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NON-PULMONARY TUBERCULOSIS

Of all the manifestations of tuberculosis, pulmonary tuberculosis gets the maximum attention. So much so that often what pertains to pulmonary tuberculosis only is mentioned as if it applies in general to tuberculosis as a whole which is not always and entirely correct. There is, however, justification for the importance given to pulmonary disease since it is the most frequent of all manifestations and is practically the only manifestation which is infectious. Even though non-pulmonary tuberculosis is non-infectious, it does lead to considerable suffering and some disability and certainly merits more attention than that given to it hitherto.

There is much about non-pulmonary tuberculosis which is not fully known at present. We do not know with any degree of accuracy about its prevalence and incidence. This holds good not only for developing countries but also for western countries with good health intelligence and authentic vital statistics. This is partly because of the lack of dependable diagnostic criteria. Very often the diagnosis is presumptive. Bacteriological confirmation of the diagnosis is exceptional. Radiology helps in the diagnosis to a large extent only in the disease of the bones and joints. Disease involving the abdomen and lymphnodes (in the absence of caseation and liquefaction) cannot be diagnosed definitely without biopsy which is often refused by the patients.

Secondly, the available information on non-pulmonary manifestations is based usually on the morbidity notifications or records of hospitals/clinics. The extent of silent and subclinical forms is anybody's guess. It is well known that in pulmonary tuberculosis, known cases are always less than the total cases present in any community or country at any point of time and these latter can only be discovered by means of a total survey. Does the same hold good for non-pulmonary tuberculosis also and if so, to what extent? Surveys on the pattern of those carried out for pulmonary tuberculosis have not been carried out so far in any part of the world for non-pulmonary tuberculosis, nor are they feasible.

There is yet another problem. Unlike pulmonary cases, non-pulmonary cases are dealt with not only in tuberculosis centres but also in many other units e.g. pediatrics, orthopaedics, nephrology, general medicine and surgery departments etc. Some of these cases may escape notification and thus the reported figures may be an under-estimate.

Whatever figures are available are very interesting. In India, the non-pulmonary tuberculous cases are about 5 to 8% of the total freshly diagnosed

tuberculous cases according to D.G.H.S. report on diagnostic activities of the district tuberculosis centres. If some allowance is made for cases diagnosed in other institutions, as mentioned earlier, the percentage may be said to be about 10. In many western countries where tuberculosis has been more or less brought under control, such as USA, UK, Sweden, Canada, Australia etc. non-pulmonary cases constitute about 20% of the total tuberculous cases. Further, the percentage in USA has risen from 8 in 1965 to 17 in 1980 and in Japan from 5 to 12 during the period 1962 to 1972. In other words, the decline in the number of cases of non-pulmonary tuberculosis is much less than the decline in the number of pulmonary cases. In Australia, the percentage amongst white nationals is about 22, but only about 3 among migrants of Asian origin. In the American Continent the extent varies from 3% to 17% according to the standard of living and therefore of tuberculosis control) of various countries.

Another interesting feature is that whereas the number of pulmonary cases amongst men is almost twice the number of cases in women, the non-pulmonary tuberculous cases amongst men and women tend to be almost equal. The relative frequency of various manifestations also seems to vary a good deal from place to place. In the western countries, genito-urinary tuberculosis is fairly frequent but it is not so in developing countries like India where most of the cases pertain to lymphnodes, followed by bones and joints.

All this shows that the state of knowledge about non-pulmonary tuberculosis is extremely deficient at present. A number of articles on non-pulmonary tuberculosis have been included in this issue of the Journal. It is hoped that this will help to focus greater attention on these manifestations and also provide the much-needed impetus for further research in this respect. The most urgent requirement is to find an authentic and practicable diagnostic test which probably would be immunological rather than bacteriological or histopathological. Once this is possible it will be easy to determine the prevalence and incidence of these manifestations.

It is commonly said that the treatment of non-pulmonary manifestations is, by and large, the same as for pulmonary disease; yet there probably are some subtle differences which may necessitate modification of regimens used in the treatment of pulmonary disease. A number of studies have been carried out in different parts of the world deploying short course regimens for tuberculosis of the spine and lymphnodes. These studies tend to show that not only short course regimens are as effective as in pulmonary tuberculosis, these also reduce the necessity for surgical intervention. Many more studies, however, are needed about these and other non-pulmonary manifestations.

REVIEW ARTICLE

TUBERCULOSIS OF SPINE

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Skeletal tuberculosis continues to be prevalent in countries where pulmonary tuberculosis is still rampant. The localisation in the spine is the commonest manifestation of skeletal tuberculosis. Thanks to the advent of chemotherapeutic agents specific against tubercle bacillus, recent times have witnessed exciting changes in the philosophy of management of tuberculosis of spine. Hence a review of history, diagnosis and current status is apposite.

Historical Review

In all branches of intellectual pursuit, a short recall of the past pays rich dividends, not only in understanding and acting in the present but also to plan effectively for the future. "If nothing else, it is pure fun".

The history of tuberculosis is long and fascinating. Tuberculosis is probably as old as mankind. The Hebrews proscribed eating of flesh of tuberculous animals and Moses forbade hunchbacks from entering the Inner Sanctuary (Eric Smith 1960).

For any disease, literature, artistic representation and human remains are usual sources of information. The latter two show evidence of tuberculosis throughout Egyptian history. (Morse et al 1964) as also artistic representations in Pre-Columbian Americas (Webb 1936).

In Greco-Roman period, Hippocrates, Celsus, Caelius Aurelianus have written on tuberculosis (Sharpe, 1962). The Hippocratic text 'On Articulations' (par. 41) was the first to suggest a possible relationship between the spinal deformity and pulmonary disease (Bick 1948).

From India, hymns in ancient Vedic texts refer to consumption. Numerous hymns in Atharva Veda refer to the pathology, the usefulness of the drug, Sipudru and benefits of heliotherapy for tuberculosis of 'the spine' (Keswani 1967). The works of Charaka (1st century A.D.) and Susruta (5th century A.D.) refer to the physiology of respiration and chest diseases (Jaggi, 1961). Galen (131-201 A.D.) has "pointed out a form of spinal deformity due to caries of vertebrae which bore

some relationship to the tubercles of pulmonary tuberculosis" (Bick 1948).

We observe that little has been added to the subject for the next thirteen centuries till Daiechamps (1513 — ?) a French Surgeon and an Editor of Galen described the relationship between vertebral caries and paralysis of lower extremities in 1570 antedating Percival Poll (1779) by a little over two centuries. Yet, as with many eponyms in medicine, the worthy get slighted and forgotten.

The writings of Nelaton (1837) on tuberculous osteomyelitis, Rokitansky (1844) on histologic morphology, Koster (1869) on tuberculous nodule in joint, Volkmann (1879) on caries sicca and Watson Cheyne (1895) on primary synovial tuberculosis were added to the impressive list of literature on pathology of skeletal tuberculosis. But the aetiology was still elusive.

With the discovery of tubercle bacillus by Robert Koch in 1882. New vistas opened for eradicating a scourge that plagued humanity in all its recorded history.

The nineteenth century will be long remembered for its contributions in medicine. It witnessed the birth of anaesthesiology by W.T.G. Morton, the development of anti-septic methods by Joseph Lister, the discovery of tubercle bacillus by Robert Koch and ended with the discovery of X-rays by Roentgen on November 8, 1895.

Diagnosis

The diagnosis of tuberculosis of the spine is not difficult in great majority of cases. Pain, muscle spasm, tenderness over the spine in early cases and deformity, abscesses and neurological deficit in late cases cry out for recognition. The radiological changes again are striking as cases come late with gross destruction of the bodies of the vertebrae. It was noted that in regions where tuberculosis is prevalent, a clinical diagnosis of tuberculosis was mostly correct as was confirmed by operation in 83 to 85% of cases (M.R.C. Reports: Madras Study). Nevertheless, atypical lesions at pedicle, spinous

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process, transverse process and posterior inter-vertebral joint may be missed if the suspicion index is not high. Such lesions are likely to be over-diagnosed if tuberculosis is not thought of. Careful correlation of clinical features with detailed study of radiograph pays rich dividends. Bone scans and computerized axial tomography have been added to the armamentarium in recent years.

The Natural History

With increase in facilities for medical care, the advent of chemotherapy and large scale BCG immunization of children, it is to be expected that the natural history of tuberculosis of spine should have changed for the better in India. The author has analysed 732 cases of tuberculosis of spine seen by him in two decades from 1961-1980 at three hospitals at Madras (Shanmugasundaram, 1980). The cases were divided into four 5-year periods and were studied for as many as thirteen factors including age, sex, extent of vertebral involvement, neurological deficit, hospital stay etc. With the exception of decrease in duration of hospitalisation, all other factors did not show any change over twenty years. The mean vertebral loss of 2.39 vertebrae showed that cases continued to come late for treatment with gross destruction. It is saddening to note that the natural history of tuberculosis of spine has not shown any significant change in the last two decades in Madras region.

Vicissitudes of Treatment

It is probable that no other disease has witnessed such whimsical, often ludicrous changes in the management of tuberculosis of the spine. It was largely empirical till recent times. As with any empirical treatment, belief held sway over reason. Hence, it is not surprising that almost all methods of treatment from benign neglect to forcible correction of gibbus were in vogue from time to time. Many a sufferer developed paraplegia and died of its sequelae. Some of the sufferers lived long years after nature's healing with gross gibbosity. At least some of the hunchbacks immortalized in literature and art were sufferers of tuberculosis of the spine. Among the methods of treatment of pre-chemotherapeutic era, two merit mention, sanatorium regimen and posterior spinal fusion.

Era of Sanatoria

“Teach me to live that I may dread
The grave as little as my bed”

(Asher R.A.J. 1947)

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The benefits of sunshine, nutritious food, and good ventilation for tubercular patients were known through the ages. A hymn in Atharva Veda extols these. The credit for organising the first country hospital exclusively for the crippled children goes to Barellai of Florence (1857). Later, similar hospitals were established in Britain and the continent. Rollier at Leysin (1903) popularised the method.

While the pendulum swung from rest to activity including horse riding for pulmonary disease, the teachings of John Hilton in 1860-62 on ‘Rest and Pain’ had influenced the clinical thought of the century for bone and joint tuberculosis. The Hippocratic principle that “a restricted and rigid regimen is treacherous, in chronic disease always, in acute, where it is not called for” had not been heeded for pulmonary cases. Thanks to the chemotherapeutics of later day the Hippocratic aphorism is valid even for bone and joint tuberculosis.

The regimen consisted of immobilisation, enforced, continuous and uninterrupted with expertly applied plasters, splints and braces, frequent turning, open air treatment and above all superb and devoted nursing care. They did not miss their schooling while in hospital bed and they thrived.

Posterior Spinal Fusion

Till recent years, operations on tuberculous spine was fraught with dangers at every stage. The high incidence of suppuration, chronicity of sinuses, and slow lingering death awaited the few who did not die soon after the operation. What cannot be approached frontally was attempted to be healed by subterfuge.

Menard called the local gibbus “orthopaedic correction essential for the restoration of stability”. Waldenstrom endeavoured to maintain an apparently normal contour by carefully adjusted pressure splinting followed by strong posterior spinal graft fixation.

Girdlestone (1950) summarizes the rationale of the posterior spinal fusion. “The support of the graft immunizes angulation; the granuloma can be organised, recalcified and soundly healed by the protection of a graft. An acute kyphosis is most undesirable by itself and for its potential damage to the spinal cord. Too many patients have walked out of hospital apparently cured and have come back with signs of paraplegia ... One should be careful not to allow a patient up until one is assured not only of the signs of healing and recalcification of focus but of a mechanical stability of the damaged part,

whether by natural process alone or buttressed by operative fusion. This is the established and most excellent rule to be disobeyed rarely and then only for sound reasons". He also states "A 'fusion' that will not fuse is a long miserable and most disheartening business".

The method was described by Hibbs at the turn of the century. In 1930's a lively controversy arose about the timing of the operation, whether it should be done during the activity of the disease or after it had healed. Thanks to the advent of chemotherapeutics in forties, the controversy had a natural death. Now-a-days, there is no need for posterior spinal fusion even though some die-hards still swear by it.

Era of Chemotherapy

With the isolation of streptomycin from *Streptomyces griseus* (Schatz et al, 1964; Schatz and Waksman 1944) a new era has started in the treatment of tuberculosis. Several chemotherapeutic agents specific against *Mycobacterium tuberculosis* have since been developed in quick succession.

With the arrival of chemotherapy, the natural history of tuberculosis has changed. For the first time, specific drugs became available against tubercle bacillus. The merits of chemotherapy are that the patients no longer die but are cured, the period of infectivity is considerably reduced, relapses are avoided and the chronicity disappears. The patients with drug-sensitive bacilli on right drugs, taken regularly, have excellent chances of cure in twelve months.

As with other organisms, the development of resistance to drugs is not uncommon with tubercle bacillus. Hence a combination of drugs is more effective than a single drug.

