demonstrate these effects. Ibuprofen has no demonstrable glucocorticoid effect.

Ibuprofen has been found to be less likely to cause gastrointestinal bleeding in doses usually used than is acetylsalicylic acid.

Clinical trials in man have shown the clinical activity of a dose of 1200-1800 mg of ibuprofen daily to be similar to that of 3600 mg of acetylsalicylic acid daily.

Indications and Clinical Uses: Ibuprofen is indicated for the treatment of osteoarthritis and rheumatoid arthritis.

Contraindications: Ibuprofen should not be used during pregnancy or in paediatric patients because its safety under these conditions has not been established. Ibuprofen should not be used in patients with a history of acetylsalicylic acid-induced bronchospasm.

Precautions: Ibuprofen should be used with caution in patients with a history of gastrointestinal ulceration.

Ibuprofen has been reported to be associated with toxic amblyopia. Therefore, precautions should be taken to ensure that patients on ibuprofen therapy report to their physicians for full ophthalmological examination if they experience any visual difficulty. Medication should be discontinued if there is any evidence of toxic amblyopia.

Adverse Reactions: The following adverse reactions have been noted in patients treated with ibuprofen:

Gastrointestinal: Nausea, vomiting, diarrhoea, constipation, dyspepsia, epigastric pain and guaiac positive stools have been noted. A few cases of gastric or duodenal ulceration, including some complicated by bleeding or perforation have occurred.

Central Nervous System: Dizziness, light-headedness, headache, anxiety, mental confusion and depression were noted in some patients treated with ibuprofen.

Ophthalmological: Blurred vision was noted in some patients and rarely a sensation of moving lights was observed following administration of ibuprofen. In addition there are three published cases of toxic amblyopia associated with the use of ibuprofen. Although a definite cause and effect relationship was not established, the attending physicians considered them to be drug-related. The condition was characterised by reduced visual acuity and difficulty in colour discrimination. Defects (usually centrocaecal) were observed on visual field examination. Symptoms were reversible on discontinuation of treatment.

Skin: Maculopapular rashes and generalised pruritus have been reported with ibuprofen therapy. Occasional cases of oedema have also been reported.

Laboratory Tests: Sporadic abnormalities of liver function tests have occurred in patients on ibuprofen therapy (SGOT, serum bilirubin and alkaline phosphatase) but no definite trend was seen indicating toxicity. Similar abnormalities of white blood count and blood urea determinations were noted. A slight fall in haemoglobin and haematocrit has been noted in some patients.

Symptoms and Treatment of Overdosage: One case of overdosage has been reported. A one-year-old child ingested 1200 mg ibuprofen and suffered no ill effects other than being drowsy the next day. Blood levels of ibuprofen reached 711 mcg/ml, which is considerably above the 90 mcg/ml previously recorded as the highest level seen in adults after a single oral dose of 800 mg. The SGPT level, nine days post-ingestion, was 72. No specific antidote is known. Standard measures to stop further absorption and maintain urine output should be implemented at once. The drug is excreted rapidly and excretion is almost complete in six hours.

Dosage and Administration: To obtain rapid response at the start of treatment, particularly when transferring from other anti-inflammatory therapy, Motrin should be given at a dose of 1200 mg per day in four divided doses. Depending on the therapeutic response, the dose may be adjusted downward or upward keeping the four-times-a-day dosage schedule. The daily dose should not exceed 2400 mg. Maintenance therapy, once maximum response is obtained, will range from 800 to 1200 mg per day. Due to lack of clinical experience, ibuprofen is not indicated for use in children under 12 years of age.

Supplied: 200 mg yellow coated tablets, 300 mg white coated tablets, and 400 mg orange coated tablets in bottles of 100 and 1000.

Product monograph available on request.

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weeks later with swelling and redness around the joint she was referred to an orthopedist. The possibility of an infection causing this lesion was raised, and aspiration of the joint was performed. The smear was negative for acid-fast bacilli and a culture was not done. However, when she returned 2 weeks later with a draining sinus, cultures of the drainage were done; when the culture results were reported 8 weeks later treatment was begun with streptomycin, 1 g/d, isoniazid, 100 mg three times a day and para-aminosalicylic acid, 4 g three times a day. This treatment was continued for 2 years, but function of the joint was severely impaired.

Comment: Monoarthritis, particularly with evidence of periarticular destruction, must raise the possibility of an infectious cause. Urgent investigation, including synovial biopsy if necessary, is needed to prevent further destruction. The use of intra-articular injection of corticosteroids prior to diagnosis is to be deplored.

