The
Indian Journal of Tuberculosis

Vol. 45 New Delhi, October 1998 No. 4

Editorial

WATCHING AIDS

According to recent estimates, there are presently 30.6 million individuals worldwide who are HIV infected and around 7 million have full blown AIDS. A majority of these persons are in poor countries, not because all these countries are more severely affected or due to a direct link between poverty and the disease but because these are more populated. Statements like - "The epidemic rages virtually out of control in South-east Asia and the Indian sub-continent" - are apparently hyperbole, needing scientific proof for credibility.

Watching the AIDS scene has become important to tuberculosis and chest disease physicians in India because of the acknowledged nexus between AIDS and tuberculosis. Half of our population is already infected with *M. tuberculosis.* And, as HIV infection spreads its tentacles in India (the AIDS pandemic reached India in 1985), the size of the dually infected segment has been gradually increasing. Consequently, the numbers coming down with tuberculosis has been rising, out of proportion to the increase expected from the rise in the population.

There are, however, no reliable statistics regarding the rise, nor are the true dimensions of this two-pronged public health hazard known. The oft and freely quoted international estimates are more scary than meaningful. Information released by the National AIDS Control Organisation (from its Sentinel Surveillance System) and the studies published by tuberculosis workers (on the extent of H V seropositivity among tuberculosis patients) do not support the international estimates, which may well be guesstimates.

News from the just conchded 12th World AIDS Conference held in Geneva also does not help. Held to review global technical progress achieved since last year's conference, its reports are more discouraging than hopeful. The rosy prospect of achieving an encouraging advance from "the cocktail chemotherapy" of AIDS, which had even led to an international initiative for arranging concessional supplies of such drugs to poor countries prior to the conference (detailed elsewhere in this issue) paled when emergence of resistant strains to these drugs was reported at the conference. The development of resistance could in fact have been expected under the somewhat dicey chemotherapy of AIDS at present, which is not easy to adhere to, and the cost is prohibitive.

A still deeper study of the pathogenic processes that ensue after HIV infection, leading to full blown AIDS, is needed to develop better anti-retroviral drugs as well as a safe and effective anti-AIDS vaccine. The good news is that full scale human trials with a promising anti-AIDS candidate vaccine are now underway in Thailand and U.S.A. (reported elsewhere in this issue). Indeed, the introduction of protease inhibitors for use along with standard AZT and 3TC anti-retroviral drugs ast year was an advance in itself. The identification now of

chemokine HIV receptors provides a better chance of achieving long term control over viral replication and plasma viremia. Chemokine receptors block the entry of HIV into CD4 T cells through the entry co-receptors. Eleven anti-retroviral drugs are now available for use in various combinations for long term treatment but their cost remains prohibitive. An attractive hypothesis being explored is that short term chemotherapy, given during the early acute stage of HIV infection, may bring down viral load to a level which may alter the pathogenic evolution of the disease itself and thus obviate the use of long term chemotherapy.

The demographic reports received from Africa and the African-American communities in the U.S.A. continue to be discouraging. Neither aggressive education/counselling, nor competent anti-retroviral chemotherapy (coupled with conditions for proper drug delivery and adherence) have proved to be practicable. Nonetheless, Senegal which had launched a very vigorous public education campaign early on has reported successful holding down to a low HIV infection rate, comparable to the around 2% range estimated for the U.S.A. In American cities, AIDS education is universal, yet, despite the sharp decline of AIDS among the whites, a higher rate persists among the blacks. While the blacks constitute 13% of the population, they contribute 57% to new HIV infections in U.S.A.

Seen from the tuberculosis standpoint, overall 1.7 billion person (one third of the global population) are infected with *M. tuberculosis* and 3.1 million have the dual infection with HIV. The dually infected population carries 10 to 20 times greater risk of breaking down to active tuberculosis compared with those having tuberculosis infection (0.1% to 0.3% per annum) only. Roughly, out of every 100 persons affected, 50 would have tuberculosis alone, 30 AIDS alone and 20 both tuberculosis and AIDS. Disease among the dually infected persons poses clinical problems of diagnosis to the unwary physicians due to unusual presentations and equivocal laboratory results. Also, there is greater need for a more carefully crafted patient management.

The demonstration of latently infected CD4 + T cells, developing despite potent anti-retroviral therapy, which cannot be eliminated by the host immune response due to the absence of a viral antigen on the cell surface (reminiscent of persistor tubercle bacilli) suggests caution when patients are being treated with both anti-tuberculosis and anti-retroviral therapy

Another significant development is the recent complete genome mapping of the tubercle bacillus. Comprising more than a thousand genes, the mapping has catapulted tuberculosis research, languishing in the classical microbiological studies, to the frontiers of science. A fresh approach to a more efficient vaccine against tuberculosis and newer drugs to kill the bacillus can now be expected.

Though anti-retroviral and anti-tuberculosis therapy have significantly reduced mortality from AIDS/tuberculosis in the U.S.A., the incidence of new HIV infections has not been correspondingly reduced, according to the CDC report covering the period 1994-1997 *(MMWR, 1998, 47, 309-314).*

This forebodes ill for India. Even granting that the risk factors for the spread of AIDS (and co-traveller tuberculosis) are somewhat different in India, the pre-eminence of educating the public sufficiently to change behaviour of the people remains the sheet anchor of our efforts. Are we going to lag woefully behind in educating the people against HIV as we have done in controlling tuberculosis due to not trying hard enough?

D.R. NAGPAUL

Ind. J. Tub., 1998, 45, 191

FIFTY YEARS OF TUBERCULOSIS CONTROL

M.L. Mehrotra*

After attainment of Independence, attention was drawn to the massive and neglected health problems of the country, and the Govt. of India appointed the Mudaliar Committee to look into the problems and suggest measures to set up an infra-structure.

Personal involvement of the national leaders and enthusiasm of devoted health workers initiated commitment to reduce suffering by initiating measures to develop a Tuberculosis Control Programme.

Realising the stupendous task, committed leaders in the medical fraternity like Dr. Bidhan Chandra Roy, Dr. Sushila Nayar, Dr. 3.K. Sikand, Dr. Frimodt - Moeller, Dr. P.V. Benjamin, Dr. P.K. Sen, Dr. M.D. Deshmukh, Dr. Joseph, Dr Kacker, Dr. Khajan Chand, and many others started looking for and locating younger persons in the few existing medical institutions of the country. They tried to locate, motivate and involve a few from every region and state of the country.

Then, with the personal involvement of committed national political leaders, like Pandit Jawaharlal Nehru, Rajkumari Amrit Kaur, Dr. Jivraj Mehta, Dr. Sushila Nayar and several others, they started planning the various strategies of Tuberculosis Control, obtaining co-operation and assistance from those countries which had already achieved a certain amount of control. They also looked for co-operation from international organizations like International Red Cross, Scandinavian Red Cross, W.H.O., UNICEF, B.M.R.C. and others.

Developing the infra-structur; throughout the country took almost twenty years.

The next generation of younger, committed medical and social workers took up the challenge with enthusiasm. There was a thruct and momentum for a decade, and future of control programme started looking bright.

The Scandinavian Red Cross in co-operation with Tuberculosis. Association of India and Government of India started training about a dozen young medical graduates in tuberculin testing, interpretation of reactions and giving B.C.G. vaccination to non-reactors. These medical graduates in turn started training a few hundred doctors and technicians to take up the work of tuberculosis control in every state of the country. At that stage the population of the country was around 500 millions. The objective was to create an awareness about tuberculosis in school children and simultaneous B.C.G. vaccination of eligibles.

Looking at the success of limited campaigns, it was decided to enlarge the programme into a Mass B.C.G. Vaccination Campaign. The Planning Commission and Union Finance Ministry promised to allocate more funds if the number of vaccinations increased. To improve the numbers, suggestions were made to start direct B.C.G. .vaccination of infants, children and young adults. This probably was a futile attempt as administrators wanted to dwell in numbers, mainly because of financial considerations.

Besides the preventive effort, there was an upsurge in the world to develop anti-tuberculosis drugs like PAS, Streptomycin, Isoniazid and Pyrazinamide which drew attention, for the first time, to develop ambitious treatment programmes, first in hospitals, sanatoria, and medical teaching centres. International community of medical workers joined in some small clinical trials and, later, in international controlled clinical trials, involving several institutions in several countries. This required large scale funding for drugs, and diagnostic procedures, specially microscopy and miniature chest X-ray for mass scale detection and case finding. Those countries which could afford financial investment started with multi-faceted control programmes.

With the initial awareness, and success of the programme, a sense of complacency started creeping in the administrators and politicians; their attention started getting diverted to other pressing

P.K. Sen - Tuberculosis Association of India Oration delivered at the 52nd National Conference on Tuberculosis and Chest Diseases held at Ahmedabad, 19-22 December, 1997.

* Former Director, TB Demonstration & Training Centre and Chest Institute, Agra-282 002.

problems resulting in financial squeeze for medical social programmes and diversion of funds to other schemes.

With the upsurge and desire for treatment, and meagre financial inputs, the technical experts started advising the use of single drug therapy with INH, or cheaper combinations like INH + Thioacetazone, A.P., PP, thoracoplasty and several other measures with variable to sometimes extremely poor results.

This in turn led to development of primary and secondary drug resistance and treatment failures.

The development of newer drugs and non-transfer of technologies for manufacture of these drugs resulted in further deterioration of mass treatment programmes, particularly the domiciliary management of cases and detection of potential cases.

With the passing away of committed political leaders and stalwarts, the second line of political leaders and medical workers started toeing the bureaucratic methods. The enthusiasm and motivation of younger workers started decreasing.

The leadership started paying attention to more pressing problems of the country and the slide back started. The inputs could not match the minimum requirements.

With the shifting priorities and vanishing commitment, the picture started looking dismal.

With increasing political and bureaucratic interference, aging workers, domestic financial difficulties, the interest and enthusiasm in the programme started diminishing, resulting in decline of case detection, treatment and follow-up. To this decline has been added the identification and prevalence of non-specific infections and H.I.V. sero-prevalence in patients. All these problems may have a dramatic adverse impact on prevalence of tuberculosis and Multi Drug Resistance.

Inspite of these increasing and dreaded problems, the aim of tuberculosis programme remains firm, i.e. to check transmission of tubercle bacilli from open cases of tuberculosis. To meet this problem the international agencies particularly the WHO and IUATLD are advocating the use of DOTS or Directly Administered Treatment and Surveillance.

Application of DOTS in small and captive populations appears to be feasible but in a vast country with innumerable problems the aims of DOTS in tuberculosis control may not be accomplished.

I have a feeling that unless the following steps are taken we may still be struggling for tuberculosis control.

1. Organising the control programme on business lines, avoiding bureaucratic controls, but insisting on accountability and achievement.
2. Allocating funds on the basis of detection and complete treatment of every case.
3. Involving almost every medical worker and his associates in the whole country. GPs are the backbone of every mass campaign in the medical field.
4. Compulsory education on the subject in all schools and colleges upto higher secondary stage.
5. Massive and repeated use of mass media both written, auditory and visual.
6. Political and national commitment as a national urgency.
7. Development of manufacturing facilities eg. factories for manufacture of simple chest x-ray, and microscopes and drugs.
8. Surveillance, guidance, and mid-way correction of on-going control programme by an independent authority.
9. Identification, training, motivation and development of social and medical personnel to be a continuous programme for shouldering the overwhelming task in remote villages and over-crowded slums.
10. Permanency of the control programme has to be kept in mind, as the programme would be needed for at least next 50 years. It has been observed that the first fifty years of independence, which we are celebrating this year, has seen the development and waning of enthusiasm in our programme and simultaneous development of many problems.

Re-invigorating the programme and achieving modest control may need another fifty years.

Ind. J. Tub., 1998, 45, 193

GYNAECOLOGICAL TUBERCULOSIS - AN UPDATE

S.N. Tripathy and S.N. Tripathy

(Received on 3.2.98; Accepted on 8.5.98)

INTRODUCTION

Tuberculosis is as old as human civilisation and was mentioned in the Rig Veda.[1] It was in the middle of 18th Century that tuberculous gynaecological manifestations received attention when Morgagni (the famous morbid anatomist) described the signs of genital tuberculosis in women. Ramymond was the first to report a case of tuberculous cervicitis, while in 1847, Kiwish first described a case of tuberculosis of uterus. The manifestations of tuberculosis in gynaecology were published as a monograph by Hagar in 1886[2].

The clinical interest of gynaecologists was aroused after the accidental finding of tuberculous lesions, by Sutherland in 1943[2], in specimens of endometrium, obtained during routine investigations for sterility and menstrua disorders. But, unlike pulmonary tuberculosis, gynaecological tuberculosis is difficult to diagnose as most cases are asymptomatic. Some have only non-specific complaints, like infertility, menstrual disorder, pelvic pain, etc. Hence, a high degree of suspicion in patients from a high risk group will help in clinching the diagnosis.

The prevalence of genita tuberculosis, in general, has never been estimited since it is not practicable. However, 0.2 to 2.0% of all gynaecological admissions are lue to tuberculosis. Various workers, including ourselves, have estimated the proportions with evidence of genital tuberculosis in patients admitted for conditions like infertility, dysfunctional uterine bleeding, secondary amenorrhoea as well as in hysterectomy specimens and in ectopic gestation sacs. We have also studied the association of genital tuberculosis with pulmonary tuberculosis in fresh, untreated bacillary cases and have found the association to be as high as 24% (Table I)[3,4].

PATHOGENESIS AND PATHOPHYSIOLOGY

Tuberculosis of the genital tract is almost invariably secondary to a primary lesion elsewhere in the body, the latter usually being quiescent by the time pelvic involvement is diagnosed. In the majority, the infection reaches the genital tract (mostly fallopian tubes) by the haematogenous route. From the tubes, the infection reaches the endometrium where it either persists in the basal layer, which is not shed during menstruation, or it gets reinfected from the lubes following menstruation. Thus, tubercles in the endometrium are always young. There may be retrograde spread of infection to the ovaries and peritoneum. In a minority of cases, tubes, ovaries and the serosal surface of uterus become involved from the peritoneal spread which occurs from an intra-abdominal lesion. Rarely, direct involvement of vulva and cervix occurs from an infected male sexual partner.