Streptomycin Sulphate

Streptomycin was isolated from *Streptomyces griseus* (Schatz et al, 1944). It is an aminoglycoside and tribasic substance. It is bactericidal in action. Among its toxic effects ototoxicity involving auditory and/or vestibular pathways of eighth nerve may occur. However, in the author's experience, the incidence of ototoxicity among the South Indian patients seems to be low. The standard dose is 20 mgm per kilogram the body weight upto 1 gramme a day reduced to 0.75 gramme for adults over 40 years of age.

Isonicotinic Acid Hydrazide

INAH was synthesized by Fox in 1951.

It is bactericidal in action. This drug is most potent *in vivo* and *in vitro*. It has the merit of oral administration as a single dose. The drug resistant strains may emerge rapidly. Hence it is given in combination with streptomycin, P. amino salicylic acid or rifampicin for synergistic action. The dose is 10 mgm per kilogramme body weight upto 300 mgm. It is a cheap drug,

Para-Amino Salicylic Acid

Lehmann (1946) devised para-amino salicylic acid as inhibitor of *Mycobacterium tuberculosis*. The emergence of resistance is rare. It synergizes well with streptomycin and INAH. The dose is 0.2 gramme per kilogramme body weight upto 10 grammes given as divided doses. Gastrointestinal upset can occur while on the drug. Further, the bulk of the drug required for action is resented by patients.

Isonicotinic acid derivatives

Ethionamide and Prothionamide are derivatives of isonicotinic acid hydrazide. They may cause gastrointestinal tract disturbances,

Pyrazinamide (Yeager et al, 1952) is a long acting drug and useful in intermittent chemotherapy along with streptomycin and INAH. It is hepatotoxic.

Rifampicin

Rifampicins are a group of antibiotics produced by *Streptomyces mediterranei*. Rifampicin is a semi-synthetic derivative of rifampicin SV. It is excreted slowly and accumulates in blood and tissue. The rifampicins interfere with RNA synthesis by binding to the DNA-dependent RNA-polymerase in transcription stage of cell growth; and the resistance is due to an alteration in the enzyme that prevents this binding. Hepatic damages can occur with the drug. It is given as a single oral drug and is still expensive. The dose is 15 mgm per kilogramme body weight upto 450 mgm for South Indian patients.

Ethambutol

The drug was described in 1961 (Thomas et al, 1961). Ethambutol shows good anti-tuberculous activity *in vitro* and in man. It is useful as a second line drug for cases resistant to streptomycin and INAH. The loss of visual acuity may occur and demands frequent ophthalmic examinations. In cases with drug toxicity, the vision may not return after stoppage of the drug. Daily dosage is 15mgm per kgm in divided doses for three to six months with frequent ophthalmic check-up.

Thiosemicarbazones

The activity of this group of drugs depend on S atom and enhanced by linkage to aromatic aldehyde. Thiacetazone is known to produce toxic effects like gastric disturbances, liver damage, anemia and agranulocytosis.

Surveillance of Drug Taking

“The absence of clinical, radiological and/or bacteriological improvement while on right drugs means CHEMOTHERAPY HAS BEEN PRESCRIBED BUT IS NOT BEING TAKEN”. Walton (1966) narrates the story of Mable who thwarted all efforts of an apparently well organized institution. Innumerable patients either stop taking the drugs out of sheer disgust or take them irregularly to promote emergence of resistant strains of organisms. Hence the importance of surveillance.

Chemotherapy and/or Radical Surgery

Mukopadhaya (1956) of India was probably one of the earliest to recognize the usefulness of chemotherapy alone for spinal tuberculosis. “In 1954, Konstam and Konstam (1958) in Nigeria embarked on a policy of ambulant out-patient treatment and in 1958 they reported interim results in 140 patients—but enough patients did well to satisfy Konstam that ambulant out-patient chemotherapy alone is the treatment of choice, at least in the circumstances of Nigeria. A later report by Dickson (1967) on 31 of Konstam’s patients tended to support this view” (Griffiths 1979). The publications of Medical Research Council Reports (MRC 1973a, 1973b, 1974a) convincingly proved Konstam’s views.

“Confronted with massive exodus of cases of tuberculosis of spine into Hong Kong from mainland China in the fifties, Hodgson and Stock (1956) started excising the lesion and fusing the spine by anterior approach with a view to shorten the period of hospital stay” (Shanmugasundaram 1978).

The anterior approach to the spine “affords full visualization of the lesion, complete excision of the debris and diseased focus and immediate fusion under compression. It enables correction of gibbosity to a greater or lesser extent. With the grafts under compression the periods of recumbency and hospitalization have been significantly shortened” (Shanmugasundaram 1978). The concept is not new (Mueller 1906; Ito et al 1934; Gjessing 1951; Nissen and Nigst 1956 and Cauchoux 1956) but the credit for popularizing the operation goes to Hodgson (1956, 1960).

Tuli (1975) has suggested a “middle path” treatment.

Studies of Medical Research Council of Great Britain

From 1969, M.R.C. Working Party on Tuberculosis of spine has initiated controlled trials in various parts of the world where tuberculosis of spine is prevalent with designs consistent with the available resources. “The clarity and logical development of the M.R.C. studies are outstanding, and it is believed that these reports are of considerable value not only for the results achieved but as an example of superbly planned field studies” (Editorial, Journal of Tropical Medicine and Hygiene-April 1974, 72). The findings of the studies have appeared in six reports and are relevant to our subject.

The following criteria were used for assessment of results; Favourable Status; Still Not Favourable Status and Unfavourable Status.

Favourable Status:

Pain free; in good health; restored to previous physical activities; no sinus or abscess; normal CNS; radiologically healed disease.

Still Not Favourable Status

Not quiescent radiographically; physical activity limited.

Unfavourable Status

Persistence of abscess of sinus; CNS involvement; death; additional surgery and/or chemotherapy for paraplegia, deterioration, etc.

The First Report (Medical Research Council 1973a) deals with the study in Masan, Korea. “At Masan, ambulant out-patient treatment, was compared with in-patient rest in bed for six months followed by out-patient treatment, a second random allocation being to chemotherapy either with isoniazid plus para-amino salicylic acid for eighteen months or with the same regimen together with streptomycin for the first three months”. At the end of three years. 84 per cent of in-patient children and 88 per cent of out-patient children showed favourable response; similarly, 90 per cent of patients on isoniazid and PAS and 82 per cent of patients on the triple regimen showed favourable response. “In conclusion, this study has demonstrated the striking but still widely unappreciated potency of standard chemotherapy in florid spinal tuberculosis in children. Furthermore,

it has established that an initial period of rest in bed offers little if any benefit”.

The Second Report (Medical Research Council 1973b) on the study at Pusan, Korea deals with a series of 150 children on ambulatory treatment with the standard chemotherapy with or without Plaster of Paris jacket immobilisation. At the end of three years, 85 per cent of children in plaster jacket for nine months and 82 per cent of children without jacket had responded favourably. The corresponding figures for the increase in the gibbus at three years were 12° and 10° respectively. 80 per cent of patients on triple regimen and 87 per cent of patients on isoniazid and PAS had a favourable response. Therefore the triple regimen was no more effective than the two-drug regimen. P.O.P. Jacket offers no benefit.

The Third Report (Medical Research Council 1974a) concerns a study in Bulawayo, Rhodesia where a controlled trial of debridement and ambulatory treatment with a second random allocation of triple or two-drug regimen for eighteen months was done. Unlike the Korean studies the series included a high proportion of adult patients. Debridement consisted of the removal of pus, caseous material, sloughs and sequestra but not deliberate removal of unaffected or viable bone. 85 per cent of the debridement series and 86 per cent of ambulatory series had favourable results at third year. There was significant mean vertebral loss in debridement series while the increase in gibbus was not significant. Bony fusion had occurred in 51 per cent of debridement series and 67 per cent of ambulatory series at three years. As in Korean series, there was little difference between SPH and PH series, 84 per cent and 86 per cent respectively responding favourable at three years.

Debridement is not a good operation. 83 per cent of biopsy specimens were histologically and/or bacteriologically positive for tuberculosis. In Bulawayo a clinical diagnosis of active tuberculosis was nearly always proved correct.

The Fourth Report (Medical Research Council 1974b) compares the anterior spinal fusion (Rad. series) and debridement on patients (Deb. series) on triple drug regimen for 18 months at Hong Kong. The mean total vertebral loss on admission was 0.7 in each of the series; at three years a mean gain of 0.2 of a vertebra in Rad. series and a mean further loss of 0.2 of a vertebra in Deb. series was seen ($P < 0.001$). There was a significant increase in the gibbus angle of 0.9° for the Rad. series

and 4.5° for Deb. series at three years ($P=0.1$). Radiographic evidence of bony fusion of affected vertebral bodies was 93 per cent and 69 per cent respectively at 36 months ($P=0.003$). The favourable response was 87 per cent and 86 per cent respectively at three years.

Eighty five per cent of 149 specimens were histologically tuberculous and/or yielded positive cultures for tubercle bacilli. The radical operation is, therefore, a better procedure.

In all there were 630 patients in four studies. The favourable status of various series were nearly identical at third and fifth years excepting in radical surgery where 89 per cent showed favourable status by 18 months.

Griffith (1979) states that “on the evidence of this (first) series of trials (Medical Research Council (1973a, 1973b, 1974a, 1974b, 1976, 1978), spinal tuberculosis uncomplicated by paraplegia should be treated by adequate chemotherapy combined with Hong Kong radical operation, if, only if, surgical expertise, adequate anaesthetic facilities and skilled nursing are readily available. If these facilities and skills are not available, the operation should not be performed, and reliance should be placed with confidence on ambulant out-patient chemotherapy. In-patient care and plaster jackets were not shown to confer any advantage and advantages that might be claimed for operative debridement do not appear adequate to justify that operation as a therapeutic measure, valuable as it may be as a means of diagnosis in an otherwise difficult diagnosis problem”.

The Rationale of Short Course Chemotherapy for Tuberculosis of Spine

The merits of short course chemotherapy are that the medication can be supervised and the case holding is easier. Several reports have appeared in recent years on short course chemotherapy in the management of pulmonary tuberculosis. “Tuberculosis of parenchymatous organs is characterized by a high bacterial population; tuberculosis of bone by a low one (Canetti, Debeyre and De Seze 1957). Debaunout (1966) showed that the total bacillary population of tuberculous spine may amount to fewer than are million organisms. A positive sputum on the other hand, may contain upto 300,000 bacteria in 1 millilitre (Boquet 1938). This low bacterial population also implies the likelihood of a lower incidence of drug resistant mutants in spinal disease than in pulmonary tuberculosis (Canetti and Grosset 1961) and it may be that this makes the spinal involvement

particularly responsive to chemotherapy” *The Series* (Griffiths 1979).

The Madras Study

The Madras Study is a joint scientific venture of the Tuberculosis Research Centre Madras, a wing of the Indian Council of Medical Research, the Working Party on Tuberculosis of Spine of the Medical Research Council of Great Britain and the Teaching Departments of Orthopaedic Surgery of Madras City. It is a logical successor of a string of controlled clinical trials in other regions of the world. The study was started in May 1975 and the intake was completed in December 1978. It would take a few years before the results are published. A short description of the Madras Study is included as it is considered relevant.

The usefulness of Isoniazid in tuberculosis is undisputed. It is a potent small dose oral drug, has good tolerability, is less toxic and, more importantly, is cheap. In 1968, among fourteen drugs of second order, Rifampicin was found to lead in good tolerability and was second only to Isoniazid in effectiveness. It is capable of fast bacterial sterilization, and has the merit of single oral medication under supervision. It is still expensive. However, both the drugs are hepatotoxic. These two drugs have been found to be an ideal combination for ambulatory short term treatment for pulmonary tuberculosis. Hence Isoniazid and Rifampicin were used in the controlled clinical trials at Madras, Hong Kong and Republic of Korea.

Ambulant cases of tuberculosis of the spine from the first thoracic to the first sacral vertebra were eligible for inclusion into the study. After careful screening from various parameters, the patients were allocated at random to one of the three regimens. In RAD/6HR, in addition to the drugs given for six months, a modified radical excision and bone grafting by an anterior approach was done within one month of allocation. AMB/6HR and AMB/9HR patients were ambulant and had drugs daily under supervision for six or nine months respectively. After the drug regimen is over, all patients are reviewed and investigated periodically. It is hoped to follow-up the patients for five years or, may be, for ten years.

The dosage of isoniazid is 6 mgm per kilogramme body weight upto a maximum of 300 mgms and of rifampicin 10 to 15 mgms per kilogramme body weight upto a maximum of 450 mgms.

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Nine hundred and sixty four patients with tuberculosis of spine were registered at six Madras City Hospitals between April 1975 and December 1978. 662 patients were rejected for various reasons and 303 patients were admitted into the study.

The first and second decades accounted for 40 per cent of patients and the third decade for 23 per cent. There was a slight female preponderance.