Discussion

The incidence of bone and joint tuberculosis is low and is declining. Accompanying this decline is a decrease in awareness of tuberculosis as a diagnostic possibility.^{2,3} The recent trend away from specialized institutions for tuberculosis treatment (and consequent decline in reliability of statistical reporting) makes a review of the subject appropriate now.

In Canada bone and joint tuberculosis accounts for less than 3% of all cases of active tuberculosis, a higher proportion than has been reported in some areas.^{4,5} This may reflect more complete notification of cases in our country.

Tuberculosis of bones and joints, as with most forms of tuberculosis, affects predominantly the elderly. Hald⁶ in Norway has demonstrated that this is a recent development, related to the fact that the decline in tuberculosis morbidity has been most striking in young people. Tuberculosis of bones and joints seems to affect both sexes equally,³ in contrast to pulmonary tuberculosis, which largely affects males. There is a

marked variation in incidence of bone and joint tuberculosis among various ethnic groups in Canada, as has also been noted in Britain⁷ and the United States.⁵ However, this variation is mainly due to differences in total incidence of tuberculosis in these groups rather than a demonstrable predisposition of certain groups for this form of the disease.

The proportion of cases of bone and joint tuberculosis in our series that resulted from reactivation of previous disease was high, particularly for hip disease. This indicates a need for additional attention in the follow-up of such cases to ensure that the disease is arrested by treatment and that its recurrence is recognized early.

Our study underscores our initial impression of the contribution of the delay in diagnosis to the harmful sequelae of the disease. The strong association of spinal cord injury with tuberculous spondylitis, and the frequency of severe joint damage are of concern, particularly since this disease, in contrast to many of the bone diseases frequently encountered, is completely curable.

What is the cause of this delay in diagnosis? We have shown that roughly two thirds of patients with bone and joint tuberculosis have other evidence of tuberculosis, and nearly one half have chest roentgenograms with changes suggestive of the disease. In addition, the interval from the onset of symptoms to the time of diagnosis does not differ between cases of new active and reactivated disease. Walker⁸ has observed that the delay is frequently avoidable, and Hunt² has suggested that the declining incidence of bone and joint tuberculosis is one of the causes for the delay in diagnosis. It is possible that, in spite of clues to the diagnosis, tuberculosis is often not considered in the differential diagnosis.

Tuberculous disease of the joints, as with other infectious arthritides, is characteristically a monoarthritis.⁸ In contrast to the more common acute pyogenic infections, however, it may present with chronic joint pain and only minimal signs of inflammation; as such, it may be mis-

taken for other more common forms of inflammatory joint disease. The frequency in our series with which intra-articular injections of steroids had been given (7% of cases) is disturbing. Aspiration of joint fluid for direct examination of a smear and bacteriologic culture prior to the institution of palliative therapy is important. But even this is frequently insufficient to make the diagnosis and, in the presence of monoarthritis, synovial biopsy should be seriously considered to ensure that what is thought to be noninfectious inflammatory arthritis is not, indeed, chronic granulomatous infection. Certainly the diagnosis of tuberculous arthritis should be made before a draining sinus demands its consideration.

Tuberculous spondylitis must frequently be differentiated from other causes of disc disease. Early changes associated with this disease fail to identify the cause, and frequently the patients are thought to have degenerative disc disease. In these cases other evidence of tuberculosis should lead the practitioner to consider tuberculosis as the cause of the back symptoms. Certainly by the time there is evidence of bone destruction in the area adjacent to the disc space an infectious cause should be considered. However, tuberculous spondylitis cannot be differentiated from other infectious spondylitides solely on the basis of roentgenographic features; surgical exploration is necessary to obtain material for bacteriologic examination. Tuberculosis, nevertheless, remains one of the most frequent infectious causes of spondylitis.⁹ The difference between tuberculosis, which is primarily a condition involving the disc space, and malignant disease, which involves the vertebrae, is usually readily apparent.

Conclusion

The information we have presented emphasizes the need for continued awareness of the possibility of tuberculosis as the cause of bone and joint disorders. Diligent search for other clues to the diagnosis, however minimal, is an important component of investigation of such cases.

In the absence of these clues, early bacteriologic and histologic examinations in possible cases will do much to avoid the regrettable sequelae that are often seen.