The tubal pathology varies according to the mode of infection. If infection is lymphatic borne, the tubercles are formed on the surface, with adhesions all around. In haematogenous spread, the tubercles are deeper and look red, oedematous and swollen in the acute infection phase and fibrosed in the chronic cases. In 50% of the cases, the tubes get blocked; blockages being multiple and the tubes thickened and shotty. Sometimes, a localised blockage at the outer end results in the formation of hydrosalpinx or pyosalpinx with thick fibrous walls

Table 1. Frequency of Genital Tuberculosis among Ob/ Gynae disorders

Disorder	Percent
Infertility	5.3
Secondary amenorrhoea	9.3
Oligomenorrhoea	2.0
Dysfunctional uterine bleeding	1.5
Hysterectomy specimens	1.0
Ectopic pregnancy sacs	1.5
Pulmonary tuberculosis	24.0

Correspondence: Prof. (Mrs.) S. N. Tripathy, 1060, Mahanadi Vihar, Cuttack - 753 004.

which may become calcified or even ossified Often, the ovaries have normal macroscopic appearance and the diagnosis is made only on histopathological study But ovaries may have tubercles, adhesions, thickening of the capsule and sometimes even caseating abscess/cavities in the ovarian substance

The tuberculous uterus usually looks normal to the naked eye even though typical tubercles may be present m the endometrium[5] Adhesions and partial obliteration of the uterine cavity may also be present In cervix, the tuberculous lesion can be ulcerative or prohferative Rarer forms like mihary and interstitial tuberculosis have also been described In the ulcerative form, the ulcers have serpigenous outline, clean cut edges and a yellow base Early ulcers are often seen near the external os The prohferative lesion has papillary formations which may be pedunculated or sessile Finally, caseation occurs which leads to progressive destruction of the cervix (Fig I)[6]

In vagina, tuberculous ulcers are very rare (Fig 2)[7] In vulva, the lesions can be ulcerative or hyperplastic

Regarding frequency of involvement of the different parts of the genital tract, the tubes are

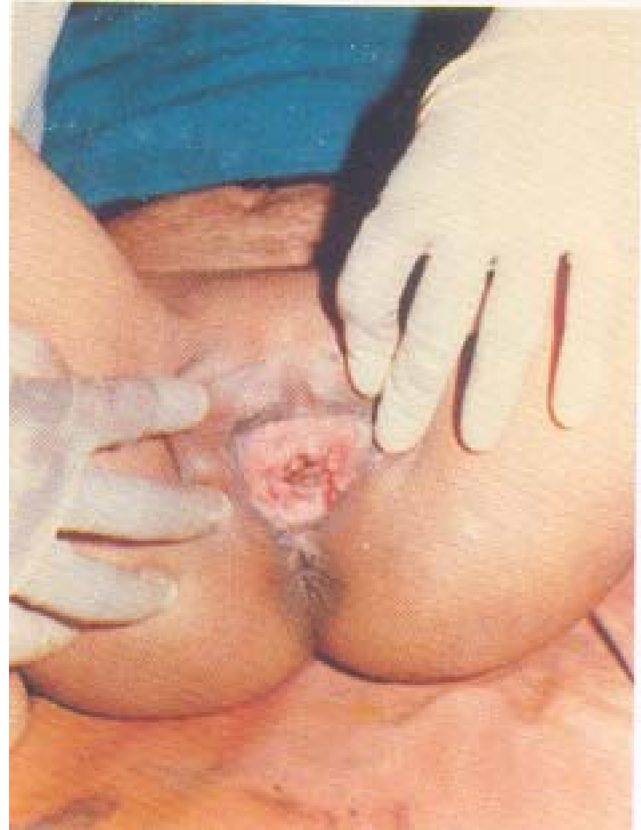


Fig. 2. Labia are pulled apart to reveal a serpigenous ulcer on the posterior vaginal wall External os cervix can be seen in the background

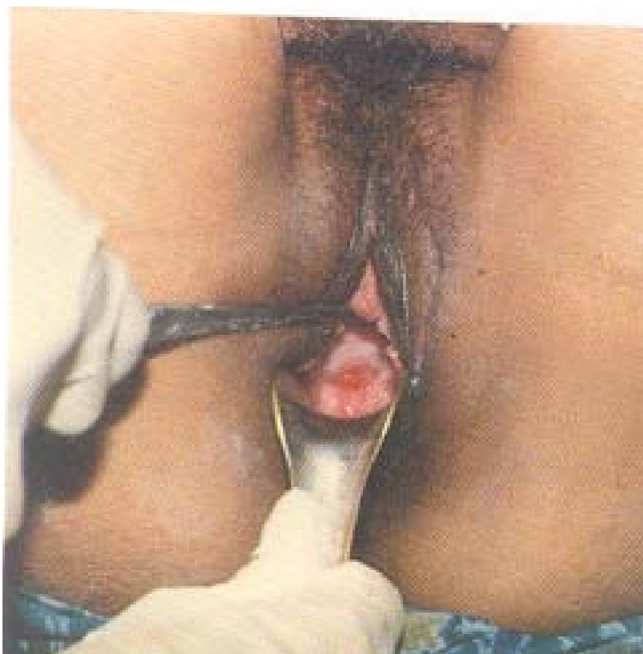


Fig. 1 Showing an ulcerative lesion of the os cervix with irregular edges and yellow base A portion of the external os is thickened and oedematous

involved m 90 to 100% cases, uterus m 50 to 60%, ovaries in 20 to 30%, cervix m 5 to 10%, vagina and vulva m 1 to 2% of the cases Myometrium gets involved very rarely We have seen only one case of myometrial tuberculosis

SIGNS AND SYMPTOMS

Till date, we have analysed 270 histopathologically proved cases of genital tuberculosis A majority belonged to the third decade of life The disease was more common m nulhparous women followed by women having more than 3 children with the last

Table 2. Common presentations

Presentation	No.	Percent 452
Primary infertility	122	
Secondary infertility	35	132
Pelvic pain	49	180
Leucorrhoea	70	260

Some had multiple presentations

Table 3. Associated tuberculosis lesions

Pulmonary	31	116
Abdominal	12	4..4%
Skeletal	4	1.2%
Glandular	2	0.8%

child birth within the previous year.

As regards presentations, some cases may not have any symptom at all while in others symptoms may be nonspecific (Table 2). Non-specific symptoms, like primary and secondary infertility are complained of by 58% cases, pelvic pain by 18% and leucorrhoea by 26% of cases.

The predominant symptom (*43%)* is secondary amenorrhoea. Among other common symptoms are oligomenorrhoea (11%), menorrhagia (17%) etc.

Palpation of the abdomen may reveal a doughy sensation due to tubercle formation on the intestinal and parietal peritoneum. On pressure palpation, a dull pain is elicited. The most significant signs are a pelvic mass and an unhealthy cervix, 21% of the former and 17% of the latter, in cur series.

Tuberculous lesions elsewhere in the body were seen in about 18% of cases in our series (Table 3). The association was perhaps low because such lesions may have become quiesccent by the time genital manifestation occurred.

From our different studies, it was noted that tuberculosis of the genital tract is comparatively common in a certain class of women, the so called high risk group. Women who have a family history of tuberculosis, chronic pelvic pain associated with infertility, past history of tuberculosis, secondary amenotrhoea associated with infertility, and women having an adnexal lump, alone or associated with infertility should be taken as the high risk group and investigated thoroughly.

About 20% of patients with gejnital tuberculosis give a history of tuberculosis in their immediate family. On careful questioning, about 30 to 40% might admit that they had had pleurisy, peritonitis, osseous or pulmonary tuberculosis in the past. Infertility associated with an adnexal lump is due to tuberculosis in about 44% of cases. Tuberculin test and ESR have diagnostic role to play in looking for the association. A careful evaluation of the chest roentgenogram by a trained chest physician is important for locating small or healed lesion, a negative chest X-ray does not rule out the possibility of genital tuberculosis.

Endometrial curettage

A thorough curettage is a must for diagnosis. The curettage material is divided into 3 portions : One portion is sent for histopathological study, another for culture and sensitivity test and the third portion should be sent for guinea-pig inoculation. However, animal inoculation is seldom done as in most places this facility is not available.

A typical tubercle found in the histopathological examination is diagnostic. Endometrial aspiration cytology is characterised by the presence of epithelioid cells, giant cells, and plenty of histiocytes in the smear. **Of course, aspiration cytology examination has many advantages : it can be done in the O.P.D; it is inexpensive and permits direct inoculation on the culture medium.** In one of our studies, out of 250 gynaecological cases, 15 were cytology positive as corroborated by histopathology[8]. Aspiration cytology can serve as a good screening procedure.

Examination of menstrual blood by direct smear for mycobacterium tuberculosis gives very poor results.

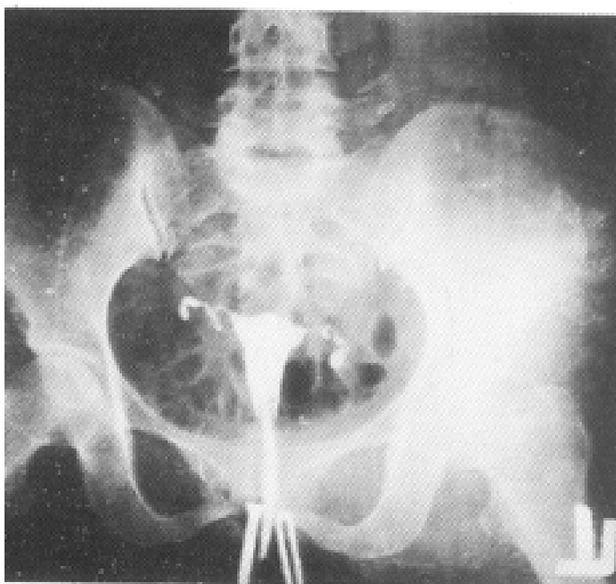


Fig. 3. Showing beaded fallopian tubes on both the sides and tobacco pouch appearance on left side on hysterosalpingography Uterus appears to be normal

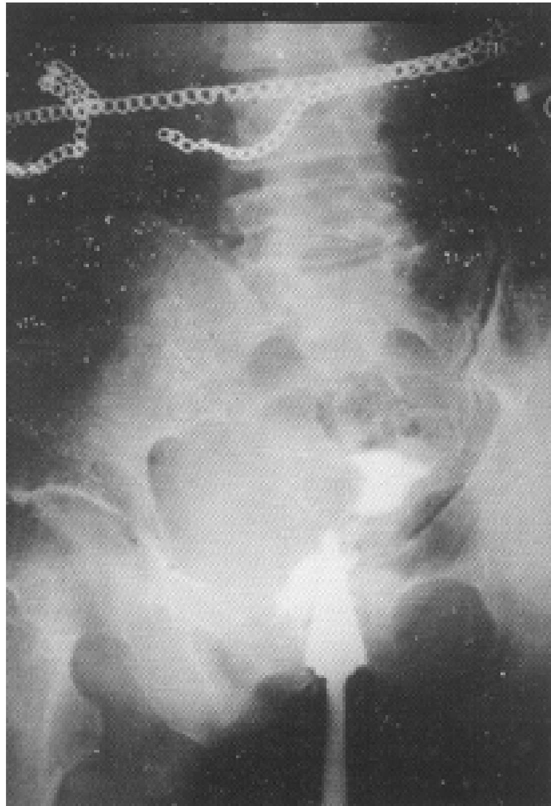


Fig. 4. Hysterosalpingography shows tobacco pouch appearance on left tube and serrated endometrium of Uterus

Hysterosalpingography

When ovaries or the tubal walls are calcified, we get a good picture but the classical picture of tuberculosis is beaded tubes or lead pipe and tobacco pouch appearance of the tube The uterine cavity is distorted in some cases but in others there is serrated endometrium (Figs 3 and 4)

Laparoscopy and Laparoscopic Biopsy

The most frequently used tool for the diagnosis of genital tuberculosis is laparoscopy The diagnosis is quite obvious when tubercles are present A biopsy taken from the site will confirm the diagnosis What is commonly encountered is salpingitis , oophoritis or a tubo-ovarian mass The signs that may help clinch the diagnosis are presence of free peritoneal fluid (looking like blood), inflamed uterus, blue uterus, caseation (mainly in the pouch of Douglas), pensalpmgitis, and on chromopertubation, the dye does not flow freely but drips And sometimes, omentum is found completely adherent to the abdominal organs, which calls for great caution in proceeding further

Hysteroscopy

Tubercles, microcaseation, distorted ostium, caseous material coming through the ostium, distorted uterine cavity, are some of the findings on hysteroscopy Biopsy material can also be obtained Endosonography is of not much help

A positive histopathological report or isolation of the *Mycobactenum tuberculosis* or definite positive findings in hysterosalpingography only should be used before treating a case as one of genital tuberculosis

TREATMENT

Treatment is usually chemotherapy A chest physician should always be consulted for planning and continuation of treatment Nowadays short course chemotheraphy is preferable for its shorter duration and better patient compliance The 2 EHRZ, 4 HR or 2 EHR, 7 HR regimens, with variation here and there could be used We add steroids, if the patient has infertility and there is no active lesion m the lungs

After 6 or 9 months of treatment, a dilatation and curettage is carried out to check up endometnal conversion In a majority, menstrual symptoms return to normal **If the patient does not conceive after one year of completion of therapy, hysterosalpingography and laparoscopy are performed again. Though tubal patency may have been restored, the tubes remain rigid and beaded in most. The conception rate in genital tuberculosis is very poor.** Sutherland, in his series of 709 cases reported conception occurring in 13% only[9] Schaffer, in a review of 7000 cases, found that only 155 cases had full term normal deliveries, 67 cases had abortion and 125 had ectopic gestation In 31 of the 155 cases, the management of tuberculosis was well documented[10] From our 270 cases, 7 had full term normal delivery, three had ectopic pregnancy and 8 had abortions Based on the reports in the literature and from our own experience, we feel that successful pregnancy is unlikely after tuboplasty, so such patients could go in for in *vitro* fertilisation and embryo transfer

Before the chemotherapeutic era, surgery was the mainstay for treatment of gynaecological tuberculosis but now surgery hits no role to play except where recurrent pelvic pain, persistence of the pelvic lump, recurrence of endometrial tuberculosis, excessive bleeding and persistence of tuberculous sinus are present.

Total hysterectomy with bilateral salpingo-ophorectomy is the operation of choice, under proper chemotherapy, both prior to and after the operation. Sutherland operated on 91 cases without any complications[9]. In our series, surgery was resorted to in 30 cases, only laparotomy was done in 21 and radical surgery in 9 cases.

To conclude, genital tuberculosis among females is fairly common. With the advent of HIV epidemic, tuberculosis as such has increased the world over. This is likely to have an impact on genital tuberculosis too. This calls for a more diligent and persistent search for genital tuberculosis in the high risk group.

REFERENCES

1. Rao K.N. History of Tuberculosis in Text book of Tuberculosis - 2nd Edition 1981. Vikas Publishing House.
2. Broune, A.W. and Willium L.M. Genital tuberculosis : Recent advances in Obstetries/Gynaecology 2nd edition, 10th Vol., 1962, London.
3. Tripathy S.N. and Tripathy S.N. Gentital affection in pulmonary tuberculosis. International J. Ob/Gyn, 1984; 19,4.
4. Tripathy, S.N. and Tripathy S.N. Genital affection in pulmonary tuberculosis Ind. J. Tb. 1991, 38, 191.
Tripathy S.N. and Tripathy S.N. Endometrial Tuberculosis, JIMA, 1987, 85, 5.
6. Tripathy S.N. and Tripathy S.N. Cervical tuberculosis : A clinicopathological analysis; Paper presented at the National Tuberculosis & Chest Diseases Conference, New Delhi -1991.
7. Tripathy S.N. and Tripathy S.N. Vaginal tuberculosis, Ind. J. of Ob/Gyn, 1986, 36, 4.
8. Tripathy, S.N. and Tripathy S.N. The scope of aspiration cytology in the detection of endometrial tuberculosis, Paper presented at the 38th All India Tuberculosis and Chest Diseases Conference, Goa-1983.
9. Sutherland A.N., Surgical treatment of tuberculosis of the female genital tract. British J. of Ob/Gyn 1980,87,610.
10. Schaeffer G. Female Genital Tuberculosis. Climical Ob/Gyn, 1976,19,1.