The patients are reviewed periodically for clinical and radiological assessment. The results will be published in the next few years. It is gratifying to note that case holding has been exceptionally good in the series. The preliminary studies seem to indicate the usefulness of short course chemotherapy with isoniazid and rifampicin for spinal tuberculosis.

Pott's Paraplegia

In the prechemotherapeutic era, paraplegia was a dreaded complication of spinal tuberculosis. Madame Sorrel-Dejerine in 1925 described two main types of paraplegia. In 1935, Seddon and Butler agreeing with Sorrel-Dejerine's classification of early onset and late onset of paraplegia, “disagreed in part with her views on pathology and wholly with her clearcut statements on prognosis. By no means all paraplegias of early onset regressed spontaneously; and about half of the patients with paraplegia coming on late made a good recovery” (Seddon 1956).

Menard (1894) did costotransversectomy. Calve (1923) and Valtancoli (1924) tried aspiration of abscess without much success. Laminectomy “removes the only part of the vertebral column that is structurally intact and invites the development of gross pathological dislocation” (Seddon 1956). Excepting for spinal tumour syndrome and posterior spinal disease the operation is not indicated for Pott's Paraplegia.

Seddon, Griffiths and Roaf (1955) have given the line of management of Pott's Paraplegia.

Antero-lateral decompression was devised by Capener (1954) in 1933 who called it lateral rachotomy. rediscovered and perfected a decade later by Dott and Alexander (Alexander 1946).

The anterior decompression and bone grafting can be done for lesions at all level for relief

of paraplegia. It is the most rational approach as it effectively deals with the causative factors for paraplegia,

Till now, controlled clinical trials for the treatment of Pott's Paraplegia have not been attempted due to the difficulties of assessment, of probable variations in the neurological deficit.

Encouraged by the interim results of the Madras Study for non-paraplegics, the workers at Madras have just started preliminary trials for a controlled study of cases of Pott's Paraplegia with two regimens chemotherapy for nine months with or without anterior radical excision decompression and bone grafting.

BCG Osteomyelitis

In recent years, no subject has generated as much heat and acrimony as the role of BCG vaccination in the prevention of tuberculosis. Without getting into the controversy, we are aware of limitations of BCG vaccine. The vagaries of the quality of vaccine and of the technique of vaccination are well known. Even under the best of conditions, 10-20% of vaccinated people will not be protected. It is ineffective for those already infected and they are in the majority. What is more alarming is that thirteen deaths from generalised BCG infection have been reported by Mande (1968) Is BCG vaccination safe? Further, Bergdahl, Fellander and Robertson (1976) felt that there is probably an increase in the incidence of BCG osteomyelitis in Scandinavian countries.

This condition runs a benign course. The interval from PCG vaccination to onset of symptoms ranges from a few months to five years. Male and female children are equally affected. The general condition of the patients remains good with moderate elevation of temperature and ESR. The lesions are mostly localised to the epiphysis and metaphysis of long bones i.e., the site of end arteries. Only 3 out of 28 patients had multiple lesions. Radiographs show well defined lesions in the epiphysis or metaphysis, occasionally extending across the epiphyseal line. Small sequestra may be seen occasionally. Some lesions are indistinguishable from chronic non-specific osteomyelitis. The growth of same strain of BCG as was given for vaccination in the culture, negative guinea pig test and histology typical of tuberculosis except for profuse occurrence of plasma cells clinch the diagnosis of BCG osteomyelitis. Bergdahl et al (1976) recommended curettage and primary closure of the lesions which makes available material for bacteriological and histo-

pathological examination and hastens healing. They gave streptomycin for 4 to 6 weeks and rifampicin and INAH for six months. There was no adverse effects on epiphyseal growth centres in their series.

Nine of 13 cases of BCG osteitis verified by culture were reported from Scandinavia (Foucard and Hjelmstedt 1971). From 1950 to 1970, there were 4 cases of verified and 23 probable cases i.e. 1 in 80,000 vaccinated children. The Stockholm region with a population of 1,500,000 has 22, 000 births per annum. All children are vaccinated at birth or in the first few weeks in Sweden. For the Stockholm region, the incidence of BCG osteomyelitis was 1 in 17,000 for the years 1961 to 1971 and 1 in 5,500 in 1972.

Are the lesions due to change in immunological reaction or change of the vaccine? Immunophoresis was negative in 9 cases (two of them BCG verified). There was no immunopathy. Are we missing these cases? How many of the skeletal lesions in the bones are unverified BCG osteomyelitis? The author suspected two lesions but could not clinch the diagnosis by bacteriology.

A Plea

We have come a long way from empiricism. With the discovery of tubercle bacillus in 1882, Robert Koch had laid the foundations for scientific endeavour in "the fight against the 'whit' plague". Thanks to the improvement in the social milieu, nutrition of the people and specific potent drugs, the developed nations have "won the battle" which we in the developing nations "have hardly joined". Now is the time to stem the tide. Before long it may be too late. Or is it already late? As long as infective cases of pulmonary tuberculosis remain, skeletal tuberculosis cannot be prevented. Let us awake and arise lest future generations blame us for dereliction of our duties.

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VISUAL PATTERN IN ETHAMBUTOL TREATED TUBERCULAR PATIENTS

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Summary : Study of visual pattern in ethambutol treated tubercular patients based on observations made in 680 cases reveals definite change of visual pattern in the form of diminution of vision and change in normal relative extent for green colour field of vision in 81 patients of whom only 24 complained of some visual disturbance.

Ethambutol, though previously used as a second line drug, is now one of the standard anti-tubercular drugs. The drug, however, has a definite toxic effect on the eyes as reported in literature (Corpe & Blalock 1965, Citron 1969). Since only a few patients complain of visual disturbances during the course of ethambutol therapy, the present study was undertaken to find out the exact magnitude of the problem, assuming that some patients may have some visual disturbance but may not complain of it. The study was conducted at Nehru Hospital of B.R.D. Medical College, Gorakhpur (U.P.) from 1976 to 1980.

Material & Method

In all, 680 patients were included in this study; out of them 471 were males and 209 were females, majority being in 20-30 years age group (Table 1).

TABLE I

Age ant! Sex Distribution

Age group	Male	Female	Total
Below 20 years		19	52
20+ to 30 years		113	394
30+to40years		52	161
40+and above		25	73
All ages	471	209	680

All the patients were on ethambutol along with other drugs. The dose of ethambutol was 25mg/kg body weight per day for sixty days followed by 15mg/kg body weight per day till completion of 18 months from the start of therapy.

All patients were subjected to general ocular examinations with special reference to vision before starting the treatment and thereafter at monthly intervals or even earlier in cases who developed any ocular symptom. **Besides** the general, the routine ocular examinations consisted of the following:-

1. Acuity of vision

- (a) for distant vision by Snellen's chart
- (b) for near vision by Jaeger's test types

2. Colour vision

by Ishihara's Isochromatic charts

3. Field of vision

- (a) Central field of vision by Campimetry
- (b) Peripheral field of vision with white, blue, red and green targets of isopter 5/330

4. Fundus Examination by

- (a) Indirect Ophthalmoscopy
- (b) Direct Ophthalmoscopy

Observations

Only 24 patients complained of ocular symptoms. Blurring of vision was the commonest symptom (66.6%). The other symptoms were diminution of vision and headache (Table 2). The

TABLE 2

Visual Symptomatology

Symptom	No. of Patients	%
Blurring of vision	16	66.6
Diminution of vision	5	20.8
Headache	3	12.5

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symptoms were recorded earliest after 4 months

TABLE 3

Time of Appearance of Symptoms

Time of appearance of symptom	No. of patients
4 Months	2
5 Months	1
6 Months	2
8 Months	7
11 Months	12

18 months of therapy their number came down to 368. The range of deterioration of vision is shown in Table 5. The near vision acuity also showed a similar pattern of change. In the symptomatic group no visual disturbance was noted prior to development of symptoms while in asymptomatic group of patients (57 cases) the visual function disturbance was noted for the first time only after 7 months of therapy (in 11 cases). No visual disturbance was noticed in any case after the treatment had continued for 12 months (Table 6).

Visual field examination revealed that central and paracentral fields were normal with both white and coloured targets, before as well as after the therapy in all the cases included in the present study. However, the peripheral fields were normal for white, blue and red colors in all the patients before as well as after the completion of therapy but were found to have changed in their normal relative extent for green color (isoptre 5/330) in 71 eyes of 39 cases. 32 patients had bilateral while 7 cases had

TABLE 4

Age & Sex distribution of patients having visual function disturbance during Ethambutol therapy.

Age Group	Symptomatic patients			Asymptomatic patients		
	Males			Total		
						4
		4	14	24	10	34
30 + to 40 yrs	4	2	6	9	3	12
40 + and above	2	1	3	4	3	7
Total	17	7	24	39	18	57

Routine monthly examination revealed a diminution of visual acuity in 81 patients though only 24 patients had suggestive symptoms. The age and sex distribution of the 24 symptomatic and 57 asymptomatic patients is given in Table 4. The proportion of males and females in both the groups is nearly the same.

It can be seen from Table 5 that before the start of Ethambutol therapy, 1200 of the

unilateral eye involvement. As regards the green field changes (77) the range of diminution for green fields was 4° to 7° in various meridians.

Fundus examination did not show any striking change during the course of therapy except for mild to moderate hyperemia of the optic disc in majority of cases. In all the 81 patients, who developed visual function disturbances the ethambutol therapy was discontinued, no sooner the visual function disturbance was

TABLE 5
Effect of ethambutol on visual acuity

Visual acuity on Snellen's chart	Before treatment		After treatment	
	Both eyes	One eye only	Both eyes	One eye only
6/6	552	96	81	206
6/9	42	36	47	139
6/12		38	5	152
6/18		2	24	246
6/24			—	102
6/36			52	51
6/60			—	—
Below 6/60			—	46

noted. In symptomatic group of patients, the symptoms disappeared within 2-5 months of stopping the therapy.

Discussion

Various ocular toxicities including the change in vision following ethambutol therapy

TABLE 6

Relationship between time of appearance of symptoms & visual function disturbance

Time after starting therapy	No. or patient showing visual function disturbance	
	Symptomatic group of patients	Asymptomatic group of patients
4 Months	2	—
5 "	1	—
6 "	2	—
7 "	-	11
8 "	7	7
9 "	—	9
10 "	—	8
11 "	12	14
12 "	—	8
Total	24	57

TABLE 7

Effect of Ethambutol on field of vision

Field of vision	Before treatment	After treatment		
Central	Within normal limits in all 680 cases for white, Blue, Red & Green colours	No Change		
Peripheral	-do-	White, Blue & Red colour fields no change		Green Colour field
			No Change Binocular 641 Cases (1289 Eyes)	Constriction 32 Cases (64 Eyes)

have been reported by many workers—Bhola & Purhoit (1976), Citron (1969), Mathur & Mathur (1981). The diminution in visual acuity and peripheral field defects have been reported as visual changes. The present study reveals a change in visual pattern in the form of diminution of visual acuity and change in normal relative extent of green colour fields in 1.2% patients treated with ethambutol, a finding similar to that of Mathur & Mathur (1981). Strikingly enough, in our study, no patient complained of colour vision defect nor was it evident on testing with Ishihara's colour vision charts. In the series reported by Mathur & Mathur (1981) 6% patients were unable to identify red and green colour on Ishihara's colour charts. This diminution of sensitivity to green colour preceding that for blue colour indicates the involvement of transmitting neural apparatus, a change which may be evident before the field for white shows demonstrable alteration. The decrease in visual acuity and loss of ability to perceive the colour green, has been attributed to optic neuritis (Mathur & Mathur, 1981). Okcu (1975) and Schimidt (1966).

It was observed that the symptoms of visual function disturbance following ethambutol therapy disappeared within 2 to 5 months of stopping the therapy on appearance of symptoms. Of course, in both the symptomatic and asymptomatic groups there was recordable functional improvement, as well, following the cessation of therapy.

Hence it is recommended that a regular visual checkup be carried out in all the patients put on ethambutol therapy, because the optic nerve changes once produced are not reversible except in mild and early cases, since once optic nerve fibres degenerate they never regenerate

The patient must be primarily made aware of the toxic symptoms which he may develop,

in which case he should report immediately at the hospital. This will prevent any permanent damage to vision due to ethambutol.

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LIVER ENZYMES DURING TREATMENT WITH RESERVE REGIMEN

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Summary : Rise of liver enzymes e.g. LDH and SGPT are common in a regimen containing Rifampicin, Pyrazinamide and Ethambutol. In spite of significant abnormal rise, the regimen was continued. The patients tolerated it well, and the values came to normal. Those who develop clinical jaundice have other contributory factors which make the liver more susceptible to damage. Malnutrition and chronic hypoxia appear to be more important factors in precipitating damage to the liver.

Introduction

All anti-tuberculosis drugs with the possible exception of streptomycin can cause hepatitis but the risk is higher with some drugs than with others (Girling, 1978).