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FATHERING. Participation in Labor and Birth. Celeste R. Phillips and Joseph T. Anzalone. 151 pp. Illust. The C.V. Mosby Company, Saint Louis, Missouri, 1978. \$8.75, paperback. ISBN 0-8016-3919-0

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SEPTRA^{*} SUSPENSION b.i.d.

■ broad-spectrum activity provides bactericidal coverage against most common causative organisms in both urinary and respiratory tract infections

- discourages development of resistance
- achieves rapid, high urine and blood levels
- well tolerated by most patients
- licorice flavor well accepted by children

■ Septra^{*} (Trimethoprim + Sulfamethoxazole) Rx. Summary
INDICATIONS: Indicated for the following infections when caused by susceptible organisms:

UPPER AND LOWER RESPIRATORY TRACT INFECTIONS—particularly chronic bronchitis and acute and chronic otitis media.

URINARY TRACT INFECTIONS—acute, recurrent and chronic.

GENITAL TRACT INFECTIONS—uncomplicated gonococcal urethritis.

GASTROINTESTINAL TRACT INFECTIONS.

SKIN AND SOFT TISSUE INFECTIONS.

SEPTRA is also indicated in the treatment of infants and children with a diagnosis of *Pneumocystis carinii* pneumonitis, especially if they are immunosuppressed.

SEPTRA is not indicated in infections caused by *Pseudomonas*, *Mycoplasma* or viruses. This drug has not yet been fully evaluated in streptococcal infections.

CONTRAINDICATIONS: Patients with evidence of marked liver parenchymal damage, blood dyscrasias, known hypersensitivity to trimethoprim or sulfonamides, marked renal impairment where repeated serum assays cannot be carried out, premature or newborn babies during the first few weeks of life. For the time being SEPTRA is contraindicated during pregnancy.

ADVERSE REACTIONS: Most frequent: nausea; vomiting; gastric intolerance; and rash. Less frequent: diarrhea; constipation; flatulence; anorexia; pyrosis; gastritis; gastroenteritis; urticaria; headache; and liver changes (abnormal elevations in alkaline phosphatase and serum transaminase).

Occasionally reported: glossitis; oliguria; hematuria; tremor; vertigo; alopecia; and elevated BUN, NPN, and serum creatinine. Hematological changes occurring particularly in the elderly, are mostly transient and reversible (primarily, neutropenia and thrombocytopenia; less frequently, leukopenia, aplastic or hemolytic anemia, agranulocytosis, and bone marrow depression).

PRECAUTIONS: As with other sulfonamide preparations, critical appraisal of benefit versus risk should be made in patients with liver damage, renal damage, urinary obstruction, blood dyscrasias, allergies or bronchial asthma.

The possibility of a superinfection with a non-sensitive organism should be borne in mind.

DOSE AND ADMINISTRATION: Adults and children over 12 years. Standard dosage: 2 Septra tablets or 1 Septra DS tablet twice daily. Minimum dosage and dosage for long-term treatment: 1 Septra tablet or ½ Septra DS tablet twice daily.

Maximum dosage: Overwhelming infections: 3 Septra tablets or 1½ Septra DS tablets twice daily.

Uncomplicated gonorrhoea: 2 Septra tablets or 1 Septra DS tablet four times daily for 2 days.

Pneumocystis carinii pneumonitis: 20 mg/kg/day trimethoprim and 100 mg/kg/day sulfamethoxazole in four divided doses for 14 days.

Children 12 years and under: †

Young children should receive a dose according to biological age:

Children under 2 years: 2.5 ml of suspension twice daily.

Children 2 to 5 years: 2.5–5 ml of suspension twice daily.

Children 6 to 12 years: 5–10 ml of suspension twice daily.

† In children this corresponds to an approximate dose of 6 mg trimethoprim/kg body weight/day, plus 30 mg sulfamethoxazole/kg body weight/day, divided into two equal doses.

DOSE FORMS:

SEPTRA DS TABLETS, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, and coded WELLCOME 02C. Bottles of 50 and 250.

SEPTRA TABLETS, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole, and coded WELLCOME Y2B. Bottles of 100 and 500, and unit dose packs of 100.

SEPTRA PEDIATRIC TABLETS, each containing 20 mg trimethoprim and 100 mg sulfamethoxazole, and coded WELLCOME H4B. Bottles of 100.

SEPTRA PEDIATRIC SUSPENSION, each teaspoonful (5 ml) containing 40 mg trimethoprim and 200 mg sulfamethoxazole. Bottles of 100 and 400 ml.

Product monograph available on request. *Trade Mark w-7021



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