FATE OF PULMONARY TUBERCULOSIS PATIENTS DIAGNOSED IN A PREVALENCE SURVEY*

A socio-epidemiological follow up after five years

Sophia Vijay[1], M.S. Krishna Murthy[2] and N. Srikantaramu[3]

Summary. The study group constitutes 86 `cases' and 341 `suspects' diagnosed in a tuberculosis prevalence survey. The area of the survey was under cover of the National Tuberculosis Programme (NTP) for more than 20 years. The observed fate of these cases after five years was : dead 58.3% , culture negative 30% and culture positive 11.7%. Comparison of these rates with age standardised rates of `cases' followed up after 5 years in an adjacent area, where control measures were not undertaken revealed that both these rates were not statistically different. The findings suggest that the same natural dynamics of tuberculosis as observed under the non-intervention situtation, obtained in the study area as well, despite the latter being under the cover of NTP for so long.

Suspects, epidemiologically, proved to be a low priority group as the breakdown rate ob-served among them over five years was as low as 3.3% again similar to the findings in the non-intervention area of a longitudinal survey.

A sociological enquiry revealed that cardinal symptoms of tuberculosis persisted even after five years in 65% of cases and 55% of suspects. Action taking behaviour indicated that more than half the patients, reported to governement health centers for remedial measures, while none of the `asymptomatics' approcehed any health center. These findings suggest that `symptoms' are the driving force for patients to seek medical advice and the NTP still has the potential to bring these self-reporting cases within its network.

INTRODUCTION

Knowledge about the epidemiological trend of pulmonary tuberculosis is enriched by prevalence surveys done from time to time in randomly selected populations. The study of fate of bacteriological cases diagnosed during such surveys over a period would help to understand the disease dynamics in an area. During a non-intervention period, the fate of cases reflects the natural dynamics of the disease and comparison of the same under control measures is likely to provide an insight into the effectiveness of the control programme.

The National Tuberculosis Institute (NTI) Bangalore, had reported[1] on the fate of cases discovered over a period of five years during the longitudinal study undertaken in rural areas of Bangalore district (1961-1966), when National Tuberculosis Programme (NTP) was not applied, being still in the formative stage. The present study was carried out in an adjacent peri-urban area where NTP was implemented in early seventies. Comparison of five year fate of cases in these studies can provide information on the impact of the current anti-TB measures in the study area.

The presence and intensity of symptoms induced by the disease is the initial force driving persons to seek medical advice. The choice of a particular source for remedial measures depends on the patient's socio-economic status, available health infrastructure in the area, besides the motivation derived from close associates. Failure to get the expected relief from a source compels a patient to shop in search of relief from alternative health sources.

Keeping in view the above factors, a socio-epidemiological study was undertaken after an interval of five years to understand, concurrently, the fate of cases and utilisation of existing health services by them over a period of time.

*Paper presented at the 52nd National Conference on Tuberculosis,and Chest Diseases, Ahmedabad, 19-22 December, 1997

1. TB Specialist, 2. Senior Investigator & 3. Statistical Assistant

National Tuberculosis Institute, Bangalore

***Correspondence**:* Director, National Tuberculosis Institute, No. 8, Bellary Road, Bangalore - 560 003

OBJECTIVES

The main objectives were to study among 'cases' and 'suspects'.

- fate, in terms of disease status and deaths, after five years.
- their health seeking behaviour between surveys, the current symptom status and probable cause of death, by sociological enquiry.

DEFINITIONS

Case : Person, having radiological abnormality and/ or cardinal symptoms of tuberculosis for 2 weeks or more and sputum culture positive for *M. tuberculosis,* irrespective of sputum smear status. *Suspect:* Person whose X-ray has been interpreted as active TB by two readers and whose sputum culture is negative for *M. tuberculosis.*

METHODOLOGY

Survey Procedure : Tuberculosis prevalence survey (Survey I) was carried out between August 1986 and October 1989 in 60 villages selected by simple random sampling, located between 19 to 24 km radius around the centre of Bangalore city (peri-urban area)[2]. The total population registered in all age groups was 56,293.

During Survey I, among 35,653 eligible persons aged $\geq$ 15 years, all those available were interviewed to obtain information regarding the presence of cardinal symptoms (CS) of pulmonary tuberculosis viz., cough, fever, chest pain and hemoptysis. Spot sputum samples were obtained from persons reporting CS for 15 days or more. These samples were subjected to smear microscopy and culture and sensitivity examinations for *M. tuberculosis.* Besides, the entire eligible population was also subjected to 70 mm photofluorographic examination (MMR) irrespective of their symptoms status. The MMR films were interpreted by two standard readers independently, and on disagreed films, opinion of an umpire reader was obtained. From persons showing radiological abnorrpality, as interpreted by any of the readers, spot sputum samples were collected and processed as stated above.

Eighty six (86) 'cases' and 341 'suspects' diagnosed from the examination of 30,141 persons aged 15 years or more during Survey 1, formed the study group for the current investigation.

These 60 villages were re-surveyed after an average interval of five years (Survey II) to estimate the prevalence of tuberculosis infection and disease in the paediatric age group. During this survey, census information of cases/suspects diagnosed in Survey I, was updated. The available cases and suspects were then subjected to MMR and one spot sputum examination. Results of these examinations were interpreted by adopting the same procedure as followed in Survey I.

Procedure for Sociological Interview at Survey II: A detailed list having identification particulars, current residential and previous symptom status of cases and suspects, was made available to Social Investigators (SIs) in pre-designed schedules. On completion of epidemiological investigation in a village, Sis contacted the available cases/suspects at their residence. Establishing a good rapport with the patient, the interviewer collected information on current symptoms with duration, action taken for relief of symptoms, sources approached, with treatment received between two surveys. Whenever required, deep probing was done to elicit the information. For cases/suspects, who were reported dead between surveys, the probable cause of death was ascertained from a responsible household member, following the procedure adopted by Census of India.

FINDINGS

1. Fate of cases and suspects : Epidemiological investigation

Cases : The fate of 60 (69.8%) cases out of the 86 detected during Survey I could be studied at Survey

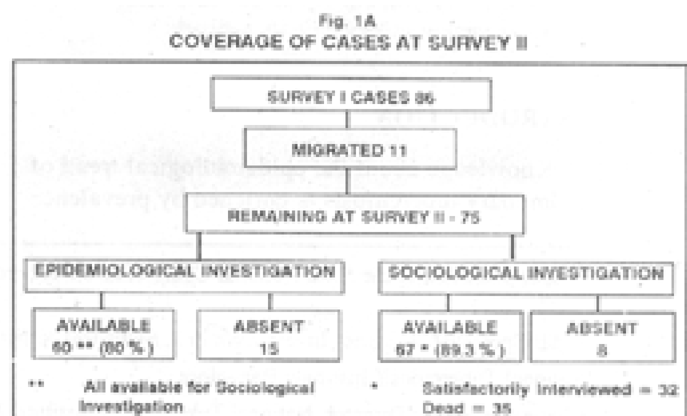


Fig. 1A
COVERAGE OF CASES AT SURVEY II

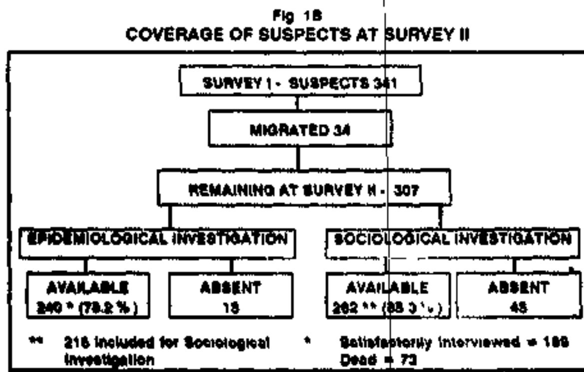
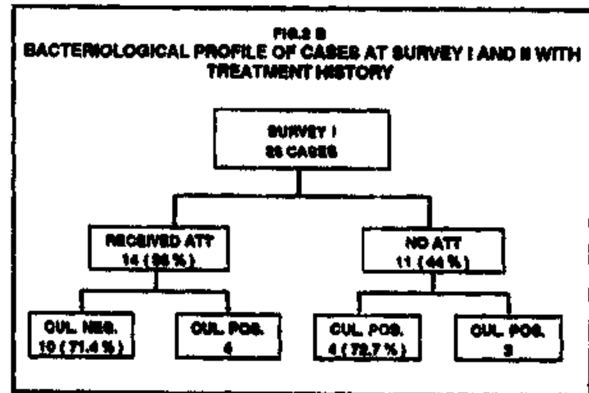


Figure 1



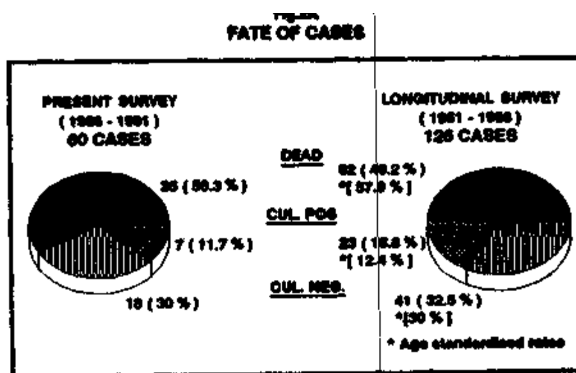
II (Fig. 1A). Among these, 35 (58.3%) cases were reported dead, 18 (30%) became culture negative, while 7 (11.7%) were culture positive, after an interval of about 5 years (Fig. 2A).

Drug resistance pattern of cases at Surveys I & II: Of the 18 cases, who became culture negative at Survey II, 13 were initially sensitive to INK while 5 were INH resistant. However, treatment history revealed that 6 of the sensitive and 4 of the resistant cases had received anti-TB treatment (ATT). Of the 7 cases who continued to be casesat Survey II, all were sensitive to INH initially, but 3 of them developed resistance to INH at Survey II, with 2 reporting history of ATT.

Influence of ATT : Treatment history for all the 25 cases available at Survey II revealed that 14 of them had received ATT of varying durations, ranging from 3-30 months in the interval between surveys. However, culture conversion at Survey II observed among the 'treated' and 'not treated' group was 71.4% and 72% respectively, without significant difference (Fig. 2B).

Suspects : Fate of 240 (70.4%) suspects could be studied at Survey II of the 341 at Survey I (Fig. IB). Among these, 73 (30.4%) were dead, 159 (66.3%) remained culture negative and 8 (3.3%) became culture positive (Fig. 3). The age standardised proportion of deaths among suspects (28.5%) was significantly lower than that among cases (58.7%) (P<0.1).

Bacteriological and radiological profile of suspects at Survey II: Excluding 73 deaths, the results of bacteriological and radiological investigations were available for 167 suspects at Survey II (Fig. 4). Among these, in 121 (72.4%), comprising 6 of the 8 suspects who became culture positive and 115 of the 159 suspects who remained culture negative, there was agreement between culture results and radiological interpretation at Survey II (Fig. 3). Further, in 44 (26.3%) of the 159



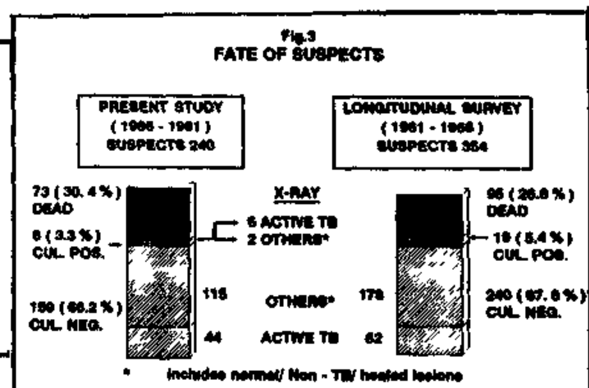


Table 1A. Distribution of "Cases " by symptoms, action taken along with treatment sources approached

No. of with source	action contacted	Symptons status	survey II		
		Cardinal 21 (65.6)		Others 1	No symptoms 10
1st	Private	9 (45.0%)	20'	1	—
action	Government	11 (55.0%)	0		
IInd	Private	2	13	—	—
action	Government	11			
IIIrd	Private	2	9	—	—
action	Government	7			
IVth	Private	1	4	—	—
action	Government	3			
All	Private	14 (30.4%)	46	_	—
actions	Government	32 (69.6%)**	46	—	—

**P<0.01

* Among satisfactorily interviewed : 32

suspects who remained culture negative, even after five years, the radiological shadows were still interpreted as active tuberculosis.

2. Symptom status & action taking pattern : Sociological Investigation

Cases : Information on presence of symptoms, action taken and probable cause of death could be obtained for 67 (89.3%) cases, comprising 32 satisfactorily interviewed and 35 reported dead at Survey II (Fig. IB). Of the satisfactorily interviewed, 21 (65.6%) cases reported CS of tuberculosis, and in 18 cough was the prominent symptom. Perusal of the action taking behaviour for relief of symptoms indicated that initially 20 (95.2%) had approached some health facility. These 20 cases, in all, had made 46 attempts to seek medical relief in the intervening period between the surveys. During these attempts, they availed services from government and private agencies, 32 (69.6%) & 14 (30.4%) times respectively with significant difference among them ($P < .01$). Although at the first action, they had shown equal preference for government and private health facilities, the overall health seeking behaviour indicated preference for government health centres (Table 1A). Ten cases reporting 'no symptoms' at Survey II, did not take any action.

Culture conversion action taken : Culture conversion to negative status observed among 'action taken' and 'no action taken' groups at Survey II was 71.4% and 75.0% respectively, showing no significant difference (Table IB).

Suspects : Sociological information was available for 262 suspects including 189 satisfactorily interviewed and 73 dead for whom the probable cause of death could be obtained (Fig. IB). Of these 189 suspects, 104 (55%) reported C.S. of various durations at Survey II. Further, 83 of those with CS had contacted different health sources for relief 170 times, availing services, 89 and 81 times from private and government health sectors respectively, between the two surveys. Though initially (first action), the suspects approached the private sector, the overall pattern revealed equal preference for private and government sources (Table 2A). Even among suspects, the non symptomatics' had not approached any health centre.

Table IB. Culture conversion among "Cases" at Survey II by action taken

	For treatment	
	Action taken	No action
	21	11
Results available	14	8
Culture Negative	10 (71.4%)	6 (75.0%)

Table 2A. Distribution of "Suspects" by symptoms and action taken along with "treatment" sources approached

No. of action with sources contacted		Symptom status at Survey II**			
		Cardinal 104(55.0)		Others 8	No symptoms 10
1st action	Private	54* (65.0%)	83	5	—
	Government	29* (35.0%)	2		
IInd action	Private	18	52	2	—
	Government	34		0	
IIIrd action	Private	12	25	—	—
	Government	13	10		
IVth action	Private	5			
	Government	5			
All actions	Private	89 (52.3%)	170	—	—
	Government	81 (47.2%)			

* P < 0.01

* Among the suspects satisfactorily:189

Table 2B. Breakdown among "Suspects" at Survey II by action taken

.	For treatment	
	Action taken 90	No action 99
Results available	69	70
Culture positive	5 (7.2%)	4 (5.7%)

Culture conversion by action taken :Culture results available for suspects at Survey II revealed that proportion of suspects breaking down as culture positive cases was 7.2% in `action taken' and 5.7% in `no action taken' group showing no significant difference (Table 2B)

3. Deaths among tuberculosis patients

Of the 35 cases and 73 suspects reported dead after five years, in 14 (40%) cases and 25 (34.2%) suspects death could be attributed to tuberculosis as inferred by Sis from the detail > of verbal autopsy collected by proxy interview (Table not presented). However, valid conclusions could not be drawn from the available data.