Hepato-toxicity due to Rifampicin and Pyrazinamide has been reported by McDermott et al (1954), Philips and Horten (1956) Macleod et al (1959), USPHS (1959) and Lees et al (1970). Re-treatment regimen consisting of Rifampicin and Ethambutol in cases where primary chemotherapy has failed, has been reported to carry a very low risk of hepatitis (Girling, 1978). Initial supplement of another drug, preferably bactericidal, can give us 100% success rate with tolerable minimal side effects in re-treatment regimen. It has been reported by East African/BMRC (1969) that mean enzyme activity of serum glutamic oxalo-acetic transaminase did not show a significant change monitored for six months at 3 months intervals during treatment with regimen consisting of streptomycin and pyrazinamide in different dosage schedules for cases who were failure of previous chemotherapy. This led us to constitute a regimen consisting of rifampicin and ethambutol with an initial supplement of pyrazinamide for a period of two months for the treatment of those who failed to benefit from previous chemotherapy. Both rifampicin and pyrazinamide are potent bactericidal drugs and are known for their hepato-toxicity. Both are metabolised in the liver (Ellard, 1969 and Pamra, 1979) and chances of liver injury will be high when two known hepato-toxic drugs are administered together. Hepatic damage is assessed at the earliest with the help of clinical laboratory by various liver function tests. Among the latter, liver enzymes are the earliest to show a rise even before the appearance of clinical signs and their monitoring at various intervals is thus an index of the extent of damage to the liver. It

was thus planned to study the possibility of addition of pyrazinamide to a combination of rifampicin and ethambutol for the re-treatment of those who failed to benefit from previous chemotherapy and secondly its effects on various liver enzymes namely serum lactate dehydrogenase (LDH), serum glutamic pyruvic transaminase (SGPT) and serum alkaline phosphatase by measuring their levels in the serum at regular intervals so as to assess the hepatic damage at the earliest

Material and Methods

Pulmonary tuberculosis patients who failed to benefit from previous chemotherapy ranging from 6-24 months were admitted in Tuberculosis and Chest Diseases Hospital, Amritsar (Punjab). All clinical conditions leading to increase in liver enzymes levels under study were ruled out. A limited number (25 cases) were selected and started on a regimen consisting of rifampicin 450mg in a patient less than 50kg body weight and 600mg rifampicin in a patient more than 50kg body weight as single dose on empty stomach in the early morning + pyrazinamide 30-35 mg/kg body weight to a maximum of 1.5gm+ethambutol 20 mg/kg body weight. All the patients were kept in the hospital during the period of study for any untoward reaction.

Liver enzymes were estimated at the beginning of treatment i.e. (Pre-treatment level) and subsequently 15, 30 and 60 days after treatment by the following methods:

1. Estimation of serum lactate dehydrogenase (King, 1965).
2. Estimation of serum glutamic pyruvic transaminase (Wootton, 1964).
3. Estimation of serum alkaline phosphatase (Wootton, 1964).

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Observations

Out of 25 cases studied, 17 were males and aged between 21 to 70 years. The observations are listed in tabulated form.

It will be evident from table 2 that mean serum LDH levels start decreasing under the effect of treatment. Decrease after 15 days is not statistically significant whereas decrease at 30 and 60 days after treatment is

TABLE 1

Grouping of patients based on pre-treatment liver enzymes levels

Liver enzyme		Range of enzyme levels	No. of patients
LDH	Abnormal	250.2-434.2 I.U/litre	10
	Normal (60-240 I.U/litre)	84.5-233.8 I.U/litre	15
SGPT	Abnormal	20-42 I.U/litre	7
	Normal (2-15 I.U/litre)	2-12 I.U/litre	18
Serum alkaline phosphatase	Abnormal	15.8-18.3 K.A. Units	4
	Normal (13 K.A. Units)	1.66-9.3 K.A. Units	21

Based on the values of pre-treatment liver enzyme levels, patients were grouped as:

1. Those who were within normal range (Normal group)
2. Those who were not within normal range (Abnormal group).

TABLE 2

Levels of serum LDH at various intervals after treatment in abnormal group

No. of days of Treatment	Mean enzyme activity (I.U/L)	S.D.± (I.U/L)	t	P
Pre-treatment	350.7	74.68		—
15 days	355.7	133.60	[10.10	More than 0.5
30 days	248.0	41.55	[3.80	Less than 0.01
60 days	235.4	95.37	3.01	Less than 0.02

TABLE 3

Levels of serum LDH at various intervals after treatment in normal group

No. of days of treatment	Mean enzyme activity (I.U/L)	S.D.± (I.U/L)	t	P
Pre-treatment	171.7	53.79	—	—
15 days	262.4	103.49	1.44	Less than 0.02
30 days	265.1	132.60	0.25	More than 0.50
60 days	162.53	49.49	0.49	More than 0.50

The above table shows that there is a transient rise at 15 and 30 days of treatment (P less than 0.02 and more than 0.5 respectively). Levels return to normal by 60 days of treatment without discontinuation of treatment.

TABLE 4

Levels of SGPT at various intervals after treatment in abnormal group

No. of days of treatment	Mean enzyme activity (I.U./-liter)	S.D. \pm (I.U/L)	t	P
Pre-treatment	37.14	8.78	-	-
15days	32.00	21.35	0.59	More then 0.5
30days	32.00	11.16	4.21	Less then 0.01
60days	6.0	2.0	9.51	More then 0.01

It is clear that levels start falling under the effect of treatment showing significant decrease by 30th and 60th days of treatment.

TABLE 5

Level of SGPT at various intervals after treatment in normal group

No. of days of treatment	Mean enzyme activity (I.U/L) (litre)	S.D. \pm (I.U/L)	t	P
Pre-treatment	5.67	3.45	-	-
15 days	18.39	15.88	3.39	Less then 0.01
30 days	15.67	10.94	5.80	Less then 0.01
60 days	8.33	4.69	1.93	Less then 0.01 More then 0.05

significant increase at 15 and 30 days of treatment but came to near normal by 60th day without discontinuation of treatment.

TABLE 6

Levels of serum alkaline phosphatase at various intervals after treatment in abnormal group

No. of days of treatment	Mean enzyme activity (K.A. Units)	S.D. \pm (K.A. Unit)	t	P
Pre-treatment	17.12	1.22	-	-
15 days	12.63	4.93	1.77	Less then 0.02
30 days	6.98	1.36	11.10	Less then 0.5
60 days	4.95	1.97	10.50	Less then 0.01

As is evident from the above table, levels fall continuously under the effect of treatment and became normal by 30th day and remain so by 60th day of treatment. Fall in the levels at 30th and 60th days of treatment is highly significant.

TABLE 7

Level of alkaline phosphatase at various intervals after treatment in normal group

No. of days of treatment	Mean enzyme activity (K.A. Units)	S.D. \pm (K.A. Unit)	t	P
Pre-treatment	4.97	2.49	-	-
15 days	5.63	4.59+	0.62	More then 0.5
30 days	4.35	2.86	0.75	Less then 0.5
60 days	3.29	1.97	2.24	Less then 0.02

It is clear from the above table that there is no significant change in the levels of serum

TABLE 8
Details of cases of Clinical Jaundice

Sl. No.	Age & Sex	Hb. (gm%)	Weight in kg	Pre-treatment level			Duration of present treatment	Level of serum bilirubin	Inter-reputation of treatment	Regimn resumed or not
				LDH (I.U./litre)	SGPT (I.U./litre)	Serum Alk. Phos. (K.A. Unit)				
1.	25 F	8.5	25	200.4	8.0	7.08	9 days	12 mg%	12 days	Pyrazinamide omitted, Rifampicin & Ethambutol restarted. Patient tolerated well.
2.	25 F	6.8	27	300.6	20.0	16.70	10 days	12.4 mg%	16 days	Pyrazinamide omitted. Rifampicin and Ethambutol restarted. Tolerated well.
3.	60 F	7.5	30	300.6	8.0	3.20	12 days	10.4mg%	18 days	Rifampicin + Pyrazinamide + Ethambutol resumed but patient had raised LDH, SGPT and serum bilirubin at 60 days of treatment and followed subsequently without any ill effect.

alkaline phosphatase at 15 and 30 days of treatment whereas fall in the levels by 60th day is significant.

3 (12 %) cases developed clinical jaundice during this study. Pre-treatment levels of liver enzymes, under study, are as shown in Table 8. All were females and their duration of treatment was from 9 to 12 days (mean 10 days) indicating the average time for clinical jaundice. Interruption of treatment was from 12 to 18 days (mean 15 days). All were severely malnourished, almost half of the average weight. One of them was severely anaemic (6.8 gm% haemoglobin) and the two others had moderate anaemia with 7.5 gm% and 8.5 gm % haemoglobin. One (4%) continued with the regimen and had raised values of LDH and SGPT and serum bilirubin at the end of 60 days of treatment and followed up subsequently without any ill effect. 2(8%) had pyrazinamide omitted thinking that this drug might be responsible for damage to the liver and rifampicin and ethambutol were restarted without any ill effect. It can be concluded that this regimen should be used with

great caution in those who have demonstrable hepatic dysfunction.

Discussion

Serum lactate dehydrogenase and serum glutamic pyruvic transaminase were used as an index of hepatocellular damage and serum alkaline phosphatase was used as an index for cholestasis. Litchman (1953) pointed out that in pulmonary tuberculosis clinical observations demonstrate a lack of parenchyma] hepatic damage contrary to the presence of such hepatic damage as revealed by sensitive hepatic tests, In our study also, none of the patients had any clinical signs of involvement of the liver or jaundice before the start of treatment though subclinical involvement of the liver was there as is revealed by the pre-treatment liver enzyme levels in the abnormal group.

It can be concluded from the given data that mean enzyme activity in abnormal group start falling after treatment by 30th day onwards whereas in normal group, mean enzyme activity

shows an increase by 15th day but there is a decline from 30th day onwards. This difference in behaviour between the two groups can be explained by the fact that pre-treatment raised liver enzyme levels are due to tuberculous toxæmia (Ban, 1955). After the start of therapy, mean enzyme activity of LDH and SGPT and alkaline phosphatase do not show any significant change at 15 days of therapy whereas in the normal group, there is a significant rise in the mean enzyme activity of LDH and SGPT after 15 days of treatment. But serum alkaline phosphatase remains unaffected. No significant change in the mean enzyme activity of liver enzymes at 15 days is explained by the fact that clearing of tuberculous toxæmia and metabolism of the drugs in the liver goes simultaneously and it appears that there is a net balance between the two resulting in no significant change. In spite of no significant change in mean enzyme activity of LDH and SGPT and serum alkaline phosphatase, regimen was not discontinued. Levels started coming down by the 30th day (P less than 0.01) and were within normal limits by the 60th day of treatment. Our results clearly support the findings of Crofton (1977) that liver enzymes improved as patients progressed under chemotherapy.

In the normal group, rise in the mean enzyme activity of LDH and SGPT at 15 days of treatment is a result of increased permeability due to hepatic cell damage associated with or without actual necrosis. (Weime, 1961; Zimmerman, 1964 and Clermont & Charmer 1967). Changes in the levels of serum alkaline phosphatase are statistically insignificant at 15 and 30 days of treatment but change is significant at 60 days of treatment (P less than 0.02). In spite of significant rise in the mean enzyme activity of LDH and SGPT, the regimen was continued and values returned to normal by the 60th day of treatment. It may be that liver finds it difficult initially to deal with the load of rifampicin but after a period of adjustment, it is capable of doing so (Lees et al, 1970). Thus, this study also demonstrates that transient abnormalities in liver enzymes are common during early weeks of treatment as opposed to no rise under regimens containing thiacetazone (Senetal, 1970). Continuation of the regimen results in their return to normal levels. Addition of pyrazinamide to a combination of rifampicin and ethambutol does not result in more involvement of the liver. Those who develop clinical jaundice have other contributory factors.

Three (12 %) cases developed clinical jaundice and all were females, undernourished, anaemic and had body weight almost half of what it should have been. It was suggested by Narang

and Sarin (1966) that chronic malnutrition and catabolism due to the effects of disease and chronic hypoxia (Refsum, 1963) made the liver more susceptible to toxicity. All these factors were present in them and made the liver more susceptible to damage under the effect of drugs. Individual susceptibility also plays a significant role. Considering the sensitivity of liver enzymes depicting the hepatocellular damage, SGPT is more sensitive to LDH during treatment because the rise in the mean enzyme activity of this enzyme is highly significant statistically.

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GENITO-URINARY TUBERCULOSIS IN PULMONARY TUBERCULOSIS PATIENTS

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Summary : Urine of 6% of 100 consecutive cases of pulmonary tuberculosis was positive for AFB on culture. Most of the genito-urinary tuberculosis cases were in the 15-45 years age-group and 5 out of 6 were males. Pulmonary lesions were cavitory in only one case and the average duration of pulmonary disease was 1-1/2 years. The commonest complaints suggestive of G.U.T. were burning micturition and frequency. Pus cells in acidic and sterile urine were a constant feature in all G.U.T

Introduction

Tuberculosis is not a rare disease in developing countries like ours. Pulmonary tuberculosis is usually initial lesion in almost all the cases. The disease spreads in other systems, usually through blood circulation or rarely local extension. The true incidence of genito-urinary tuberculosis (GUT) in cases of pulmonary tuberculosis is uncertain because of wide variations in the figures reported in the literature.

Wildbolz (1937) introduced the term "Genito-urinary Tuberculosis" as a separate clinical entity on the assumption that tuberculosis of kidney and epididymis were actually the manifestations of the same disease, disseminated by the blood stream. Medlar & Spain (1949) reported that in 168 cases in which genito-urinary tuberculosis was seen at autopsy, 134 (80%) had lesions in the lungs.

Sporer et al (1956) reported a series of autopsy examination on 736 tubercular cases who had not received chemotherapy. They found genito-urinary involvement in 117 (16%) cases, whereas it was 7 % in those who received anti-tubercular drugs.

Mygind (1960) found that tubercle bacilluria is demonstrable in 2% of patients with pulmonary tuberculosis. Sarinder Man Singh et al (1975) studied 36 cases of pulmonary tuberculosis in India and showed that 3 cases (8.3%) had urine culture positive for A.F.B.

Material and Methods

One hundred consecutive cases, who were admitted in T.B. Hospital attached to S.P. Medical College, Bikaner, were studied. All the cases were sputum positive for AFB. Detailed history and findings were recorded. The urogenital system was thoroughly investigated

i.e., urine examination complete, urine smear for AFB, urine culture for pyogenic organisms, urine culture for AFB, plain skiagram abdomen. IVP and hematological investigations.

The method for isolation of mycobacteria was the method used by Vestal (1969) modified by Bentz et al (1975).

Observations

The youngest patient was 14 years of age and the eldest was 70 years. The mean age of the patients in the present series was 32.6 years in males and 28 years in female patients. Maximum cases were encountered in the age group 20-30 years and these constituted 43% of the total cases. Out of 100 cases, 90 were males and 10 females (Table I).

TABLE I

Showing Age and Sex Distribution in 100 Cases of Pulmonary Tuberculosis

Sl. No.	Age group in years	Male	Female	Total
1.	10-20	10	2	12
2.	20-30	38	5	43
3.	30-40	20	1	21
4.	40-50	15	1	16
5.	50-60	6	1	7
6.	60-70	1		1
Total		90	10	100

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68% of the cases had bilateral pulmonary lesions as compared to 32% unilateral lesions. 73% patients had cavitory lesions either unilateral or bilateral, while 27% cases were non-cavitory.

Maximum number of cases (68%) attended the hospital within I year of their complaints and this number gradually decreased as the duration of complaints increased (Table II).

TABLE 2

Showing Duration of Pulmonary Lesion

Sl. No.	Duration of pulmonary lesion (in years)	Number of patients
1.	0	68
2.	2	22
3.	5	4
4.	8	4
5.	More than 10	2
Total		100

First hour ESR was found to be raised in all cases. The range of ESR was 51-75 mm in 43% and more than 100 mm in 3% cases.

Frequency of urine was the commonest symptom in 29 % cases. In one patient frequency was 20-22 times in 24 hours and he was miserable because of this. Hematuria was not a conspicuous feature and was seen only in 4 % of cases. History of renal colic was present in 13% cases. 18% cases had grossly turbid urine, while red coloured urine was observed in only 8 cases. Acidic reaction of urine was present in 18 cases, while 82% had alkaline reaction. Albuminuria was observed in 15 cases. Microscopically, pus cells were seen in 64% cases. Microscopic hematuria was found in 15 cases. Calcium oxalate and amorphous phosphate crystals were seen in 15 cases.

The urinary smears of all the 100 cases were examined for AFB and also cultured. None of the smears was positive for AFB, whereas culture could detect AFB in the urine of 6

cases. All these six cases were taking haphazard anti-tubercular treatment.

Urine of 51 cases out of 100, who had symptoms referable to genito-urinary tract or had pyuria, albuminuria etc., was subjected to culture for pyogenic organism. 24 had sterile urine and in 27 cases, culture was positive for pyogenic organisms.

All the 6 cases with urine culture positive for AFB had pyuria in acidic urine and the urine was sterile for pyogenic organisms. 4 cases were in the age group 15-45 years while two cases were in the age group 50-60 years. Bilateral pulmonary lesions were present in 4 cases, while two patients were unilateral. Average duration of respiratory symptoms was 1½ years. Commonest genito-urinary complaints were burning sensation on micturition, increased frequency and renal colic. Renal angle tenderness was appreciable in 4 cases and thick, craggy and tender epididymis was palpable, again in 4 cases. Out of these six cases, two did not have radiological evidence of G.U.T. on IVP. while the other 4 showed early tubercular involvement of kidney as shown in Table III.

Eighty seven patients were on triple-drug therapy (SM, INH, PAS or TH), whereas 13 cases were on two drugs only. Isonex was being taken by 87 cases at the time of study. Most of the cases (88) had been under treatment for a period of less than one year, while 12 cases were such who had taken drugs for more than 1 year.

Discussion

In the present study, detection of AFB in the urine by culture was taken as a conclusive evidence of tubercular involvement of the genito-urinary system.

Regarding age and sex incidence of G.U.T., Borthwick (1956) noted that genito-urinary involvement was rare in the extremes of age and most of the cases were seen between 16-40 years. Bayu et al (1976) had maximum number of cases in the age group 30-40 years. The findings in the present series is in consonance with the above authors, 4 cases being between the ages 15-45 years and the other 2 above 45 years. Out of the 6 cases having G.U.T., 5 were males and 1 female. This finding is in conformity with the findings of Borthwick (1956) who found the male/female ratio to be 2:1.

Truly, tuberculosis of the genito-urinary system cannot be a primary manifestation of the disease and is usually secondary to the

TABLE 3

Showing the important observations of the six cases of genito-urinary tuberculosis (urine culture positive) out of 100 cases

Sl. No.	Age (Yrs.)	Sex lesion	Site of pulmonary lesion	Duration of Treatment taken Pulm. Tub.	Duration of treatment	I.V.P, findings
1.	21	Male	Bilateral non-cavitary	Streptomycin, Isonex, Thiacetazone	2 months	Normal
2.	50	Male	Unilateral cavitary	Ethambutol Cycloserine	1 year	Normal
3.	44	Male	Bilateral non-cavitary	Ethambutol Cycloserine	5 years] irregular	Rt. calyces spastic, irregular, and crowded, Lt. calyces, improperly outlined.
4.	22	Female	Unilateral non-cavitary	Streptomycin, Isonex, Thiacetazone	2 months	Superior and middle right calyces, shows linear filling defect. Inferior irregular.
5.	35	Male	Bilateral non-cavitary	Streptomycin, Isonex, Thiacetazone	2 months	Rt. pelvis irregular and small. Poorly functioning both kidneys.
6.	35	Male	Bilateral non-cavitary	Ethambutol, Ethionamide	3 years irregular	Lt. calyces spastic, irregular. Persistent pooling of dye in lower calyx. Pelvis also spastic.

presence of a primary lesion, active or inactive elsewhere.

In the present series, out of the 6 cases of G.U.T., 4 were having bilateral pulmonary lesions and 2 unilateral, only one unilateral case having a cavitary lesion. This finding is contrary to Medlar (1949), 80% of whose G.U.T. cases had cavitary or caseous pulmonary lesions. Since Medlar's series consisted of autopsies, the difference could have been due to the patients in his series having prolonged and more extensive disease.

Lattimer (1968) reported 4 to 8% of their cases on the whole having genito-urinary tuberculosis. In the same article, the authors analysed the findings in 25 physicians with pulmonary tuberculosis and found that 72% of them had advanced lesions in the kidneys, but none of them showed any clinical symptom suggestive of G.U.T. The probable reason of this high detection of G.U.T. in pulmonary

tuberculosis was that they received special care and proper attention in diagnosing G.U.T. Secondly, the number (25) is too small statistically.

Lattimer (1968) and Ehrlich (1974) reported involvement of G.U. system to be directly proportional to the duration of pulmonary tuberculosis. In the present series, however, 68% of the cases had history of pulmonary lesions for less than 1 year and only 2 cases had pulmonary lesions for more than 11 years, with a mean duration of illness of 1½ years.

In our series, urine culture for AFB was positive in six out of 100 cases of pulmonary tuberculosis. Sporer et al (1956) found 7% genito-urinary tuberculosis in the pulmonary tuberculosis patients who were under anti-tubercular drugs. The percentage of G.U.T. in those cases who were not receiving anti-tubercular treatment was 16%. This means that at least an equal number of cases cease to pass

AFB in urine as a result of anti-tubercular treatment. In the present series, about 6% of cases of pulmonary tuberculosis continued to excrete AFB in urine inspite of anti-tuberculous treatment. The findings cited by others are comparable to our findings.

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A CORRELATIVE STUDY ON ISOTOPE RENOGRAPHY, INTRAVENOUS PYELOGRAPHY AND URINE CULTURES POSITIVE FOR MYCOBACTERIUM TUBERCULOSIS IN TUBERCULOUS PATIENTS

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Summary : Urine specimens from patients of pulmonary tuberculosis (100 patients) and osteo-articular tuberculosis (50 patients) were submitted routinely for mycobacterial cultures. 16 patients (10.7%) were found to have positive urine culture for *M. tuberculosis*. Isotope renography depicted abnormalities of various types in 13 (81.2%) patients, while I.V.P. indicated abnormalities only in 7 (43.7 %) patients. It was evident that isotope renogram is a much better marker to detect renal involvement. In 7 patients (4.6%) a positive urine culture for *M. tuberculosis* was not anticipated, and in 3 patients isotope renograms and I.V.P. were also normal. Thus normal symptoms or normal tests do not necessarily exclude the possibility of genito-urinary tuberculosis.

Introduction

Tuberculosis bacilluria is known to be associated with tuberculosis of various sites of the body and many workers believe that renal tuberculosis can exist without clinical manifestations (Hobbs, 1923; Medlar, 1926; Medlar Spain and Holliday, 1949; Wechsler, Westfall and Lattimer, 1960; Bentz et al 1975). In the present work we have tried to determine the frequency of this occurrence and to correlate the positive urine cultures for *Mycobacterium tuberculosis* with isotope renography and intravenous pyelography,

Material and Methods

100 bacteriologically confirmed patients of pulmonary tuberculosis and 50 patients of osteo-articular tuberculosis were included in the study. Basis of diagnosis in the latter group was clinical and radiological evidence with a positive tuberculosis reaction. Following specific investigations were conducted:—

- (a) Urinalysis and routine urine culture for *Mycobacterium tuberculosis* was done in all patients.
- (b) Isotope renography was performed in those patients where urine culture was positive for *mycobacterium tuberculosis*.
- (c) Intravenous pyelography was performed in those patients, where urine culture was positive for *mycobacterium tuberculosis*.

(b) Urine Culture for *Mycobacterium Tuberculosis*

All drugs were discontinued for at least 5

days prior to collection of urine. Early morning, first voided urine specimens of all the patients were submitted for mycobacterial culture (Kenny, Loechel and Lovelock 1960; Agarwal, Srivastava and Prasad 1981). Cultures were done under strict sterile condition on Lowenstein—Jensen media by Petroff's concentration technique (Cruickshank 1975). The media were incubated in an incubator at a temperature of 37°C for a period of 6 to 8 weeks. *Mycobacterium tuberculosis* was identified by typical colony morphology and bio-chemical test (Cruickshank 1975).

(b) Isotope Renography

Isotope renography was done according to the standard method (Witcofski et al 1961). Site of kidney was localised earlier by a plain X-ray abdomen or by an intravenous pyelogram. After proper preparation of the patients, I-¹³¹ Hippuran (Orthiodo hippuric Acid). 25 uci/Kg. body weight was injected rapidly by intravenous route. Isotope renogram charts were obtained and analysed for any abnormal findings.

Qualitative analysis was done according to the criteria of Kennedy et al (1965). Renograms were classified into unilateral or bilateral abnormalities and were grouped into three types:—

- (1) Flattening of all the phases suggesting parenchymal damage (Type A).
- (2) Flattening of secretory phase, lowered somewhat delayed peak, indicating impaired vascular and tubular functions (Type B).

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- (3) Normal vascular and secretory phase with delay in fall of curve in excretory phase, indicating impairment of drainage (Type C),

(c) Intravenous Pyelography

After proper preparation of the patient, a check film of abdomen was taken. If satisfactory, 40 c.c. of Conray 420 was injected intravenously. 15" x 12" X-ray films were exposed at intervals of 7-1/2, 15 and 30 minutes. Pyelograms were analysed for any abnormal findings.

Observations

The 16 patients with urine cultures positive for *M. tuberculosis* were reviewed in terms of their initial clinical diagnosis. Nine patients had a possible or probable initial diagnosis of renal tuberculosis based on urinary symptoms or abnormalities demonstrated by urinalysis at the time of admission. The remaining 7 (4.7%) patients had normal urinalysis and positive urine culture was not anticipated.