The death rates observed among different age group of cases was similar, but among suspects the death rate in the age group *55+* was significantly higher compared to that in other age groups (p < .05) (Appendix).

Appendix
Distribution of deaths among Cases and Suspects by age

Age	Cases		Suspects	
	No.	Death rate	No.	Death rate
15-34	7	4 (57.1%)	26	3* (11.5%)
35-54	28	16 (57.1%)	75	6* (7.7%)
55+	25	15 (60.0%)	139	64* (45.1%)

* P < 0.05
** P<0.05

DISCUSSION

The study area was under the cover of NTP for more than two '"decades. Besides, with the geographic proximity of the study area to Bangalore city, the population had better access to the well developed network of health services available in the city, including the private sector facilities.

The factors that could influence the fate of cases over time are the natural dynamics of the disease and the effect of control measures in the area,

the criteria of diagnosis and the period of observation (5 years) in the present study and the Longitudinal study[1] were similar. Hence, comparison of these two seperate findings on fate of cases becomes valid.

The status of cases in terms of death and bacteriological conversion after five years in the present study did not show significant difference at 5% level with the corresponding age standardised rates of the Longitudinal study (Fig. 2). Similarly, the observed fate of suspects in these two studies also failed to show significant difference[4].

Further, Jagota et al have reported fate after five years, of cases with poor treatment compliance as 49% dead, 38% sputum culture negative, and 13% sputum positive[5]. These rates were also similar to the rates observed in the current study.

From all the above findings and **the similarity observed in culture conversion among cases, irrespective of action taken and ATT received, it could be inferred that in the NTP area study had no influence on fate of cases.**

Inspite of adopting the standard technique for X–ray interpretation, 26.3% of the suspects continued to be labelled as having active disease after five years (at Survey II). This perhaps supports the contention of the inherent limitation of X-ray interpretation to ascertain activity of the lesion. **Besides, the lower standardised death rates observed among suspects (28.5%) compared to cases (58.7%) and a breakdown rate of only 3.3% over five years, suggests that suspects could be considered as epidemiologically low priority group. This supports the programme policy of subjecting suspects to repeat sputum examination before initiating them on treatment.**

The symptom status at Survey II revealed that more than half of the cases/suspects reported CS despite majority of them having sought remedial measures between surveys. Persistence of chest symptoms after five years has also been reported among 44.8% of cases in a DTC treated by Balasangameshwar et al[6]. Even with good health facilities available in the study area, a large proportion of patients reported persistence of symptoms.

Either dissatisfaction with treatment or persistence of symptoms had resulted in cases and suspects changing the source of treatment frequently. Nevertheless, the proportion of suspects having CS seeking advice and frequency with which they changed the source of treatment was relatively less compared to cases. Cases/suspects having no symptoms had not approached any health agency indicating that symptoms were the driving force for seeking medical advice and treatment.

The first point of contact for 55% of the cases seeking relief was government health facility. But, among suspects, the initial preference was for private sources (65%). Considering the overall action taking behaviour of cases and suspects, it was found that the cases had preferred the government source. From earlier studies in adjacent area, Banerji *et al* and Radha Narain *et al*[8] had reported that 50% of the cases approached government facility for alleviation of symptoms. **It is obvious from the present study findings that even after 3 decades, the pattern of health seeking behaviour of patients in these areas has remained the same in spite of the private sector having expanded by leaps and bounds.**

Valid conclusions could not be drawn as to the probable cause of death among cases/suspects by verbal autopsy. The limitations of adopting such technique may be due to respondents' recall, social stigma related to tuberculosis and interviewer's inability to probe the matter. However, the observed significantly higher death rate among suspects aged > 55 years may be attributed to advanced age rather than tuberculosis.

ACKNOWLEDGEMENT

The authors are grateful to Dr (Mrs) P. Jagota, Director, NTI and the faculty members for their valuable suggestions. They are also grateful to Dr. A.K. Chakraborty, former Addl. Director, NTI under whose guidance the study was planned and conducted. We gratefully acknowledge the services rendered by the staff of Sociology and Epidemiology Sections for carrying out the field work meticulously, Mrs Kamala Rathnaswamy, Mrs B. Vijayalkshmi, and Mr P. Perumal for their secretarial assistance and Mr B. Narayana Prasad, draughtsman for graphics.

REFERENCES

1. National Tuberculosis Institute, Bangalore : Tuberculosis in a rural population of south India : A five year epidemiological study, Bull Wld Hlth Org., 1974,51,473.
2. Chakraborty, A.K., Channabasavaiah, R., Krishna

Murthy, M.S., Shashidara, A.N., Krishna Murthy V.V. and Choudhary K. Prevalence of pulmonary tuberculosis in a peri-urban community of Bangalore under various methods of population screening, Ind J Tb 1994,41, 17.

3. Raj Narain, Ramanatha Rao, Chandrasekhar, Pyare Lal. Fate of cases diagnosed in a survey : Proceedings of the 21ft Tuberculosis & Chest Disease Workers' Conference, Calcutta, Feb. 1966.
4. Krishna Murthy V.V. Prevalence, incidence and fate of suspect cases of tuberculosis. NTI Newsletter, 1982,90,75
5. Jagota, P, Venkatarama Gupta E.V. and Channabasavaiah R. Pate of smear positive patients of pulmonary luberculosis at an urban District Tuberculosis Centre, five years after treatment; Ind J Tub, 1994,41, 223.
6. Balasangameshwara, V.H., Jagota, P., Channabasavaiah R. Persistence of chest symptoms in smear positive pulmonary tuberculosis patients treated with standard and short course chemotherapy regimens under a District Tuberculosis Programme - a five year follow-up; Ind J Tub; 1996,43, 143.
7. Banerji D. and Andersen, S. 1963. A sociological study of awareness of symptoms among persons with pulmonary tuberculosis; Bull Wld Hlth Org; 1963,29,665.
8. Radha Narain, Prabhakar S., Susy Thomas, Pramila Kumari, S., Suresh, T. and Srikantaramu, N. A sociological study of awareness and action taking of persons with pulmonary tuberculosis (Re-survey) Ind J Tub; 1979, 26, 3, 136.

Original Article *Ind J Tub, 1998, 45, 207*

REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME : AN URBAN EXPERIENCE

Sunil Bhat[1], Rohit Sarin[2], Anand Jaiswal[3], Anil Choudhary[4], Neeta Singla[5] and Subroto Mukherjee[5]

Summary. Under the National Tuberculosis Programme in India, treatment completion rates of only 30% to 40% were achieved, using the standard chemotheraphy refimens. This was particularly difficult to achieve in the bigger cities because of no primary health care delivery system there. This shortcoming was addressed with the introduction of the Revised National Tuberculosis Control Programme and the use of short course regimes under the DOTS strategy.

A part of the domiciliary treatment area of the LRS Institutes of Tuberculosis & Allied Diseases was used to test the feasibility of the DOTS strategy in an urban setting.

The study lasted from October 95 to September 97. It was found that case-finding went up to 70% of the "estimate"; the smear positive to smear negative ration among the newly discovered cases was 2:1. Sputum conversion among new smear positive cases was nearly 81% and the cure rate was 80%

INTRODUCTION

The National Tuberculosis Programme (NTP) has been in operation in India since 1962 but no epidemiological impact has been reported Meanwhile, an increase in the absolute number of patients has occurred because of the increase in population Besides, there is the impending threat of TB-HIV co-infection and the emergence of multi-drug resistant tuberculosis

An in-depth review of the NTP was conducted in 1992 by a team comprising national and international experts, leading to the formulation of a revised strategy named Revised National Tuberculosis Control Programme(RNTCP)[12] The revised strategy emphasizes case-finding through quality sputum microscopy and putting the patients on Directly Observed Treatment with Short Course Chemotherapy (DOTS) to achieve cure rate of at least 85%.

The revised methodology is different for rural and urban areas because of the difference in demographic and health infrastructure characteristics[3] In the urban setting, health services in general, and tuberculosis services in particular are provided through specialized institutions because primary health care infrastructure is not well developed And, organised tuberculosis services have not evolved in cities, as was envisaged under NTP

In Delhi, the tuberculosis services are offered by 13 Area TB clinics, of which 9 are under the Municipal Corporation of Delhi (MCD), currently controlled by the Delhi State Government The L R S Institute of Tuberculosis & Allied Diseases runs one of the 13 Area TB clinics and has been assigned a definite geographic area for offering domiciliary services

With the introduction of the revised strategy in Delhi, a part of the said domiciliary treatment area was taken up (under phase II extension of RNTCP) for testing the operational feasibility of the strategy in an urban setting

METHODOLOGY

Project Area

The total population alloted to the Institute is more than 1 million (Census, 1991), of which 700,000 population was taken under the RNTCP Eight TB treatment centers were opened for the population of 700,000 and a TB health visitor was

Paper presented at the 52nd National Conference on Tuberculosis and Chest Diseases, Ahmedabad 19-22 December, 1997

1 Senior Research Officer, 2 Assistant Medical Superintendent, 3 Chest Physician, 4 Medical Officer, 5 Research Officer

L R S Institute of Tuberculosis and Allied Diseases, New Delhi

***Correspondence**:* Dr Sunil Bhat, L R S Institute of TB & Allied Diseases, Sri Aurobmdo Marg, New Delhi - 110 030

posted at each centre. Sputum collection was done at those centres but specimens were brought to the central laboratory of the Institute for microscopy. DOTS was applied in each centre individually.

TB Treatment Centres

The identification of the sites for establishing the 8 out-reach facilities was decided on the basis of maximum "feeder area" in respect of tuberculosis patients who are seeking treatment at the Institute's OPD. Six centres were set up within the existing Government health care facilities while two were put up in rented premises provided by a non-government organisation. All the centres were located within twenty kilometer radius from the Institute.

Study period

The activities carried out from October 1995 till September 1997 were analysed as 2 yearly cohorts.

Activities

As per the operational guidelines of RNTCP, issued by the Government of India, all the symptomatics who reported to the Treatment Centres were told to submit three specimens of sputum (one an early morning collection) for microscopy. However, a departure was made from the guidelines in that the slide-making and examination of the slides was done at the Institute's main laboratory.

In all, 8 Health Visitors, one for each Treatment Centre, and one Senior Treatment Supervisor (STS) from the Institute performed the field activities. In addition, three Laboratory Assistants and one Senior Tuberculosis Laboratory Supervisor (STLS) of the Institute's laboratory performed sputum microscopy and ensured quality control. The job responsibilities of these categories of staff were as per the operational guidelines for the RNTCP.

FINDINGS

Case -finding

Over the two year period, 867 tuberculosis cases were found in the first year (October 96 - September 96) and 1308 in the second year (October 97 - September 97). The respective numbers of new smear positive cases were 345 and 464, as compared with the estimated case-load of over 10 thousand cases hi the community, of which 2,800 would be infectious, on the basis of the National Sample Survey.

The different types of patients found are shown in Table 1 and the age sex distribution of the new smear positive cases is shown in Table 2.

A total of 2175 patients were enrolled during the two years. It can be seen that the new smear positive patients decreased from 40% in the first year to 35% in the 2nd year while the retreatment cases increased from 23% to 30%. The proportions of smear negative and extra-pulmonary cases, however, remained unchanged. Male : Female ratio was 2 : 1 and a majority of the patients (82%) were 16 to 44 years old. In both the years, the ratio of new smear positive to new smear negative cases was as high as 2 : 1.

Table 1. Distribution of cases found according to clinical type and year

Year	Pulmonary					Extra-pulmonary	Total
	New smear	For retreatment			New smear negative		
		Relapse	Others	Total			
First	345 (40%)	63	141 (23%)	204	167 (19%)	151 (18%)	867 (100%)
Second	464 (35%)	79	313 (30%)	392	232 (19%)	220 (16%)	1308 (100%)
Total	809 (37%)	142	454 (27%)	596	399 (18%)	371 (18%)	2175 (100%)

Table 2. Age and sex distribution of new smear positive cases according to year

Year	Age groups																Total
	0-15		16-24		25-34		35-44		45-54		55-64		>64		Total		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
First	3	11	81	35	80	30	42	12	20	3	14	7	5	2	246	99	345
Second	6	10	115	7J	87	49	40	15	30	8	16	4	5	2	299	165	464
Total	9	21	196	112	167	79	82	27	50	11	30	11	10	4	545	264	809

Table 3. Sputum conversion at 3 months among new and retreatment smear positive cases

Year	Category of smear positives	Number	Sputum status at 3 months		
			Negative	Positive	N.A.
First	New	345	289 (84%)	32	24
	Retreatment	68	41	19	8
Second	New	464	364 (78%)	61	39
	Retreatment	123	73	42	8

Note : Not all retreatment cases were sputum positive; N.A. - Result not available

Progress

Sputum conversion

Conversion of the new smear positives to negative status at 3 months was §4% during the first year and 78% in the second year, giving an average rate of sputum conversion at 3 months of 81% (Table 3). The average sputum conversion at 3 months of retreatment cases who were smear positive at the time of enrolment was 60%.

Treatment outcome

The treatment outcome of all the patients enrolled during the first year is shown in Table 4. New smear positive patients had cure/treatment completion rate of 80% and failure rate of 9%. Retreatment cases had cure/treatment completion rate of 65% and failure rate of 13%. Death rate was 6% in retreatment cases compared with 1% in new smear positive cases.

DISCUSSION

Compared with the situation under the NTP, i.e. inefficient case-holding and poor treatment completion with standard chemotherapy, the Revised National Tuberculosis Control Programme

Category	Number	Treatment outcome					
		Cured	Treatment completed	Died	Failed	Defaulted	Transfer
New smear positive	345	256	20	5	30	32	2
Retreatment	204	123	10	12	33	26	—
New smear negative	167	—	151	3	3	9	1
Extra-pulmonary	151	—	140	3	3	5	

Annexure

Estimated numbers of tuberculosis patients, based on the presumed Annual Risk of Tuberculosis Infection of 1 % (Styblo Model[4]):

□	New Smear positive cases will be	50 (37%)/lakh/year
□	New smear negative cases will be	50 (3 7%)/lakh/year
□	Retreatment cases will be 50% of new smear positives	25(19%)/lakh/year
□	EP & paediatric cases will be 20% of new smear positives	10 (7%)/lakh/year
		135(100%)/lakh/year

- Total no. of cases under ARI of 2 =135 * 2 = 270/lakh population/year
- Total no. of cases for our 7 lakh population = 270 x 7 = 1890

(RNTCP), introduced in 1993, provided directly observed intermittent short course regimens with which high cure rates of around 90% could be obtained[4,5].

The present study was conducted to test the technical soundness and operational feasibility of the RNTCP strategy in an urban context, in the 700,000 population living in an area which forms part of the domiciliary treatment area allotted to the LRS Institute of Tuberculosis and Allied Diseases, New Delhi. The target for case-finding under the RNTCP is 70% of the 'estimated' cases during the two year study period. The "estimated" number of cases to be found was calculated on assuming an average ARI of 2 and using the Styblo[4] equation of 50 new smear positives added every year for each ARI of 1. Thus, for 700,000 population and an ARI of 2, the annual incidence of smear positives came to 700. Further, the proportions of retreatment, smear negative and extra-pulmonary and paediatric cases were also calculated based on the guidelines given by RNTCP. (Annexure).

Not only was case-finding improved under "RNTCP but the quality of diagnosis also was much better. The proportion of new cases confirmed bacteriologically was as high as 67%, which is higher than the international standard of quality sputum diagnosis i.e. 50% bacteriological confirmation by smear.

The treatment effectiveness of DOTS was evident from the smear conversion at 3 months among the newly diagnosed smear positives which was about 81%. The treatment outcome ampng new smear positive cases was around 80% cure/ completion rate (Treatment Success Rate). However, smear conversion for retreatment cases was 60% at 3 months. Further evaluation in terms of level of drug resistance, chronicity of the disease, final treatment outcome, failures and deaths in this category is, therefore, required.

This study clearly demonstrates the technical soundness and operational feasibility of DOTS in the urban set up.

ACKNOWLEDGEMENTS

Our thanks are due to Mr. Sunil Kumar Basak, Mr. Bhaskar Bose and Mr. Anand P. Thachil for writing up the text, and the sincere work done by our Health Visitors as well as the laboratory staff.

REFERENCES

1. WHO. Tuberculosis control and research strategies for the 1990s. Bulletin of WHO 1992, 70, 1.17.
2. Sarin R, Dey L.B.S. Indian National TB Programme; Revised Strategy. Ind. J. TB 1995, 42, 95.
3. Chakraborty A.K. *et al.* Prevalence of pulmonary tuberculosis in a peri-urban community of Bangalore under various methods of population screening. Ind. J. Tub. 1'994, 41, 17.
4. Styblo, K. Overview and epidemiologic assessment of the current global TB situation with an emphasis on control in developing countries. Rev. Infec. Dis. 1989,11, Suppl. 2 : 339.
5. Enarson, D. Principles of IUATLD collaborative TB programmes. Bull Int. Union Lung Diseases 1991; 66 (4): 195.

FIELD STUDY TO EVALUATE THE BACTERIOLOGICAL PARAMETERS IN THE DIAGNOSIS OF LYMPHNODE TUBERCULOSIS IN CHILDREN

P. Narang[1], Rahul Narang[2], D.K. Mendiratta[3], S.M. Sharma[4], R. Narang[5] and S. Nayar*

(Received on 2.12.97; Revised version receivedon 9.6.98; Accepted on 10.7.98)

Summary. A study was undertaken to evaluate the efficienacy of histopathology and bacteriology- ical investigations in the diagnosis of lymphode tuberculosis in children. Since hospitals generally get cases with more advanced lesions, a door to door field study was undertaken to pick up early cases as well. A total of 64 children from 35 villages were motivated for biopsy, The tissue obtained was subjected to (i) impression smear examination by Ziehl Neelsen and Auramin 0 staining (ii) culture on 2 Lowenstien Jensen media and one 7H9 OADC liquid medium and (iii) routine histopathology (HP).

A total of 23 (35.94%) biopsied nodes were found to be positive for tuberculosis by any of the three methods; 9 (14.06%) on HP, 13(20.31%) by culture and 21(32.81%) on smear. Addition of smear and culture to histopathology increased the yield of tuberculosis by 21.88% (14 additional cases). Impression smear examination yielded best results, particularly in early cases. This method could prove useful in the peripheral hospitals where other facilities do not exist.

INTRODUCTION

Superficial lymphnode involvement or 'Scrofula' is the most commjon form of extra-pulmonary tuberculosis in children and often presents as a diagnostic dilemma to the clinicians. Seth *et al*[(have stated that lyrrjphadenopathy may be the sole manifestation of the disease without even the associated features of tyw grade fever, loss of weight, cough or other respiratory symptoms. There is no symptom which either by its presence or absence can clinch the diagnosis". The clinician, therefore, has to depend on the various laboratory parameters for confirmation.

In the past, most of the studies on tuberculous lymphadenitis had based their data taking only histopathology as their gold standard'. In the routine hospital practice even today, we find that microbiological investigations for extrapulmonary tissue specimens are hardly ever requisitioned even though Jawahar **et** al[4] have reported 4 culture positive but HP negative cases and Vanaja Kumar **et al**[5] have reported 98% isolation of *M. tuberculosis* from lymphnodes when the specimens were properly transported and cultured on one solid and one liquid medium.

The present study was, therefore, undertaken to compare the results of simple microbiological investigations like impression smear examination and culture with histopathology in the diagnosis of tubercular lymphadenitis, particularly in early cases picked up in a field survey.

MATERIAL AND METHODS

This study was part of an ICMR field study where door to door survey of tuberculous lymphadenitis in children was taken up in 35 villages of Wardha district. A total of 64 children with enlarged lymph nodes were motivated and brought to the hospital for lymphnode excision biopsy. At the time of biopsy, the surgeon, on basis of clinical assessment and parameters like positive Mantoux test, radiology and/or history of contact with a tuberculous case, classified them into clinically tuberculous (33) and clinically non tuberculous (31); and in order to prevent any bias, did not communicate his diagnosis to the laboratory till the time of analysis.

1: Prof. & Head, 2. Post Graduate, 3. Assoc. Prof. Department of Microbiology, 4. Prof. & Head, Department of Pathology, 5. Prof. & Head, Department of Surgery, 6. Director, Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha - 442 102

Correspondence: **Dr** (Mrs) P. Narang, Prof. & Head, Department of Microbiology, M.G.I.M.S., Sevagaram, Wardha 442102

The excised lymphnode was immediately sent to the microbiology laboratory in a dry sterile container where it was cut into two halves along the lonitudinal axis through the hilum with a sterile scalpel and impression smears were prepared from the cut surfaces on to two clean sterile slides for staining by Ziehl Neelsen method and fluorescent staining with Auramine O. One half of the lymph node was then sent in 10% formalin to pathology laboratory for histopathology and the other half was homogenised in a sterile pestle and mortar. A portion of the triturated material was processed for routine bacteriology and fungus isolation, while the rest was concentrated by Modified Petroff's technique[6] and cultured on 2 slopes of Lowenstein-Jensen medium and one tube of Middlebrook 7H9 broth with OADC (oleic acid albumin dextrose catalase) (HiMedia). Both the media were incubated at 37°C for 8 weeks before discarding them as negative. The growth of acid fast bacilli on these media was identified as *Mycobacterium tuberculosis* by standard methods described by Collin and Lyne[7] and Collins *et al*[8].

OBSERVATIONS

Out of the 64 biopsied nodes, 23 (35.94%) were found to be tuberculous by one or more of the three methods, 20 (60.61%) in the clinically tuberculous group and 3 (9.68%) in the non-tuberculous group (Table 1). Histopathology (HP) was positive in 9 (14.06%), culture in 13 (20.31%) and impression smear in 21 (32.81%) cases.

Amongst the 33 subjects clinically suspected to be tuberculous, histopathology was positive in 9

Table 1. Results of different investigations

Clinical Type	Positive by			Total Positive Cases
	Smear	Culture	Histo-pathology	
Ttiberculous n = 33	18 (54.54)	10 (30.30)	9 (21.27)	20 (60.61)
Non-TB n = 31	3 (9.67)	3 (9.67)	0	3 (968)
All n = 64	21 (32.81)	13 (20.31)	9 (14.06)	23 (35.94)

Figures in parentheses are horizontal percentages

(21.27%), culture in 10 (30.30%) and smear in 18 (54.54%) cases, while in the clinically non-tuberculous cases, HP was negative in all the 3 cases detected positive by smear and culture (Table 1).

The positivity frequency of various investigations is shown in Table 2. Seven (30.4%) out of the 23 cases were positive by all the three methods, 6 (26.08%) by any two methods, 2 (8.7%) by culture alone and 8 (34.8%) by smear alone. Thus, the addition of smear and culture to histopathology detected additional 14 (21.88%) cases of lymphnode tuberculosis.

Table 2. Positivity status by various laboratory investigations

Investigations	Result					Total positive
Smear	+	+	+	—	+	21
Culture	+	-	+	+	—	13
H.P.	+	+	_ _	_ _	_	9
No.	7 (30.4)	2 (8.7)	4 (17.4)	2 (8.7)	8 (34.8)	23

Figures in parentheses are percentages

Impression smear proved to be the most sensitive technique. Its sensitivity was 100% in HP proven cases and 84.62% in culture positive cases i.e* 11 out of 13 cases. The sensitivity of culture in HP positive cases was 77.78%, while vice versa was only 53.85%, culture having detected 6

Table 3. Status of 8 smear positive children

	H/O TB	Site	Size (cm)	No	Type	MX	X-ray
1	—	G	<3	M	D	+	+
2	+	A	<3	S	D	+	—
3	+	A	<3	M	D	ND	—
4	—	G	>3	M	MT	—	+
5	—	G	<3	M	D	+	+
6	-----	C	<3	S	D	+	—
7	+	C	<3	S	Q	_	_
8	+	C	<3	S	£)	—	—

A = Axillary, C = Cervical, D = Discrete, G = General, S = Single, M = Multiple, MT = Matted, ND = Not done, MX = Mantoux test, H/o = History of

additional cases and missed 2 which were positive on HP.

The breakup of the 8 subjects positive only on smear is shown in Table 3. They were considered as tuberculous on the basis of additional positive parameters like strong clinical suspicion, history of contact, positive tuberculin test of more than 10 mm or chest X-ray findings suggestive of tuberculosis.

Ziehl Neelsen staining was positive in 18 (85.70%) of the 21 (32.81%) cases positive for tuberculosis by fluorescence microscopy. There was no case positive by Ziehl Neelsen which was negative on fluorescence microscopy.

All isolates on culture were characterised as *M. tuberculosis.* No *M. bovis,* BCG or NTM strain was isolated.

All lymph node cultures put Up for routine bacteriology were sterile except for two that grew *Staphylococcus epidermidis* which were taken as skin contaminants.

DISCUSSION

This study differs from those undertaken earlier by other workers in being fleld based rather than hospital based. The fleld studies have an advantage in bridging the gaps and providing clues to the natural history of any disease. This study picked up cases in the very early stage of infection, may be much before the actual disease process started. In many cases the parents were not even aware of the symptoms and thfc presence of enlarged nodes in their children. Miller[9] has stated that in children lymphnodes get infected early in childhood along with primary focus but may remain quiescent for long only to manifest as disease later or whenever the resistance is lowered. This is also probably stage 1 of Jones & Campbell[10] where the enlarged nodes are staged as firm, mobile, discrete, slightly tender showing reactive hyperplasia on histopathology.

> In the natural history of tuberculous lymphnode enlargement, there appears to be an early stage, probably soon after infection, when tubercle bacilli could be Seen in smears (including impression smears) and culture but the histopathological examination is negative.

According to Hooper", this stage is not diagnosable except by indirect means or by the demonstration of acid fast bacilli in the lymph nodes. **The demonstration of bacilli in the additional 8 freshly prepared impression smears and 6 cultures compared with 9 histopathology positive cases (Table 2) clearly indicates that in the early stage of the disease histopathology is not likely to be diagnostic.** Moreover, 3 cases from clinically non-tuberculous group, again early cases, were positive also by smear and culture and negative on histopathology (Table 1). In the present study, smear was found to be a very sensitive technique. In Stanfield's[12] book on interpretation of lymphnode biopsy, G.R. Latham has advocated the use of impression smear for cytology and though many reports on staining of histopathology slides for AFB are also available, the authors have not come across any study which reports on the utility of imprint smears in detecting *M. tuberculosis.* In these smears, the morphology of the bacilli was observed to be mostly short and stumpy unlike the long beaded organisms seen in the sputum specimen from a pulmonary tuberculosis case. This is probably due to the fact that lymphnodes, being the active sites for immune response, keep the bacilli in a metabolically reduced state. In an immunocompromised or AIDS patient the bacilli are again reported to be long and well formed.

> The morphology of tubercle bacilli in smears and cultures of tuberculous lymphnodes, especially those from early stage enlargement is different : The rods are short and stumpy unlike the long and beaded organisms seen in smears and cultures from sputa of pulmonary tuberculosis cases.

Thus, this technique can be easily adopted in the peripheral hospitals that undertake lymphnode biopsies particularly as Z.N. staining was also found to be fairly sensitive. However, some caution must be exercised in interpreting the results, especially if flourescence microscopy is used. Four cases in the present study were false positive for acid fast bacilli : culture, HP and other clinical parameters being negative. In another 3 cases, culture was positive for Nocardia instead of

Mycobacterium. Both the organisms are acid fast but differ in their treatment. On the other hand, smear also detected 2 cases each of microfilaria and fungus.

It is, therefore, concluded that no single technique is totally dependable and till such time that more sensitive methods are available for use for routine diagnosis of tuberculous lymphnodes, in the hospitals where facilities are available, all the three investigations must be requisitioned simultaneously in order to get the maximum diagnostic yield from a specimen. In the peripheral hospitals, however, impression smear staining of lymphnode biopsies may prove to be of immense benefit by preventing much delay in the diagnosis of tuberculous lymphadenitis.

ACKNOWLEDGEMENT

The authors are grateful to the Indian Council of Medical Research for financing the field study.

REFERENCES

1. Seth V., Kabra S.K., Jain Y. *et al.* Tubercular lymphadenitis. Clinical manifestations. Indian J Pediatr; 1995, 62 : 565.
2. Pamra S.P. and Mathur G.P. Cooperative study of tuberculous cervical lymphadenitis. Indian J Med Res; 1974,62: 1631.
3. Lake S.K. and Oski F.A. Peripheral lymphadenopathy in childhood. Am J. Dis Child; 1978, 132 : 357.
4. Jawahar M.S., Sivasubramaniam S, Vijayan V.K., Ramakrishnan C.V., Paramasivan C.N. Vanaya Selvakumar, Sare Paul, Tripathy S.P. and Prabhakar R. Short course chemotherapy for tuberculous lymphadenitis in children. BMJ, 1990. Vol. 301,18-25 Aug., 359.
5. Vanaja Kumar N, Vanaya Selvakumar, Jawahar MS, Rajaram K. and Pramasivan C.N. Transportation of lymphnode biopsy specimens in selective Kirchner's liquid medium for culture of tubercle bacilli. J. Med. Microbiol., 1997, 46, No. 3,260.
6. Marks J. and Thomas CHH. Notes on cultivation of tubercle bacilli. Mon Bull Min Health and PHLS; 1958, 17, 194.
7. Collin C.H. and Lyne P.M. Microbiological Methods, 5th ed, 1979, Butterworths London.
8. Collin C.H., Grange J.M. and Yates M.D. Organisation and paractice in tuberculosis bacteriology, 1st edition, 1985, Butterworths, London.
9. Miller F.J.M. (Ed). Tuberculosis in Children : Evolution, epidemiology, treatment, prevention. B.I. Churchill Livingstone, New Delhi : 1994, 1-294.
10. Jones P.O. and Campbell P.E. Tuberculous lymphadenitis in childhood : The significance of anonymous mycobacteria. Br J Surg, 1962, 50, 302.
11. Hooper A.A. Tubercular peripheral lymphadenitis. BrJ Surg; 1972,59 (5): 359.
12. Stanfield A.G. (Ed). Lymph node biopsy interpretation. 1985, Churchill Livingstone, Edinburgh.