Out of 16 patients with urine culture positive for *M. tuberculosis*, 13 (81.2%) patients had abnormal renograms. Type B abnormality was most common and was seen in 9 patients on left side and in 2 patients on right side.

TABLE 1

The frequency of Urine Culture Positive for M. tuberculosis in various patient categories

Patient Categories	No. of Patients	Patients with positive urine cultures	
		(No.)	(Percentage)
Total patients studied	150	16	10.7
Patients of Pulmonary Tuberculosis	100	9	9
Patients with Osteoarticular tuberculosis	50	7	14

TABLE 2

Urinalysis Findings of 16 Patients with Urine Culture Positive for M. tuberculosis

Urinary Findings	Patients					
	Pulmonary Tub.		Osteoarticular Tub.		Both	
	(No.)	(%)	(No.)	(%)	(No.)	(%)
Acidic reation	9	100	7	300	16	100
Albuminuria	5	55.6	4	57.1	9	56.2
Microscopic :						
Pus cells	5	55.6	4	57.1	9	56.2
R.B.C.	4	44.4	3	42.9	7	43.8
Casts	2	22.2	1	14.3	3	18.8

TABLE 3

Qualitative Analysis of Isotope Renograms of 16 Patients with Urine Culture Positive for M. tuberculosis

Side	Type of abnormality in renogram			Abnormal		Normal	
	Type A	Type B	Type C	(No.)	(%)	(No.)	(%)
Right	0	2	0	13	81.2	3	18.8
Left	2	9	0				

TABLE 4

Analysis of Intravenous Pyelograms (I. V.P.) of 6 Patients with Urine Culture Positive for M. tuberculosis

I.V.P. Findings	Site of Abnormality			Total	
	Right Kidney	Left Kidney	Both Kidneys	No.	%
Normal pyelograms				9	56.3
Abnormal pyelograms				7	43.7
(a) Moth eaten appearance of calyces	1	3	0	4	57.1
(b) Calycectasis with poor visualization	0	1	0	1	14.3
(c) Calycectasis with hydro-ureter	0	1	0	1	14.3
(d) Non-visualisation	0	1	0	1	14.3

Out of 16 urine culture positive patients, 7 (43.7 %) patients had abnormal I.V.P. findings. The most common abnormality was 'moth eaten' appearance of calyces (57.1 %). However, no bilateral abnormality could be found in these patients.

On correlation with I.V.P. findings and abnormalities in renograms, it was observed that all the seven cases who had abnormal findings I.V.P., also had abnormal renograms. However, among 9 cases with normal I.V.P., 6 patients (66.7%) showed abnormal renogram and all presented with "Type B" abnormality.

It was observed that out of 16 patients with urine culture positive for *M. tuberculosis*, 3

patients (18.8%) had no abnormalities, while 4 patients (25%) had abnormality in isotope renograms only. In 7 patients (43.7%) all the parameters were abnormal.

Discussion

Positive urine cultures for *Mycobacterium tuberculosis* of 150 patients suffering from pulmonary (100 cases) and osteo-articular (50 cases) tuberculosis was found in 16 (10.7%) patients. This supports the concept that renal tuberculosis is the most common extra-pulmonary form of tuberculosis (Bentz et al 1975). In pulmonary group the yield of positive urine culture was 9 %. This findings is well in agreement with other workers (Hobbs, 1923;

TABLE 5
Correlation Between Intravenous Pyelogram (I. V.P.) and Isotope Renograms of 16 Urine Culture Positive Cases

I.V.P. Findings	Total No. Abnormal isotope Renograms		Type of Abnormality		
	(No.)	(%)	A	B	C
Normal	9	66.7	0	6	0
Abnormal	7	100	2	5	0
(a) Moth eaten appearance of calyces	4	100	0	4	0
(b) Calyceulasis with pour visualization	1	100	1	0	0
(c) Culycectasis with hydro-ureter	1	100	0	1	0
(d) N on- visualization	1	100	1	0	0

TABLE 6

Grouping of Urine Culture Positive Cases According to all the three parameters

Groups	Findings				
	Urinary Symptoms Urinalysis	I.V.P,	Isotope Renogram	No.	Percent
I	A	A	A	7	43.7
II	A N	A		2	12.5
III	N	N	A	4	25.0
IV	N	N	N	3	18.8

Rosencranz, 1940 and Medlar, 1942). On the other hand, the yield of positive urine culture for M. tuberculosis in osteo-articular group was 14%. Higher percentage of urine culture positivity in osteo-articular group has been reported (Harris, 1928; McLell and Davis, 1942; Snellman 1950).

On routine urinalysis, overall abnormality in urine was present in 9 (56.2%) of 16 culture positive cases and 7 (43.8%) had normal urine analysis. Bentz et al (1975) reported that a total of 58% urine culture positive cases in their series were having normal urine

findings. Various investigators from time to time have emphasized that bacilluria due to M. tuberculosis can exist without causing clinical manifestations (Cunningham, 1911; Bernstein, 1914; Hobbs, 1923). These investigators also believed that bacilluria with M. tuberculosis could occur in the absence of renal lesions and was not necessarily a proof of genito-urinary tuberculosis,

To study the frequency to this occurrence, we performed isotope renography and intravenous pyelography (I.V.P.) in these 16 patients with tuberculous bacilluria. Isotope renography de-

pected abnormalities of various type in thirteen (81.8%) patients. Left kidney was involved in eleven patients and right kidney in two patients. Type B abnormality, indicating impaired vascular and tubular function, was most common and was observed in 11 patients. In the remaining 2 patients, renograms suggested Type A' abnormality indicating parenchymal damage (Table III). On the other hand I.V.P. indicated abnormalities only in seven (43.7%) patients. Nine patients (56.3%) showed no evidence of renal tuberculosis (Table IV). Our findings are well in agreement with other workers, who failed to demonstrate evidence of renal tuberculosis in majority of their patients by the help of I.V.P. (Band, 1950; Biehl, 1958 and Bentz et al 1975).

On correlating the findings of isotope renograms and I.V.P., it was evident that isotope renogram was a much better marker to detect renal involvement. It was found that all the seven cases with abnormal I.V.P. were showing abnormalities in isotope renograms. Besides this, 6 out of 9 patients having normal I.V.P., showed abnormalities in isotope renograms. Moth eaten appearance of calyces were observed in 4 patients and calycectasis with hydro-ureter in one patient on I.V.P. and all of them showed Type B' abnormality during renography indicating impaired vascular and tubular functions. Calycectasis with poor visualization or non-visualization was associated with 'Type A' abnormality in renograms indicating parenchymal damage. Comparison between various I.V.P. findings and isotope renographic findings have been summarized in Table V. We are not aware of any study where both isotope renography and I.V.P. have been performed in patients having urine cultures positive for *M. tuberculosis*.

In 7 (4.7 %) patients a positive urine culture for *M. tuberculosis* was not anticipated. They had denied current genito-urinary symptoms and had normal urinalysis on routine examination, Bentz, et al 1975 reported unanticipated urine cultures positive for *M. tuberculosis* in 7 % of their cases. Out of these 7 patients, 3 had no urinary symptoms and routine urinalysis, renograms and pyelograms were normal (Table VI). A question arises naturally as to the cause of tuberculous bacilluria in these cases. It is very difficult to accept it as a purely physiological process because of the available experimental (Medlar and Sassano, 1924; Helmholtz and Millikin, 1926; Lieberthal and Von Huth, 1932) and pathological evidence (Cunningham, 1911; Hobbs, 1923; Medlar, 1926). Medlar 1926 demonstrated that cavitation and calyceal communication in renal tuberculosis was

later manifestation of advanced diseases, which was present only in minority of cases. He concluded that physiological or excretory "Tuberculous Bacilluria" does not exist without tuberculous lesion in the kidney. Thus a patient with a urine culture unexpectedly positive for *M. tuberculosis* should not be dismissed as having incidental bacilluria, even in the face of normal urinalysis, normal renogram and normal pyelogram, but should always be treated as a case of renal tuberculosis.

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CASE REPORTS

TUBERCULOSIS OF THE BREAST

S.H. KULKARNI,* H.R. TATA,** ANP M. JAIRAMAIAH***

Summary : Mammary gland is an unusual site for tuberculosis and it appears to have peculiar resistance to tubercular infection. Eighty biopsy proved cases of tuberculosis of the breast are reported. Most of the cases were in 21-30 years age-group. 91.25% patients presented with a lump and 32.5% patients presented with lump and sinus both. Both the breasts were involved in one case. Six cases had associated pulmonary tuberculosis. Eleven patients were lactating. Associated malignancy was found in two cases. Excision followed by chemotherapy was the treatment given.

Introduction

Sir Astley Cooper in 1829 had described this entity as a "Scrofulous swelling in the bosom of young women". Since then, several cases have been reported. In the present study, 80 cases of breast tuberculosis seen during the last 16 years, i.e., 1963 to 1979, are reviewed.

Patients and Methods

The cases included have been taken up from the patients attending the surgical department of the Wanless Hospital, Miraj. Some cases are also included whose histopathology was reported from the Pathology Department of the hospital, though the cases were treated elsewhere.

Seventy eight patients were females and two were males. The majority of the patients were under the age of 40 years (63 out of 80). Largest number of cases was in the age group 21-30 years. Youngest patient was 15 years and oldest 70 years old. Two patients were pregnant and 11 were lactating. The mode of presentation was a lump in 73 patients and both lump and discharging sinus in 26 patients. The lump was painful in 20 patients. The axillary lymph nodes were enlarged on the side of breast lesion in 16 patients. Six patients had associated pulmonary tuberculosis and one had cervical lymphadenitis. In the remaining 57 cases no other tuberculous focus could be detected anywhere in the body.

In all the patients the diagnosis was made by biopsy of the lesion with histological examination. Diagnostic criteria included the presence of granulomatous inflammatory infiltration or the presence of tubercles with central cassation. Acid fast bacilli were seen in only 5 cases.

the mass or wedge excision of the abscess cavity and overlying sinuses, followed by antituberculous chemotherapy for 18 months.

Discussion

Most of the cases occur below the age of 40 years. In the present series, 63 patients out of 80 were below 49 years. In the series of Dharkar et al (1968) most of the cases were in the age group 18-25 years. Thirteen out of the 14 cases reported by Dubey and Agarwal (1968) were between 20 and 40 years in age.

Involvement of the breast tissue by a tuberculous disease is not common. It may be due to mammary tissue itself being unsuitable for multiplication and survival of tubercle bacilli. Raw (1924) observed only 7 cases in 10,000 necropsies in a T.B. Sanatorium. Nagashima (1925) did not find a single case of breast involvement in 34 autopsies on the patients with miliary tuberculosis.

There is a controversy regarding the possible route of entry of bacilli in the breast. The bacilli may reach the breast tissue via blood stream, lungs or from contiguous structures (Nagashima, 1925; Hall, 1936; Raven, 1949). According to McKeown and Wilkinson (1952) infection travels from the lungs to the breast tissue via tracheobronchial lymph nodes. In the present series 6 patients had pulmonary and 17 patients had nodal involvement. In the remaining 57 cases no other tuberculous focus could be detected anywhere in the body.

McKeown and Wilkinson (1952) classified tuberculosis of the breast in following sub-groups on the basis of clinico-pathological correlation.

These patients were treated by excision of

(i) Acute miliary tuberculous mastitis in

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which the breast disease is part of a generalised miliary disease.

(ii) Nodular tuberculous mastitis in which there is caseation and abscess formation.

(iii) Disseminated tuberculous mastitis where miliary lesions are limited to the affected breast only.

(iv) Sclerosing tuberculous mastitis in which there is a hard fibrous mass.

(v) Tuberculous mastitis obliterans in which there is duct involvement producing marked epithelial fibrosis.

In the present series following was the distribution in each group—

(i) Acute miliary tuberculous mastitis	Nil
(ii) Nodular tuberculous mastitis	60
(iii) Disseminated tuberculous mastitis	2
(vi) Sclerosing tuberculous mastitis	10
(v) Tuberculous mastitis obliterans	8

Acid fast bacilli were seen on smear in only 5 cases and all the cases were from nodular tuberculous mastitis group.

Ten cases underwent simple mastectomy in which the breast was riddled with sinuses and abscess. In two cases radical mastectomy was carried out due to the presence of malignancy and in the remaining cases excision biopsy was done. All these cases were put on routine anti-tuberculous treatment.

It would be appropriate to conclude that if a young woman comes with a lump in the breast with loss of appetite and general weakness the possibility of tuberculosis is to be considered

first and then malignancy. If a patient comes with a sinus and matted axillary lymph nodes clinically diagnosis is highly probable.

Acknowledgements

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TUBERCULOUS OSTEOMYELITIS OF THE STERNUM

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Summary : A case of tuberculous osteomyelitis of the sternum is reported and the diagnostic and therapeutic aspects reviewed. It should be considered in any indolent infection of the sternum even when there is no evidence of tuberculosis elsewhere in the body.

Osteoarticular tuberculosis is a therapeutic problem and tuberculous osteomyelitis of the thoracic cage (including the vertebrae) forms 7% of all cases of bone and joints tuberculosis (Nicholson, 1974). Involvement of the sternum without and tuberculous focus elsewhere is uncommon enough to warrant special mention and more so because of the morbidity associated with the intrathoracic spread of the disease and the therapeutic challenge the entity poses.

Case Report

A 50 years old male labourer came with a history of a chronic non-healing ulcer over the body of the sternum, gradually increasing in size, and not responding to antibiotics and dressings in different hospitals. On initial presentation the diagnosis of rodent ulcer/dermatitis artifacta was considered. Radiologically, no lesion was evident over the sternum then. Microscopic examination of tissue biopsy showed a chronic nonspecific infection.

Examination of the patient was unremarkable except for a punched out ulcer over the body of the sternum measuring 5 cms in diameter with seropurulent discharge. Tenderness was present over the adjoining sternal body and left fourth costal cartilage. No systemic abnormality could be made out clinically. A lateral radiograph of the chest showed periosteal reaction of the deep surface of the second piece of the sternum and destruction of the lower piece of the sternum. Mantoux test was positive (24 mm). The sedimentation rate was high (60 mm/hr). Sinogram showed the dye in the anterior mediastinum suggesting complete destruction of the bone. Lung fields were clear. There was no evidence of any tuberculous lesion elsewhere also.

Without further delay, the excision of the sternum along with the ulcer from the second piece to the xiphoid and the adjoining costal cartilages from the ITI to the VII was undertaken (Fig. 1). The right VII rib was used to replace the sternum and it was held in position

by stainless steel wire G-24. The lower part of the rib was fixed by chromic catgut sutures to the rectus abdominus.

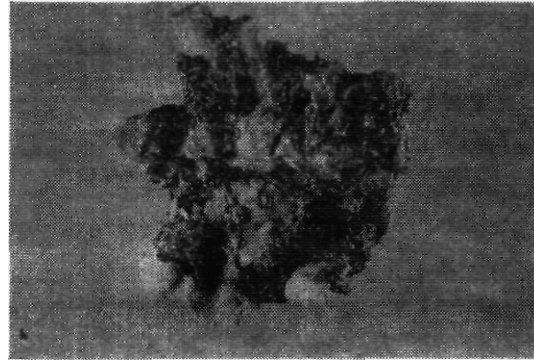


Fig.1. Photograph of the posterior surface of the excised specimen showing irregular destruction of the bone.

Postoperatively the patient was put on Gentamicin and Fiagyl. The tissue histology showed tuberculous granulation tissue. Antibiotics were discontinued following subsidence of toxemia and the patient was started on anti-tuberculous regime. Postoperative wound infection due to staphylococcus aureus was managed by specific antibiotics and wound irrigation. The cortex of the rib was perforated over a small area to allow granulations to proliferate and the raw area was skin grafted. Patient was discharged with antituberculous drugs and when seen six months later he was asymptomatic and the wound healed well.

Discussion

Pyogenic osteomyelitis of the sternum has been described after median sternotomies for cardiovascular surgical procedures, and secondary to mediastinal sepsis (Wray et al, 1973). Spread of specific infections from ribs, vertebrae, paravertebral or internal mammary lymph nodes may also be postulated. Tuberculous osteomyelitis of the sternum can occur following a

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focus of infection in the lung or lymph nodes, which resulted in bacteraemia. Secondary staphylococcal and pseudomonas infections may vitiate the clinical picture and diagnosis, as in our case. Costochondritis was an usual association of nonspecific osteomyelitis (Culliford et al, 1976).

The usual clinical presentation is of a dull aching pain restricting deep breathing and coughing, indolent ulcers, sinuses and persistent discharge of serous fluid without much of constitutional symptoms or septicaemia. If intrathoracic (intrapleural, intrapericardial or mediastinal) spread occurs the onset is more acute.

The diagnosis of osteomyelitis is suggested when there is chronic ulceration or sinus with bony thickening and tenderness. Sternal radiography is suggestive by the irregular cortical destruction with periosteal reaction but may be normal in the early stages. Specificity of the infection may be established by demonstrating acid fast bacilli from the discharge or by culture and guinea pig inoculation. The associated secondary infection or paucity of the organisms may negate the above investigations and one may have to resort to tissue examination to clinch the diagnosis. Tomography and radionuclide scanning with ^{67}Ga $^{99\text{m}}\text{Tc}$ are advances in diagnostic techniques (Mittapalli, 1979).

The treatment in early cases may be limited to antituberculous drugs and antibiotics combined with frequent check-X-rays to assess healing. Occasional curettage of necrotic tissue with preservation of the posterior periosteum to maintain support to the cage, may be necessary. After healthy granulations form, the raw area can be skin grafted. If full thickness destruction of the sternum occurs, excision of the sternum with repair to the defect should be undertaken.

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TUBERCULOSIS OF THE OESOPHAGUS

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Summary : A case of tuberculosis of the oesophagus is reported. The patient complaining of dysphagia had oesophagoscopy which showed a proliferative type of growth occluding almost whole of the lumen of the lower end of the oesophagus, resembling oesophageal malignancy. Biopsy done twice failed to reveal any evidence of malignancy. Gastrostomy revealed tubercles on the oesophageal wall. Histopathology clinched the diagnosis of tuberculosis.

Tuberculosis of the oesophagus is a rare condition (Thomson and Negus, 1948; Terracol and Sweet, 1958). In a review of the literature in 1954, Wexels encountered reports of 125 cases. Since then a few more solitary case reports have been found in the literature (Fehmy, 1969; Annamalai, 1972, Ito et al, 1976; Pradhan et al, 1976).

Case Report

A 50-year-old-man was admitted to the E.N.T. unit of P.B.M. Hospital, Bikaner for progressive dysphagia for solids and liquids of 3 months' duration. Physical examination showed a poorly nourished thin built old male with evidence of marked anaemia and mild dehydration. ENT check up was normal. Barium swallow (Fig. 1) revealed lower oesophageal narrowing with almost complete hold up of the barium and proximal dilatation.

Oesophagoscopy disclosed an exophytic, red highly vascular fragile mass occluding near about whole of the circumference of the lumen of the lower oesophagus i.e. at a distance of 38 cm from the upper central incisor teeth. Biopsy tissue taken from the lesion showed no evidence of malignancy, A repeat oesophagoscopy was done and second tissue biopsy was again reported as chronic granulomatous lesion with no evidence of malignancy.

During the period of 15 days after admission, the dysphagia became more marked. A nasogastric tube could not be passed through this stricture so the patient was referred to the gastro-intestinal surgeons to perform gastrostomy for feeding purpose. At operation, tiny mass like a tubercle was found over the wall of lower end of the oesophagus suggesting tubercular lesion of the oesophagus. Biopsy of the tissue this time was reported to be tuberculous.

Subsequent to this histological diagnosis,

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the patient was thoroughly re-investigated in detail to locate any tubercular lesion in any other part of the body. A re-interrogation of



Fig 1: Oesophagogram showing complete holdup of barium at the lower end of the oesophagus with dilatation of proximal segment.

the patient did not reveal any history or complaints suggestive of tuberculosis. Detailed systemic examination also failed to reveal any evidence of tuberculosis. Smear examination of the sputum did not show acid-fast-bacilli. In

the skiagrams of chest, there were opacities in the hilar region suggestive of an old tuberculous lesion. His E.S.R. was 38 in 1st hour (Westergren's method). He was prescribed anti-tubercular therapy. Follow up examination after 8 weeks showed opening out of the narrowed segment of the oesophagus, the dilated proximal oesophagus showed regression in size. Gastrostomy wound was closed. The patient was advised to continue anti-tubercular therapy.

Discussion

Tuberculosis of the oesophagus is a rare entity and its presence without active primary lesion in the chest or elsewhere in a 50 year old man makes the case interesting clinically.

Involvement of the oesophagus by tuberculosis is usually secondary to already existing disease in the lungs or other parts of the body, although primary tuberculosis has been reported (Fehmy, 1969). There have been many hypotheses as to the mode of affection of the oesophagus. Most of the cases are due to swallowing of highly infectious sputum of cavitory disease in the lungs. Sputum may get stagnated proximal to oesophageal stricture. Lymphatic (Fehmy, 1969) or hematogenous (Lockward, 1913) involvement is also possible and occasionally oesophageal tuberculosis has been described in miliary tuberculosis (Thomson and Negus, 1948). Involvement of the oesophagus also occurs by continuity as in downward extension or tubercular ulceration of the pharynx. Rarely it may be affected by contiguity as in Pott's disease of spine and by tuberculous lymph nodes in the mediastinum and may be responsible for traction diverticulum of the oesophagus.

Although there are many patients with pulmonary tuberculosis, oesophageal tuberculosis is not frequently met with (as against frequent involvement of the intestinal tract) in spite of the fact that the oesophagus is so frequently exposed to tubercle bacilli from the swallowed sputum of patient with pulmonary tuberculosis. This local resistance of the oesophagus is difficult to explain. However, it might be due to difference in blood supply, lymphatic drainage, mucous secretion and local pH. A relative paucity of lymphoid tissue in the oesophageal wall (for which tubercular bacilli have a great affinity) could perhaps be an additional factor responsible for the rare occurrence of tubercular lesions in the oesophagus.

Both the gross and the microscopic pathology of oesophageal tuberculosis are similar to that of other tuberculous lesions in the gastrointestinal tract, Endoscopic examination may

show an ulcer, granuloma or at times tubercles scattered here and there. The present case revealed a tumour like lesion occluding the whole of the circumference of the lumen. The most common site for lesion is the mid-portion of the oesophagus near the bifurcation of the trachea.

No characteristic symptoms are ascribable to tubercular lesion of the oesophagus. Clinically, the symptoms depend on the type of the lesion, whether it is ulcerative or stenotic. Progressive dysphagia and pain are common complaints at the time of presentation (Wexels, 1954; Rubinstein et al, 1958, Fehmy, 1969; Pradhan et al. 1976). In the present case, complete oesophageal obstruction required gastrostomy for feeding.

Prognosis is usually favourable with recent anti-tubercular drugs. Resection of the part is usually not required. Drug therapy was found to be beneficial in the present case.

This case reveals that a tubercular lesion of the oesophagus should be kept in the mind when dealing with oesophageal lesions. It may pose a diagnostic problem when repeated biopsy is negative for malignancy in spite of suggestive clinical and radiological evidence. Biopsy is essential for final diagnosis.

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GASTRIC TUBERCULOSIS ERODING SPLENIC ARTERY—AN UNUSUAL CASE OF HAEMETEMESIS AND MELAENA

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Summary : A case of gastric tuberculosis (secondary to pulmonary tuberculosis) presenting with two deep ulcers in the fundus (one of which perforated into a sealed off space), fatal haemetemesis and erosion of splenic artery is reported.

Introduction

Gastric tuberculosis is an extremely rare manifestation of tuberculosis. Palmer in an exhaustive review of literature could collect only 400 cases documented upto 1950. From 1950 to 1979, there are not more than 16 cases reported in English literature to the best of our knowledge. (Stirk, 1968, Page et al 1975, Wani & Rashid 1977, P. Sengupta 1978, Bhansaii 1977 Amesu, et al 1962, Chazan & Atchison 1960, Novis et al 1973, Tuchel et al 1969, Kakar et al 1979). In the light of this rarity, the preoperative or antemortem diagnosis of gastric tuberculosis, an otherwise curable disease, is a real challenge.

Case Report

Patient, 34 years old male, was perfectly well till February 1980 when he started complaining of mild upper abdominal discomfort following meals. 10 days prior to admission he lost appetite and 5 days subsequently he had melaena on one occasion. On the day of admission (21.5.1980), he had two massive bouts of haemetemesis in the morning. There was no history of drug intake, fever, cough or liver disease. During his 16 hours stay in the hospital, he continued to have repeated bouts of haemetemesis and passed tarry stools on two occasions. He was given repeated gastric lavage with ice cold water, intravenous fluids and seven pints of blood. Upper gastro-intestinal endoscopy revealed frank blood and clots especially in the fundus. In addition, there was an ulcer in gastric fundus with irregular and edematous margins and blood oozing from it. No varices were seen in the oesophagus and fundus. The duodenum was normal. The clinical diagnosis of bleeding gastric ulcer (benign) was made. Sixteen hours after admission, patient d

Autopsy Findings

Stomach— Contained 200 ml. of fresh blood and at its fundus was adherent to spleen, tail of pancreas and splenic flexure of colon. There were two ulcers measuring 1.5 cm and 1 cm. situated high up in the fundus along greater curvature (Fig. I). In addition, (here were four superficial erosions nereby (Fig. 1). Ulcers had undermined and ragged margins with dark-brown slough silting on their floors. On separating the fundus from spleen the larger ulcer was



Fig. I. Gross photograph showing ulcers and erosions in gastric fundus. Spleen (Sp) is adherent to stomach and shows a healed infarct.

found to communicate with a sealed off space which was filled with a large thrombus near the splenic hilum (Fig. II). Pancreatosplenic group of lymph nodes were caseous (Fig. III). Histological sections through ulcers showed extensive caseation and tuberculous inflammatory exudate extending from mucosa down to serosa. In areas adjacent to ulcers including the erosions, inflammatory reaction was rather productive characterised by the presence of caseating and non-caseating granulomas (Fig. IV). Submucosal

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Fig. II-Gross photograph showing stomach (S) pulled apart and probe, passed through an ulcer, communicating with a space.