Original Article

Ind. J. Tub., 1998, 45, 215

TUBERCULOUS RHEUMATISM (PONCET'S DISEASE) -A CASE SERIES*

Anurag D. Bhargava[1], Anand N. Malaviya[2] and Ashok Kumar[3]

INTRODUCTION

The occurrence of polyarthritis in patients with active tuberculosis was first reported by Antonin Poncet in 1897[1]. In contrast to the usual tuberculous arthritis which is monoarticular, infectious and destructive, tuberculous rheumatism (Poncet's disease) is a non-destructive para-infective polyarthritis occurring in patients with active tuberculosis, which resolves completely on anti-tuberculosis therapy. Although the existence of this entity had been questioned in the past[2], more than 25 cases have been published in the English language literature since 1974[2,4-12]. We present here a case series of four patients of this illness. The pathogenetic mechanisms underlying this condition are also discussed

CASE REPORTS

Case I:

A 26 year old housewife presented with continuous fever of 3 weeks' duration. Three days following the onset of fever she developed arthralgia associated with morning stiffness and limitation of movement in both Shoulders, wrists, and small joints of the hands. A week later she also developed painful limitation of movements in both knees and feet. There was no other significant medical history. There was no family history of rheumatic, or autoimmune disease. On examination she had temperature of 38 degrees Celsius. She had palpable lymph nodes in the right supraclavicular and left axillary regions which were non-tender, firm in consistency, and varying between 1.5 - 2 cm in diameter. The lymph nodes in the left axilla were matted. Tenderness was elicitable on pressure bilaterally over the following joints : shoulder, all metacarpophalangeal and proximal interphalangeal joints, knees, ankles, mid-tarsal and 1st metatarsophalangeal joints. There was no evidence of significant effusion in joints except for swelling in mid-tarsal region bilaterally. The spine was normal. Rest of the systemic examination was normal.

Lvestigations

Hemoglobin 9.6 g/dl. WBC : 11 x io»/J with 83% granulocytes, 16% lymphocytes and 1% monocytes, ESR was 68 mm in the 1st hour. Serum bilirubin, Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) levels were normal but serum alkaline phosphatase (SAP) was 673 IU/L.

Mantoux test performed with 5 TU was 20 mm. Antinuclear factor (ANF), rheumatoid factor (RF), and Anti-Streptolysin O (ASLO) liter were negative. X-rays of the chest and the joints of the feet were normal. Biopsy of the cervical lymph node revealed necrotising granulomatous lymphadenitis suggestive of tuberculosis. AFB stain of the biopsy specimen was negative. Her HLA DR haplotype was (9,11).

Course

The patient was put on four drug anti-tuberculosis therapy since the evidence was strongly suggestive of active lymph node tuberculosis. The patient's rheumatic symptoms showed a remarkable improvement within two weeks of initiation of therapy. Non steroidal anti-inflammatory drugs were used only occasionlly.

Case 2 :

A 17 year old girl was admitted with history of

*Paper presented at the 52nd National Conference on Tuberculosis and Chest Diseases, Ahmedabad, 19-22 December, 1997

1. Assistant Professor (Medicine), P.S. Medical College, Karamsad, 2. Professor of Medicine, University of Kuwait, Kuwait, 3. Associate Professor (Medicine), All India Institute of Medical Sciences, New Delhi.

***Correspondence**:* Anurag Bhargava, Assistant Professor (Medicine), P.S. Medical College, P.O. Box 8, Karamsad - 388 325.

moderate grade fever of one month duration. One week after onset of fever she noticed onset of swellings in pre-auricular and post-auricular regions bilaterally, which were not painful. One week prior to entry she developed pain and swelling in both knee and ankle joints, associated with morning stiffness, and significant restriction of movement. She was treated with non steroidal anti-inflammatory drugs with partial relief. On examination, she was pyrexial (Temp. 39°C). She had evidence of bilateral small pre-auricular and post-auricular lymph node enlargement. She 'also had bilateral supraclavicular and axillary lymphadenopathy which was non-tender, discrete and firm in consistency. There was mild hepatomegaly. Both the knees and ankles were tender and showed limitation of movement. Examination of the knees revealed a mild effusion. Rest of the musculoskeletal and general examination was normal.

Investigations

Hemoglobin : 12 g/L, WBC : 4.7 x 10' 1 with a normal differential count. ESR was 48 mm in the 1st hour. SAP was 417 IU/L with normal levels of serum bilirubin and liver enzymes. Mantoux test with 5 TU was 17 mm. RF, ANF, ASLO were negative. The Cheast X-rays were suggestive of right paratracheal adenopathy. Ultrasound of the abdomen revealed presence of lymph nodes in the superior mesenteric and celiac artery regions. X-ray of the knee joints was normal. Synovial fluid aspirated from the right knee joint was turbid with cell count of 10 x 10^9/L and a differential count of 50% lymphocytes and 50% granulocytes. AFB stain of the synovial fluid as well as culture for AFB on L-J medium were negative. Lymph node biopsy of the right supraclavicular node showed caseating granulomas suggestive of tuberculosis.

Course

This patient was also put on standard short course chemotherapy and showed consistent improvement and subsequent resolution of symptoms over 2 weeks of therapy.

Case 3

A 39 year old labourer presented with history of fever of 3 weeks' duration. Two weeks before admission, he started complaining of pain in both ankles which was accompanied by swelling and limitation of movements. He had significant anorexia and associated weight loss.

Examination revealed a well built man. Temperature was 38°C. There were 1.5 cm diameter nodes in the right supraclavicular and left axillary regions which were non-tender, firm in consistency. The lymph nodes in the right supraclavicular region were matted. There was mild hepatosplenomegaly. Musculoskeletal examination revealed mild swelling, tenderness and painful limitation of movement in both ankle joints.

Investigations

Hemoglobin 14.4 g/dl. WBC : 7.5 x 10^9/L with a differential count of 70% granulocytes, 27% lymphocytes and 3% monocytes. ESR was 34 mm in the 1st hour. ANF, RF and ASLO were negative, Mantoux test with 5 TU was 20 mm. X-ray chest revealed features of right paratracheal and right hilar lymphadenopathy with an infiltrate in the right middle zone. Sputum could not be obtained even after saline induction. Lymph node biopsy of the right supraclavicular node showed caseating granulomas. AFB stain was negative. His HLA DR haplotype was (2,4).

Course

The patient's fever and arthritis resolved completely within 3 weeks of starting anti-tuberculosis therapy.

Case 4

A 20 year old student came with a history of remittent fever of more than 4 months' duration. One month after onset of fever he developed pain in both wrists, knee and elbow joints. Pain was also felt in the carpometacarpal joints, proximal and distal inter-phalangeal joints of the right hand. He also reported significant weight loss. He had been treated as having rheumatoid arthritis on the basis of these complaints. On examination he was febrile, (Temperature-40°C), had two discrete, non-tender axillary lymph nodes 2-3 cm in diameter and firm in consistency. He had mild enlargement of liver and spleen. On examination of the musculoskeletal system, he had mild swelling of the wrist joints, and

tenderness elicitable over both wrists, knee joints. There were no significant effusions. Rest of the systemic examination was normal.

Investigations :

Hemoglobin 10.4 g/1. WBC 10.8 x $1Q^{9/2}$ with a normal differential count. ESR was 102 mm in the 1st hour. SAP was 470 IU/L. ALT was 50 IU/L, while AST was 46 IU/L. Serum bilirubin, albumin and prothrombin time were normal. Mantoux reaction with 5 TU was omm, ANF, RF, ASLO were negative. Biopsy of the right axillary lymph node showed features compatible with reactive lymphadenitis. Liver biopsy showed presence of non caseating granulomas.

Course

The patient was given anti-tuberculosis therapy in view of clinical and investigative features suggestive of disseminated tuberculosis. The patient had resolution of fever and arthitic symptoms within two weeks of therapy.

DISCUSSION

Tuberculous rheumatism (Poncet's disease) has been defined as a "polyarthritis associated with visceral tuberculosis in which there is no evidence of bacteriologic involvement of the joints themselves."[2]. The arthritis in Poncet's disease resolves completely on anti-tuberculosis therapy. **The diagnosis of this entity is largely clinical and is made by excluding other causes of polyarthritis in a patient with documented active tuberculosis.**

The controversy surrounding the existence of tuberculous rheumatism had been due largely to Poncet's rather broad concept of tuberculous rheumatism, which was based on the association of polyarthritis with

(*i*) active or inactive visceral tuberculosis
or
(ii) a family history of tuberculosis
or
(iii) the presence of a true tuberculous joint in any patient before, coincident with, or following a polyarthitis of any type [2].

This definition lacked diagnostic precision and led to the inclusion by Poncet of patients who clearly had other rheumatic diseases like rheumatiod arthritis, solely on the basis of a family history of tuberculosis, or a history of tuberculosis in the past. This was criticized by later workers, who even questioned the existence of such an entity[2,13].

Fever of 3-17 weeks' duration (usually > 38°C) followed by polyarthritis were the presenting features in our patients. The arthritis was acute to subacute in onset, and varied in extent and severity. Symmerrical involvement of large joints was uniformly observed, but small joint involvement (which was asymmetrical in one patient) was been in 2 patients. **In our patients knee joint involvement was most commonly observed followed by ankle and wrist joints.** In other case reports also knee joint involvement has almost invariably been observed. Effusions were present in 2 patients but was large enough in only 1 patient to enable a diagnostic aspiration. **Although it has ben described as a polyarthritis, a review of the recent literature reveals Poncet's disease to be more often a pauciarticular, symmetrical, arthritis of predominantly the large joints.[2,4,12]** None of our patinets had axial skeleton involvement as part of the polyarthritis. This is also in conformity with the recent literature. Although the arthritis in Poncet's disease may be acute or subacute in onset and duration, as observed in our series, chronic arthritis has also been observed. In one case report the rheumatic symptoms had been present for 18 months[9].

The synovial fluid aspirated in one of our patients was found to be inflammatory in nature with no evidence of direct tuberculosis infection of the joint, by conventional culture methods. In a recent report, however, even a polymerase chain reaction, used to detect *Mycobacterium tuberculosis* target DNA in the synovial fluid of a patient with Poncet's disease, was found to be negative[14].

Could the arthritis observed in our patients have been due to other causes? Tuberculous rheumatism may be confused with other arthritides like rheumatic fever, rheumatoid arthritis (as in patients no. 2 and 4), or arthritis associated with connective tissue disorders. However, these were carefully excluded in our patients on the basis of clinical, radiological, serological and microbiological evidence. In all our patients, investigations revealed the presence of active tuberculosis. Complete

resolution of arthritis within 2-3 weeks of initiation of anti-tuberculosis therapy was seen, and there was no recurrence of rheumatic symptoms on follow up. The consistent association of arthritis with presence of active tuberculosis, the resolution of symptoms on anti-tuberculosis therapy, and the lack of evidence of any other known rheumatic disease are all compatible with the diagnosis of Poncet's disease in our patients.

Lymphadenopathy was a consistent finding in our cases. This was especially important since the presence of active tuberculosis had not been suspected initially, but it was subsequently established on the basis of lymph node biopsies in 3 patients. Lymphadenopahty was most frequently encountered in the cervical and axillary regions, but involvement of mediastinal and retroperitoneal nodes was also seen. In our series, Poncet's disease was more commonly associated with active extrapulmonary tuberculosis, notably that involving the lymph nodes. Although Poncet's disease can be associated with tuberculosis at other sites, a large series also noted its frequent association with lymph node tuberculosis[15].

A strongly positive reaction to tuberculin, frequently observed in the literature was also noted in 3 out of our 4 patients. One patient with evidence of disseminated tuberculosis was non-reactive to tuberculin.

Our patients were all young adults in the age group 17-39 years. Other case reports describe patients ranging from 2 years to 40 years indicating that Poncet's disease predominantly occurs in young adults and children[2,4-12].

Poncet's disease has been called a para-infective arthritis[4], a term which requires explanation. A para-infective arthritis is like reactive arthritis, an aseptic arthritis triggered by an infection outside the joint[16]. However, in para-infective arthritis, treatment of the infection leads to cure of the arthritis unlike true reactive arthritis where this does not lead to resolution of the arthritis[16].

PATHOGENESIS

The pathogenesis of Poncet's disease is still uncertain but is considered to be immune cells mediated, since there is no direct bacteriological involvement of the joint itself. In the last decade, there is accumulating experimental evidence implicating mycobacteria in the pathogenesis of arthritis. However, both host factors as well as mycobacterial antigens have been implicated.

Poncet's disease has been considered to represent a hypersensitive immune response to tuberculoprotein, which may produce a reaction in the joint spaces, similar to that produced in skin in erythema nodosum occurring in active tuberculosis[6]. In one patient with Poncet's disease, lymphocyte proliferation assays showed increased reactivity of synovial fluid lymphocytes compared to peripheral blood lymphocytes". Since Poncet's disease apparently occurs only in a small proportion of patients with active tuberculosis, a genetic predisposition might be involved. In one patient with Poncet's disease the HLA haplotype was DR4[10], which was so in one of our patients too. Genes coding for this allele are associated with rheumatoid arthritis and may also influence the immune response to mycobacterial antigens. DR4+ patients are hyper-responsive to mycobacterial antigens[17]. Poncet's disease might result from a genetically determined (HLA linked) hyperresponsiveness to mycobacterial antigens[17] disseminating into joint spaces[18]. However, this issue of a specific HLA linkage of Poncet's disease needs further study.

While host factors may be important in the pathogenesis of Poncet's disease, the role of mycobacteria and their antigens also needs to be considered. It is known that mycobacteria are arthritogenic. Injection of the heat killed and desicated *Mycobacterium tuberculosis* in oil (complete Freund adjuvant) in animals can produce a chronic synovitis resembling rheumatoid arthritis[19]. BCG immunotherapy given to cancer patients has been shown to produce arthritis as an adverse effect, possibly caused by a similar adjuvant effect[20,21]. Molecular mimicry between mycobacterial antigens and host tissues and the resulting immunological cross reactivity may also pay a role. Antigenic similarity between a fraction of *M. tuberculosis* and human cartilage has been shown[22]. A T cell mediated cross-reactive autoimmune response might also be operative in the pathogenesis of Poncet's disease.

CONCLUSIONS

1. Tuberculosis can present with predominantly

rheumatic features (Poncet's disease) which may confuse the unwary clinician. Therefore, active tuberculosis (often of lymphnodes) should be strongly considered in the differential diagnosis of patients with fever and polyarthritis of obscure cause, especially in regions of high prevalence of tuberculosis.

2. The diagnosis of Poncet's disease remains clinical and is established on excluding other potential causes of arthritis in a patient with active tuberculosis. The complete resolution of arthritis of Poncet's disease on anti-tuberculosis therapy also furnishes further proof of the diagnosis.

The entity of tuberculous rheumatism deserves a mention in the standard text-books of medicine and rheumatology on the strength of the current evidence. Also, further studies to elucidate the pathogenetic mechanisms underlying Poncet's disease are required.