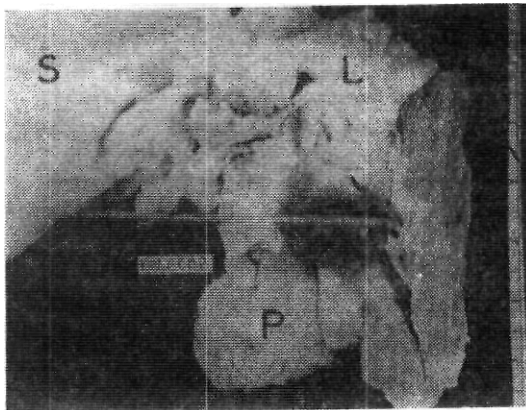


Fig. III-Gross photograph showing caseous lymph nodes (L), and splenic artery over superior border of pancreas (P) lost in the space near splenic hilum.

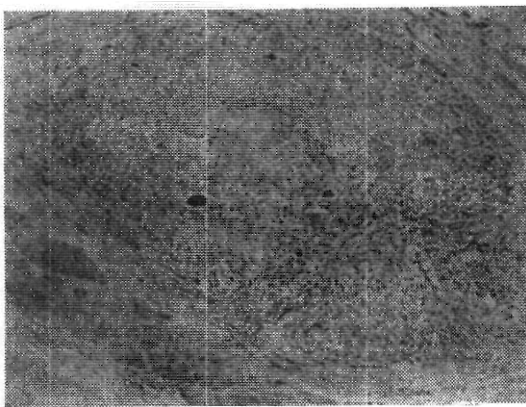


Fig. IV-Photomicrograph showing a granuloma in gastric submucosa (H&E x 110).

vessels showed intimal fibrosis and tuberculous arteritis. Random sections from rest of the stomach revealed normal histology. Tubercle bacilli were demonstrated in histological sections with Ziehl Neelsen stain.

Splenic Artery—identified on the superior border of pancreas was found lost in the space near splenic hilum (Fig. 1T1). Multiple histological sections through this space revealed an elastic structure (Splenic artery) infiltrated by exuberant tuberculous inflammatory exudate.

Spleen—showed tuberculous granulomas and a large healed infarct (Fig. I), resulting from erosion and occlusion of splenic artery by a large thrombus.

Liver—although grossly normal, showed granulomas both in lobules and portal tracts.

Right lung—had an apical scar which on histology revealed marked fibrosis and occasional ill-formed granulomas. Hilar and tracheobronchial lymph nodes showed calcification and occasional granuloma.

Rest of the organs including intestines were found to be normal both grossly and microscopically.

Discussion

Isolated case reports of primary gastric tuberculosis are available in the literature (Stirk 1968, Page et al 1975, Wani & Rashid 1977, P. Sengupta 1978, Kakar et al 1979). It is almost always secondary to tuberculosis elsewhere in the body—pulmonary tuberculosis being held responsible in 50% of the cases (Henery Bockus, 1974). Our patient has had tuberculosis of right lung, with involvement of hilar and tracheobronchial lymph nodes. The route by which the disease spread from the lungs to the stomach, pancreas, liver, spleen is, however, not absolutely clear. Three routes are possible: haematogenous; direct extension from neighbouring organs particularly caseating lymph nodes, and retrograde spread along lymphatics (Palmer 1950). It is likely that in our case the disease process spread haematogenously from lungs to stomach, spleen, pancreas and liver with subsequent involvement of draining lymph nodes (pancreatosplenic). However, it is also possible that the disease spread through lymphatics from hilar and tracheobronchial lymph nodes to pancreatosplenic lymph nodes with subsequent affliction of stomach, spleen and pancreas. This however, fails to explain tuberculous lesion in the liver.

Out of the various form which gastric tuberculosis may assume, ulcer form is the commonest (Palmer 1950). Further, these ulcers are most often shallow (Palmer 1950), Though our patient had the commonest form of gastric tuberculosis the ulcers were unusually deep extending down to serosa, one of them having resulted in a sealed off perforation. Gastric tuberculosis can involve any part of the stomach, most favoured sites being ant rum and lesser curvature (Palmer 1950). However, in our patient, ulcers were situated high up in the fundus along the greater curvature. The splenic artery got eroded because of its anatomical proximity to the tuberculous ulcers (stomach) and caseous lymph nodes (pancreatosplenic group)—another unusual feature in our case.

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NEWS AND NOTES

33RD TB SEAL CAMPAIGN

The 33rd nation wide TB Seal Campaign organised by the Tuberculosis Association of India and its affiliates in the States was inaugurated on 2nd October, 1982—the Gandhi Jayanti Day by Shri M. Hidayatullah, Vice-President of India at a special function held at his residence 6, Miulana Azad Road, New Delhi, Being the Centenary Year of the Discovery of Tubercle Bacillus by Robert Koch, the Association has selected for this year's Seals the pictures of Robert Koch., a microscope and a slide showing tubercle bacilli. The annual TB Seal Campaigns have been the one single-all-India effort calculated to involve our people in the anti-tuberculosis movement and ensure their full participation in implementing the "National Control Programme. The collections amounting to over Rs. 400 lakhs realised from the past campaigns are being utilised by the State Associations for assisting poor TB patients and their families, Organising Conferences, Refresher Courses, Seminars. Health Education, etc.

In a special message issued on the eve of the Campaign, Shri Zail Singh, President of India and Patron of the Association has conveyed his good wishes for the success of the Campaign and appealed to the nation to donate generously towards this great humanitarian cause. Shri S. Ranganathan, President of the Association has also appealed to the people to strengthen the TB Associations by buying TB Seals in large numbers and helping them to intensify the campaign against TB.

KOCH CENTENARY CELEBRATIONS

Andhra Pradesh: To mark the Centenary of the discovery of Tubercle Bacillus by Robert Koch, special functions were organised in some of the Districts in Andhra Pradesh. In Anantapur an Anti-TB Week was organised in co-operation with the staff of the Chronic Diseases Hospital. The function was presided over by Dr. C. Lakshminarasa Reddy, District Medical and Health Officer and it was inaugurated by Dr. B. Govindarajulu, Superintendent of the Headquarters Hospital. Dr. V.K. Rajaram Rao, Honorary Secretary of the District Association outlined the activities of the Association and Dr. (Smt.) B. Seetha Devi distributed clothes to patients. 5,000 copies of an educative pamphlet on TB in Telugu were distributed on the occasion.

A TB Camp and multi-disciplined diagnostic

and treatment camp was conducted at Dharmavaram on 28th March. The Camp was inaugurated by Dr. C.L.N. Reddy, D.M.O. & Health Officer and the function was presided over by the Revenue Divisional Officer. Doctors in the various specialities rendered free services. Dr. M. Chandrasekhar, DTO, was incharge of the Camp which was attended by 42 patients. Two such camps were organised in West Godavari District, and these were attended by 630 patients. During the TB Week celebrations a total of 3027 BCG vaccinations were given to children in the age group 0-5 years. An anti-TB Sibir was also organised at Elluru on the 18th July, 1982 and 264 symptomatics attended it.

In Visakhapatnam District, a TB Camp was organised at Pedagadi on the 15th July. The Camp was inaugurated by Dr. (Mrs.) V. Chittiseshu., ADMHS (TB & BCG), Andhra Pradesh. Dr. G.S. Prakasa Rao, Regional Director of Medical and Health Services, was the Chief Guest. In all 1020 patients attended the camp. Shri Madan Mohan Reddy, District Development Officer also participated in the Camp.

In Hyderabad, the Superintendent and staff of the TB Hospital, Irrumnuma, in collaboration with the State TB Association, organised a Centenary meeting on 24th March, 1982. Dr. P. Raehu Ram Reddy, Superintendent, Hospital for Mental Diseases, presided. Dr. (Mrs.) V. Chiltiscshu inaugurated the function and eminent specialists spoke on various aspects of tuberculosis.

In Medak, the District TB Association observed the Anti-TB Week by organising an exhibition and distributing health education material to the public. A public meeting was organised at Sanga Reddy on 29th March 1982 with Kum. Gayathri, IAS, District Collector, in the Chair. Shri M. Madhava Rao, Executive Director, BHWL, Ramachandrapur, was the Chief Guest. Dr. G. Sree Krishna, Civil Surgeon and District TB Control Officer and Joint Secretary and Treasurer. Medak District TB Association, gave a report on the anti-tuberculosis activities in the district. Smt. A. Madhava Rao distributed incentives to poor TB patients,

A seminar on Tuberculosis was conducted at Ibrahimpatnam, Ranga Reddy District on the 7th August, 1982. The Seminar was in-

augurated by Dr. O.A. Sharma, ADMS, Andhra Pradesh and presided over by Shri K. Yadagiri Reddy, President, Panchayut Samiti. Dr. D. Umapathy Rao, Honorary General Secretary, State TB Association, delivered the Key Note Address on the life of Robert Koch. The scientific session was Chaired by Dr. O.A. Sharma. Shri K. Yadagiri Reddy distributed clothes donated by the Teachers and Merchants Association of Ibrahimpatnam. Papers on various aspects of tuberculosis were presented by leading specialists in the district.

KERALA CONFERENCE

The first Kerala State Conference on Tuberculosis and Chest Diseases was held in Trivandrum on the 6th and 7th August, 1982. The conference was inaugurated by Shri K. Karunakaran, Chief Minister of Kerala and the inaugural session was presided over by Shri K. G.R. Kartha, the State Health Minister. Prof S. Ananthanarayanan, Retd. Principal, Medical College, Calicut, presided over the Conference and Dr. C.F. Sivadas, Director TB Centre, Trivandrum and Honorary Secretary, State TB Association welcomed the delegates. The inaugural function was addressed by Shri K. Ramachandra Nair, IAS, Health Secretary and Dr. V.T. Jayalakshmi, Director of Health Services, Kerala. Shri P.N. Raman, Secretary-General, Tuberculosis Association of India, conveyed the greetings and good wishes of the Central Association. The scientific programme included papers on various aspects of tuberculosis and Guest Lectures by Dr. S.P. Pamra, Honorary Technical Adviser, Tuberculosis Association of India, on "Diagnosis of Pulmonary Tuberculosis", Dr. K.V. Krishnaswami, Director, Institute of Chest Diseases, Madras on "Fate of sputum Negative Pulmonary Lesions" and by Dr. C. Thirugnana Sambandam on "Tuberculosis in Children". Dr. A. Ananthaswamy, Organising Secretary of the Conference proposed the Vote of Thanks.

REFRESHER COURSE

The Tamil Nadu Tuberculosis Association

conducted a Refresher Course on TB and Chest Diseases for the districts of Tirunelveli, Ramnad and Kanyakumari on the 11th July, 1982 at the Bio-Chemistry Hall, Medical College, Tirunelveli. Dr. R. Hariharan, Principal of the Medical College, inaugurated the course and Dr. G. Chandrasekharan, Deputy Director of Medical Services (TB) and Honorary Secretary, Anti-TB Association of Tamil Nadu, welcomed the gathering. Dr. R. Subramanian, Honorary Secretary, District TB Association, Chaired the sessions. 91 doctors, including a large number of Professors, Senior students and private practitioners, attended the course. Prof. K.V. Krishnaswami, Dr. G. Chandrasekharan, Dr. Abraham Balachandran, Dr. S. Ganpatisundaram, Dr. M.K. Srinivasan, Dr. G.V. Seshanarayanan, Dr. M.S. Srinivasan and Dr. (Mrs.) L.M. Sarojini delivered lectures at the course.

SHORT FILMS

The Tuberculosis Association of India has produced three short films, in colour, of about 3-4 minutes' duration each, on diagnosis, treatment and prevention of tuberculosis. These films are available in English, Hindi, Assamese, Punjabi, Marathi, Gujarati, Tamil, Malayalam, Telugu, Oriya, Bengali and Khasi languages. The cost of one set of these films is Rs. 1,500/- plus forwarding charges. Those who wish to procure prints of these films, may kindly contact the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi 110001.

XXV WORLD CONFERENCE

The XXV World Conference on Tuberculosis, organised under the joint auspices of the International Union Against Tuberculosis and Liga Argentina Contra La Tuberculosis Buenos Aires will now be held in Buenos Aires (Argentina) from the 12th to 19th December, 1982.