REFERENCES

1. Poncet A. De la polyarthrite tuberculeuse deformante ou pseudorheumatisme chronique tuberculeux. *Congres Francaise de Chirurgerie* 1897;! :732.
2. Isaacs A.J., Sturrock R.D. Poncet's disease; fact or fiction? *Tubercle* 1974; 55: 135.
3. Brav E.A., Hench P.S. Tuberculous rheumatism. *J Bone Joint Surg* 1934; 16 : 839.
4. Bloxham C.A., Addy D.P. Poncet's disease : Para-infective tuberculous polyarthropathy. *Br Med J* 1978; 1 : 1590.
5. Alien S.C. A case in favour of Poncet's disease. Br Med J 1981; 283: 952.
6. Dall L., Long L., Standford J. Poncet's disease : Tuberculous rheumatism. *Review of Infectious Diseases* 1989; 2(1): 105.
7. Malik S.K., Khatri O.K., Deodhar S.D. Tuberculous rheumatism. *J Indian Med. Assoc.* 1977; 69: 201.
8. Benatar A., Hill I.D., Bowie M.D. Poncet's disease. *SAfrMedJ* 1984; 65 : 930.
9. Wilkinson A.G., Roy S. Two cases of Poncet's disease. Tubercle 1984; 65 (4): 301.
10. Ames P.R.J., Capasso G., Testa V., Maffulli N., Tartora M., Gaeta G.B. Chronic tuberculous rheumatism (Poncet's disease) in a gymnast. *British Journal of Rheumatology* 1990; 29 : 72.
11. Southwood T.R., Hancock E.J., Petty R.E., Malleson P.E., Thieseen P.N. Tuberculous rheumatism (Poncet's disease) in a child. *Arthritis Rheum* 1988; 31 : 1311.
12. Arora V.K., Verma V. Tuberculous rheumatism (Poncet's disease) : three case reports. *Ind J Tuberculosis* 1991; 38 : 229.
13. Summers S.D., Jayson M.I.V. Does Poncet's disease exist? Rheumatology and Rehabilitation 1980; 19: 149.
14. Qurtom M.A.F., D'Almeida *E.,* Sattar S.A., Malaviya A.N., Mustafa A.S. Reactive arthritis due to tuberculous lymphadenitis (Poncet's disease) in a Sri Lankan woman. *Med Principles Pract* 1997 (In press).
15. Ku F-S, Li C-L, Shen L-H, Hsing S : Differential diagnosis of rheumatic fever and allergic arthritis due to tuberculosis. Chin Med J (Engl) 1966; 85. 477.
16. Toivanen A. Reactive arthritis *in* Klippel JH, Dieppe PA, Eds, Rheumatology. London: Mosby Year-Book Europe, 1994 : 4.9.1.
17. Ottenhof T.H.M., Torres P, Terencio de las Agnas J *et al.* HLA-DRA associated immune response gene for *Mycobacterium tuberculosis :* a clue to the pathogenesis of rheumatoid arthritis. *Lancet* 1989; *ii*, 310.
18. Southwood T.R., Gaton J.S.H. The molecular basis of Poncet's disease. Br J Rheumatol 1990; 29:491.
19. Pearson C.M. Development of arthritis, periarthritis and periostitis in rats given adjuvants. *Prof Soc Exp Biol Med* 1956; 91 : 95.
20. Torisu M., Miyahara T., Shinodhara N, Ohsato K, Sonozaki H. A new side effect of BCG immunotherapy-BCG induced arthritis in man. *Cancer Immunol Immunother* 1978; 5 : 77.
21. Hughes R.A.,Allard S.A., Mami R.N. Arthritis associated with adjuvant mycobacterial treatment for carcinoma of the bladder. *Ann Rheum Dis* 1988; 48: 432.
22. Holoshitz J., Drucker I., Varetzky A. *et al.* T lymphocytes of patients with rheumatoid arthritis patients show augmented reactivity to a fraction of mycobacteria cross reactive with cartilage. *Lancet* 1986; II: 305.

Ind. J. Tub., 1998, 45, 221

PULMONARY TUBERCULOSIS : A PREDISPOSING FACTOR FOR COLONISING AND INVASIVE ASPERGILLOSIS OF LUNGS*

B.N. Panda, D. Rosha and M. Verma

Summary. Aspergillus is an ubiquitous fungus capable of invading lung parenchyma. Disease can be caused by allergic manifrstation or by chronic tissue colonization leading subsequently to tissue invasion.

We have analysed case records of 29 cases of Aspergillus lung disease at a tertiary referral center. This group included 14 cases of allergic bronchopulomonary aspergillosis (ABPA) and 15 cases of tissue colonization or invasion. This latter group included 2 cases of invasibe and disseminated asoergillosis and 8 cases of aspergilloma, Diagnosis was confirmed histologically in 13 of these cases. All these cases had a single positive denominatoe, i.e. history of treatment for pulmonary tuberculosis leaving residual cavity/bronchiectasis. There was one death in this group. Response to surgery with or without systematic antifungal therapy was good in 13 of them. Based on clinical, radiological and histological evidence, aspergilloma, semi-invasive aspergillosis and iinvasive aspergillosis can be regarded as various stages of a single entitiy.

INTRODUCTION

In earlier studies, it was observed that 11% of residual pulmonary post-tuberculosis cavities can have a fungal mass due to Aspergillus[1,2]. In our practice, we have come across Aspergillus infection of lungs presenting with varied clinical manifestations in treated cases of pulmonary tuberculosis. This study analyses the clinical spectrum of Aspergillus infections as observed in a tertiary referral Respiratory Medicine Department of Armed Forces.

MATERIAL AND METHODS

In the Armed Forces, all cases of pulmonary tuberculosis are followed up every six months, after completion of short course chemotherapy, for 2 years and cases with residual cavity/bronchiectasis/ radiological evidence of volume loss are further followed up every 6 months for any residual complications. This study is based on proved cases of Aspergillus lung disease from (a) all post tuberculosis follow up cases, (b) all cases of diffuse/ localised pulmonary opacities, and (c) chronic asthmatics. Diagnosis of Aspergillus colonisation/ invasion was established on demonstration of fungus in tissue bronchial lavage specimens and ABPA was diagnosed on criteria like (i) peripheral eosinophilia, (ii) changing pulmonary opacities (iii) skin hypersensitivity for Aspergillus antigen and (iv) central bronchiectasis in CT scan of chest.

RESULTS

Out of 9543 indoor patients, we diagnosed and treated 29 cases of Aspergillus lung disease. This included 14 cases of allergic broncho-pulmonary aspergillosis (ABPA). The association with tuberculosis disease was tried to be established in all these cases. Though majority (8 of 14) had received anti-tuberculosis treatment, sometime or other, sputum or bronchoscopic lavage did not yield any bacteriological proof to suggest a diagnosis of tuberculosis in any of the cases of ABPA.

There were 15 cases of tissue colonisation with Aspergillus. All these 15 cases were treated cases of pulmonary tuberculosis. Diagnosis was confirmed by sputum smears and culture positivity in 11, only culture positive in 2 and 2 cases were bacteriologically negative but showed excellent clinical and radiological response to short course chemotherapy. In all these cases, diagnosis of aspergillosis was confirmed by invasive methods/ by demonstration of fungal hyphae in the tissue/

*Paper presented at the 52nd National Conference on Tuberculosis and Chest Diseases, Ahmedabad 19-22 December, 1997

From the Department of Respiratory Medicine, Army Hospital (R & R), Delhi Cantt

Correspondence: Col B.N. Panda, Sr. Advisor, Respiratory Medicine, Med Div, Army Hospital (R & R) New Delhi-110 010.

cavity. There were 2 cases of invasive aspergillosis with multi-organ involvement. In both these, the organism was demonstrated from different sites through tissue sampling. One patient responded well to Amphotericin therapy, whereas there was resistance to Amphotericin in the other case. Even high dose of liposomal Amphotericin was found to be ineffective.

There were 5 cases of semi-invasive aspergillosis where partial tissue invasion was noted from the resected lung specimens. In another 8 cases, we found the fungal ball lying completely separated from the surrounding pulmonary cavity. This latter group was easier to handle surgically. All these 15 cases had history of previous treatment for pulmonary tuberculosis and 11 of these had far advanced sputum positive cavitary disease.

DISCUSSION

The fungus Aspergillus is an opportunistic organism that survives on decaying organic matter. The presence of Aspergillus as a causative factor for asthma was first described by Hinson in 1952 in England[3]. Subsequent studies, both in Europe and USA have revealed presence of Aspergillus colonisation even in asymptomatic adult[5]. This disease is being increasingly recognised in this subcontinent[2,4-6] too. Though many workers have come across ABPA cases who have been given anti-tuberculosis chemotherapy at different times, a definite causal relationship indicating a tuberculous etiology was lacking[5,6]. However tuberculosis of lung as a predisposing factor in colonising aspergillosis (in cases with aspergiloma) was found by other workers[4,7]. Even today, tuberculosis remains the most important cause of sub-acute and chronic respiratory morbidity in our country which most often leaves behind a scarred pulmonary parenchyma vulnerable to fungal colonisation. Other diseases causing residual scarring and cavitation are sarcoidosis, rheumatoid lung, Wegner's granulamatosis, but they are relatively rare. However, in our series there were two distinct groups. One group was of ABPA in hypersensitive adults with evidence of raised IgE, peripheral esoniophilia and structural damage in the medium sized (proximal) bronchi where prolonged stasis by fungal hyphae resulted in destructive lesions and resultant proximal bronchiectasis. The other group occurred in a post tuberculosis scarred lung resulting in fungal colonisation, either in the form of mobile fungal ball or as semi-invasive aspergillosis where the fungi gradually started penetrating the walls. The unusual associations were disseminated aspergillosis in two apparently healthy, adults, with a fairly well preserved immunological status as indicated by positive response to tuberculin and monilial antigens. Possibly, tuberculosis was a common denominator in cases of Aspergillus colonisation. Complete spectrum of Aspergillus colonisations starting from Aspergilloma, semi-invasive aspergillosis and invasive aspergillosis were seen in this group of patients possibly indicating different stages of tissue invasion in the setting of tuberculous scarring. The other important observation was that in two cases of invasive aspergillosis with histologically proved multi-organ involvement there were no overt causes of immunodeficient state. Hence, this study show that though fungal diseases of lungs are uncommon in our country, in respect of colonising/invasive aspergillosis, previous tuberculosis treatment may be a strong predisposing factor.

REFERENCES

1. Research Committee of British Thoracic and Tuberculosis Assn. Aspergiltosis and Residual Tuberculous Cavities - The Result of Survey - Tubercle 1970; 50 : 227.
2. Mohapatra, L.N., Pande, J.N. Pulmonary Mycotic Infections *in :* Ahuja, M.M.S. Ed. Progress in Clinical Medicine in India, 1978. Hememann A. New Delhi,
3. Hinson, K.F.N., Moon, A.J., Plumme, N.S. Broncho pulmonary aspergillosis : A review and report of of eight new cases, Thorax, 1952; 7 : 317.
4. Sobti, K.L., Hoon, R.S. Dutta, R.N. Incidence of pulmonary aspergillosis in Indian Armed Forces. J. Assoc. Phy. Ind. 1978; 26: 871.
5. Shah A. Allergic Bronchopulmonary Aspergillosis - An emerging disease in India. Ind. J Chest Dis and All. Sc. 1994; 36: 169.
6. Behera, D., Guleria, R., Jindal, S K., Chakrabarti, A., Panigrahi, D. Allergic Bronchopulmonary Aspergillosis : A retrospective study of 35 cases. Ind. J. Chest Dis & All. Sc. 1994; 36 : 173.
7. Sahoo RC, Rao PVP, Shivananda, P.O., Kumar A., Mohanti, L.K. A Profile of Aspergillus lung disease. J. Assoc. Phy Ind. 1988, 36 : 711.

Ind J Tub, 1998, 45, 223

INCREASING THE EFFECTIVENESS OF THE REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME

Debabar Banerji[1]

Summary. As RNTCP is already being implemented extensively in the country, it was felt worthwhile to initiate a debate which could lead to suggestions to make it more cost-effective. A massive case finding effort to do sputum microscopy of symptomatic persons and administration of the DOTS are the two major pillars of the programme. A major obstacles to assessing the performance of the RNTCP is that very scanty information, and that too of questionable quality, validity and reliability, is available. A detailed ac-count of the two phases of the Pilot Projects, baseline information on the annual risk of infection, feedback data from a surveillance system and operational research studies to optimize RN-TCP as a system, as envisaged in the WHO\World Bank document on RNTCP, should form a priority area for action. Decentralization of DOTS administration by tapping the enormous potential for community action through Panchayats and other local mechanisms and increase of epidemiological coverage by including the sputum negative, culture positive and pre-sputum positive radiological cases forms another set of suggestions, It is also suggested that action ought to the initiated to respond to the felt needs of the 75 per cent of the population, which falls outside the purview of RNTCP. There ought also to be plans for integrating RNTCP into NTP after the five year period of World Bank support expires.

The focus is on RNTCP implementation

The focus here is on analyzing the recently introduced 'Revised National Tuberculosis Programme' (RNTCP) of the Government of India with a view to suggesting ways of more effectively implementing it. The RNTCP is taken as given. A studied effort has been made here to leave behind the very lively debate that had preceded the development of the policy postulates, planning, programming and implementation of the RNTCP[1].

Early in the nineties, WHO and the World Bank had come to the conclusion that the problem of tuberculosis has taken the form of a global epidemic and the concurrent pandemic of AIDS had made the situation much more serious[2] They got together to launch the Global Programme of Tuberculosis to combat the menace The target set was to find 70 per cent of the cases and to cure at least 85 per cent of them The Government of India have joined the global movement and launched the RNTCP The Directorate General of Health Services of the Union Ministry of Health and Family Welfare (DGHS) has produced an unpublished document in 1995 *(The Revised National Tuberculosis Programme A Brief),* which embodies an analysis of the reasons for poor performance of India's National Tuberculosis Programme (NTP) and the rationale for adopting the RNTCP It contains the details of the RNTCP and the phases in which it is to be implemented This is used as the main source of information on RNTCP for this presentation

The RNTCP conforms to the WHO/World Bank guideline of having the objective of finding 70 per cent of the cases and attaining at least 85 per cent of cures Creation of 'sub-distiict supervisory unit' for case finding and employing what is called Directly Observed Treatment, using intensive short course chemotherapy (DOTS), form the centrepiece of the strategy for attaining the objectives Data from Phases I and II of the Pilot Projects, a surveillance system for the implementation of the different components of what it calls the 'World Bank TB Project' and feedback information from 'operational research', were meant to 'optimise' the working of the programme The Brief recognizes that after the end of the five-year term of the RNTCP, it will be covering only '25% population (271 27 million)' The estimated expenditure for this population coverage alone was Rs 442 crores Under the heading, 'Future Plans', the Government of India proposes to 'revitalize the National

1 Professor Emeritus, Jawaharlal Nehru University, New Delhi
***Correspondence**:* Nucleus for Health Policies and Programmes, B-43 Panchsheel Enclave, New Delhi -110 017

Tuberculosis Programme (NTP) in non-project areas'.

Some major problems in implementing RNTCP

Very scanty data are available to tuberculosis workers on the two phases of the Pilot Project and the project covering the population of 271.21 million. Nevertheless, availability of considerable data on some vital epidemiological, sociological, technological and organizational and managerial aspects of the NTP can also be used for analyzing the functioning of the RNTCP and for offering suggestions for strengthening it.

Three fundamental epidemiological issues emerge from the line pursued in the formulation of the RNTCP:

(a) very convincing empirical evidence produced by epidemiologists like Grzybowski[3] and Chakraborty[4] has demonstrated that even the admittedly poor performance of the NTP, which left an overwhelming proportion of infectious and often drug resistant cases totally uncared for, did not result in a proportionately rapid increase in the prevalence and incidence rates of the disease in the country in the past three decades or more;

(b) even if it is possible to attain the very unrealistic coverage envisaged in the RNTCP for 25 per cent of the population, this still leaves the fate of the remaining 75 per cent of the population, which is due to come 'for revitalization of the NTP in the future plans of the Government of India', uncertain, at least for a long span of time; and,

(c) even if the desired coverage is attained in the RNTCP, this will still leave those who are culture positive but are repeatedly found smear negative and those who belong to the 'pre-sputum positive stage of the pathogenesis of the disease', outside the purview of diagnosis and cure. Both epidemiologically and sociologically, they form a significant group.

It is very encouraging that RNTCP has taken care of two of the fundamental issues which had shaped the NTP : it deals with the felt needs of the people and the first level of the diagnostic procedure is based on the screening of the symptomatics by sputum microscopy. However, in adopting the approach of DOTS, it makes the questionable assumption that the drug administration must be directly observed by the RNTCP staff. This not only involves considerable expense, which includes the high cost of the technology used, but it also requires enormous managerial and organizational efforts to ensure that the patients, who are scattered over large areas, receive the treatment.

One of the most crucial problems in assessing the implementation of the RNTCP and offering suggestions for improvement is that the data on some vital aspects of its functioning - the Management Information and Evaluation System (MIXES) are often non-existent or very scanty or are of questionable quality, validity or reliability. The DGHS Brief referred to the Pilot Projects, baseline data on Annual Rate of Infection (ARI), monitoring and evaluation of RNTCP and the use of the approach of operational research and systems analysis, in the true scientific definition of the term used by the National Tuberculosis Institute, Bangalore (NTI). However, they do not seem to have published or even produced documents which contain such vitally needed information.

Under such circumstances, it was fortuitous for us to have an opportunity to have a first hand study of the functioning of three centres for implementing RNTCP in Hoogly District of West Bengal and have detailed exchange of views with the workers involved at the diferent levels of the administration. We are fully conscious of the limitations of the data base and will be grateful to get corrected, if better information is made available to correct our assumptions. Analysis of the RNTCP on the basis of such scanty data can thus serve as a stimulus to provoke the authorities concerned into coming out with more comprehensive information to have better standard of debate on this important programme.

The performance data in these three centres in Hoogly revealed that, epidemiologically, the RNTCP covered less than a fifth of the sputum positive cases as assessed by the prevalence figures of the National Sample Survey of 1955-58[5]; there

are serious logistics problems in getting the patients for administering DOTS; even sub-district level physicians in charge of RNTCP did not have adequate understanding of the RNTCP; the efficiency of the staff involved was below par; and, certainly, RNTCP is sucking in a substantial proportion of the resources from the already resource - starved infrastructure, thus causing problems for implementing other health programmes, including, ironically, implementation of NTP in non-project areas.

Some suggestions for a debate on improving the performance of the RNTCP

Though it does not find an explicit mention in the DGHS Brief, indications have been given elsewhere which suggest that the authorities concerned are amenable to adopt a flexible approach towards the details of programme implementation. Some of the areas where a debate can be initiated to improve implementation of the RNTCP within the range of the allowed flexibility are presented below :

1. *Additional Sociological Issues :* Giving primacy to the already existing felt need among tuberculosis patients to seek relief from the suffering has been the sheet anchor of not only the NTP of India, but also almost all over the world[8]. Sociological studies in this country have given a different meaning to the so-called problem of 'default' or 'non-compliance' by putting the problem of non-adherence to treatment within the wider systems perspective, which takes into account the myriad organisational and management and technological issues which affect this phenomenon.

Studies conducted by us in 19 villages, covering eight states of the country, for the period 1972-95 have brought into focus the profound changes that have taken place in the social relations within rural and urban communities[7]. People feel much more empowered and capable of taking responsibility concerning activities which are of concern to them. The constitutional amendments concerning Panchayats and Nagar Palikas are early indications of social recognition of the changes that have occurred. A recent visit to West Bengal, (which incidentally led to the small study of RNTCP in the Hoogly District) revealed that panchayat functionaries have developed considerable political and administrative competence over more than two decades of implementation of Panchayati Raj in that state. It seems but logical that the task of administration of DOTS be handed over to them, more particularly when it is now a constilutional obligation to have at least a third of the membership for women. The contrast between the very poorly functioning, bureaucratic rural health institutions and the panchayat functionaries, who are accountable to the villagers, was very striking. There are many other states in the country which have panchayats of similar levels of performance. Furthermore, with the passage of time, others may also catch up.

It appears that social scientists have not yet adequately taken note of the, enormous increase in the capabilities for self-governance among the people of the country. One such instance was discovered by the DANIDA Leprosy Programme (DANLEP)[8] at Rajnandgaon District and elsewhere in Madhya Pradesh, where they could 'unearth' enormous untapped potential for community initiative for case finding, treatment and disability prevention activities, which far outshone the lethargic, victim blaming government functioning. Two movements in the form of Medical Manthan and Health Camps, which were held in Punjab about a decade back[9], also provide another instance of such mass mobilization for health action. It is a fit problem for interdisciplinary operational research to determine the optimal ways of decentralizing the administration of DOTS lo the patients or Panchayats.

2. *Logistics and Supervisory Support to Panchayats and Other Institutions :* An assured system of supply of drugs (may be in the form of ' drug banks' in the name of the Panchayats), forms/ cards for reports and records and referral facilities will be an integral component of this decentralisation process. The sub-district level supervisory units can provide the vitally needed supportive supervision. A well designed information programme which passes along these responsibilities of the local functionaries to the people at large will be of use in promoting these activities.

3. *Increasing the Epidemiological Effectiveness of*

the RNTCP : Smear negative, culture positive and pre-sputum positive cases of pulmonary tuberculosis can also be included in the RNTCP if the NTP system of referral, radiological or even culture diagnostic facilities at the District/ Taluk Tuberculosis Centres are incorporated within the RNTCP. Once cases are diagnosed, the necessary treatment regimen can be administered according to the norms adopted by that programme.

4. *Strengthening of the Feedback, Information and Evaluation System :* As pointed out in the foregoing, data on baseline ARI, monitoring of the different aspects of the RNTCP, the data obtained from the Pilot Projects and repeat ARI surveys must become available to provide the feedback to make the programme more effective.

5. *Operational Research and Systems Analysis on RNTCP :* For incorporating the changes proposed in the foregoing, these will prove to be most potent tools for increasing the effectiveness of the programme.

6. *Taking Care of the 75% Non-RNTCP Population and Planning for the Post RNTCP Era :* Preoccupation with RNTCP must on no account lead to any form of neglect of the NTP. Indeed, with the changes suggested for increasing the epidemiological coverage of the RNTCP population and decentralization of DOTS, very little difference will remain between an efficiently and effectively run NTP and RNTCP, except perhaps the enormous difference in the cost. It may be recalled that NTP too had very rigorous standards for treatment supervision, once the rest of the elements of that programme were put on the ground.

REFERENCES

1. Banerji, D., Serious Implications of the Proposed Revised National Tuberculosis Programme for India. Voluntary Health Association of India and the Nucleus for Health Policies and Programmes, 1997: New Delhi.
2. World Health Organization, WHO Reports on Tuberculosis Epidemics, *WHO, 1995, Geneva.*
3. Grzybowski, S., Epidemiology of Tuberculosis with particular reference to India, Ind. J. Tub 1995,42, 195.
4. Chakraborty, A.K., Tuberculosis Situation in India : Measuring it through Time Ind. J. Tub. 1993,40,215.
5. Indian Council of Medical Research, Tuberculosis in India : A sample survey, 1955-58, Special Report Series, 34, ICMR, 1959 : New Delhi.
6. Banerji, D., A Social Science Approach to Strengthening India's National Tuberculosis Programme, Indian Journal of Tuberculosis, 1993, 40,61.
7. Banerji, D., A Socio-cultural, Political and Administrative Analysis of Health Policies and Programmes in India in the Eighties, 1991 : Lok Paksh, New Delhi.
8. Danlep, Leprosy Eradication : An experiment in Community Action, 1988 : DANLEP, New Delhi.
9. Government of Punjab, Mobilising People for Healthy Living : An Experiment initiated by Sardar Swam Singh Boparai, *Chandigarh : Department of Health and Family Welfare, 1987.*

Ind. J. Tub, 1998, 45, 227

MULTIDRUG RESISTANT TUBERCULOSIS : SUCCESSFUL TREATMENT WITH AN UNCONVENTIONAL REGIMEN

Anil K. Agarwal, Inder Mohan Chugh and Ashok Shah

(Received on 12.5.98; Accepted on 11.8.98)

Summary: We report a case of multidrug resistant pulmonary tuberculosis successfully treated with drugs which are not commonly used against tuberculosis.

INTRODUCTION

Over the counter availability of anti-tuburculosis drugs associated with indiscriminate use, in inappropriate combinations by practitioners not well-versed in the proper use of drug therapy in tuberculosis has aggravated the problem of drug resistance. Multidrug resistant tuberculosis (defined as *M. tuberculosis* resistant to Isoniazid and Rifampicin, with or without resistance to other drugs) has recently been reviewed and data on the prevalence of multidrug resistant tuberculosis (MDR-TB) in different countries have been summarized by the WHO/IUATLD Global Surveillance Project[1]. The highest rate of MDR-TB has been reported from Nepal (48%) followed by Gujarat, India (33.8%), New York City (30.1%), Bolivia (15.3%) and Korea (14.5%)'. In, India, primary MDR-TB is reported to be ≤3.2% and acquired MDR-TB is ≤6.0% except in Gujarat[2]. The report presents a worrisome picture of the patients with MDR-TB from different parts of the world[2]. This grim situation, along with the advent of AIDS, has led to the search for appropriate anti-tuberculosis agents amongst currently available drugs[3].

We present a HIV negative case with MDR-TB who was on continuous ATT in various combinations including reserve drugs for the last 3 years without relief. He, however, eventually responded to an unconventional regimen with the help of four new drugs which are not generally used against tuberculosis.

CASE REPORT

A 30-year-old, non-diabetic, HIV negative Tibetan male, diagnosed as a case of pulmonary tuberculosis was referred to our Institute with haemoptysis of 2½ years' duration. He also had low grade intermittent fever without chills or rigours. One month prior to presentation, the patient had developed exertional breathlessness. Three years prior to referral, based on radiological appearances but without bacteriological confirmation, he was initiated on ATT. Since then, he had been on continuous therapy in various combinations (Table 1). Once before, 17 years ago, the patient had received regular ATT for 3 months which he had stopped of his own accord. He was then given Streptomycin injections along with some yellowish coloured tablets which were most probably a combination of Isoniazid and Thiacetazone. For the last 3 months, he was receiving Rifampicin 600 mg and Ethambutol 800 mg once daily.

On examination, his nutrition was poor and he appeared to be ill. He was afebrile and chest revealed evidence suggestive of bilateral upper lobe fibrosis along with cavity on the left side (Fig. 1). A review of eight serial chest radiographs over a period of 3 years revealed a steady deterioration in the lesion. Six direct sputum smears were positive and *M. tuberculosis* was also isolated on culture. Tuberculin test with 1 TU PPD showed induration 18 mm. His haemogram, blood sugar, electrocardiogram, liver function as well as renal

Department of Clinical Research, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi

Abbreviations :, AIDS = Acquired Immunodeficiency Syndrome; ATT = Anti-tuberculosis Therapy; HIV = Human Immunodeficiency Virus; MDR-TB = Multidrug Resistant Tuberculosis

Correspondence : Dr. Ashok Shah, Department of Clinical Research, Vallabhbhai Patel Chest Institute, University of Delhi, P.O. Box, 2101, Delhi -110 007.

Table 1. *Previous Treatment History*

Month	Year	ATT given	Duration (Months)	Sp. for AFB	Comments
	1978-79	S + 7HT	3	ND	- Inadequate treatment; Drugs stopped too early
November	1992	$R_{450}H_{300}E_{800}$	$2^{1}/_{2}$	ND	- ATT started without bacteriological evidence
February	1993	$R_{450}H_{300}Z_{1500}E_{800}$	1	ND	- Only one drug (Z) added
March	1993	$R_{450}H_{300}E_{800}$	4	ND	- Needless change in treatment regimen
July	1993	$R_{600}H_{300}E_{800}N_{500}C_{500}$	21	ND	- 2 new second-line drugs (N,C) added
May	1995	$R_{600}E_{800}$	3	ND	- Inappropriate treatment

ND - Not done; S - Streptomycin, H - Isoniazid, T - Thioacetazone, R - Rifampicin, E - Ethambutol, Z Pyrazmamide, N - Ethionamide, C - Cycloserine.

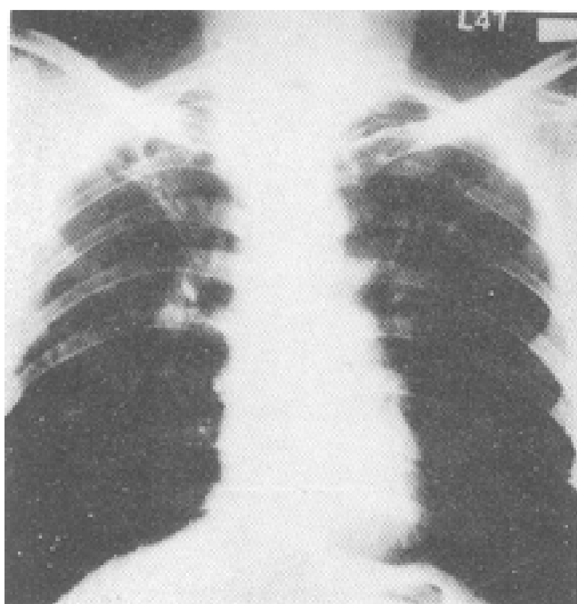


Fig. 1. Post therapy chest radiograph showing marked resolution of the lesions

function tests were within normal limits.

Based on drug history, sputum status and radiological picture, a clinical diagnosis of drug resistant tuberculosis was made. The patient was initiated on a domiciliary regimen comprising Streptomycin 1 gm intramuscularly once daily, 5 days a week; Clofazimine 200 mg once daily; Ciprofloxacin 750 mg twice daily; Pyrazinamide 1500 mg once daily; a combination of Isoniazid 150 mg and Para-aminosahcyclic acid (PAS) 5 gm twice daily along with symptomatic treatment. Three months later, although the patient had experienced symptomatic relief, 3 direct sputum smears were still positive and the chest radiograph did not show significant improvement. The sputum sensitivity report, which became available at that time, showed that the mycobacterium was resistant to Isoniazid, Rifampicin, Streptomycin, Ethambutol and Kanamycin but was sensitive to Thiacetazone, Cycloserine, Ethionamide, Ciprofloxacin and Ofloxacm. Sensitivity to Pyrazinamide was not tested. Based on the sensitivity report, the ATT was revamped. Streptomycin was stopped and Capreomycin 750 mg once daily intramuscularly, 5 days a week; Cycloserine 500 mg once daily and Ethionamide 500 mg once daily were odded.

Within 2 months of commencement of the revamped ATT, the patient was asymptomatic. Haemoptysis had stopped and appetite had improved with significant gain in weight. Sputum for AFB and cultures for *M tuberculosis* were negative and continued to remain so. The chest radiograph also showed marked improvement (Fig.2.) Liver and kidney function tests along with audiometry were monitored regularly throughout the treatment and remained within acceptable limits. Cycloserine had to be stopped after 5 months of initiation due to non-availability of the drug. Capreomycin could only be withdrawn after 9 months as the patient did not report for follow up though he continued taking his medicine regularly. The anti-tuberculosis regimen was stopped after a total duration of 24 months. Patient continues to remain well after cessation of therapy.

DISCUSSION

The development of drug resistance in our

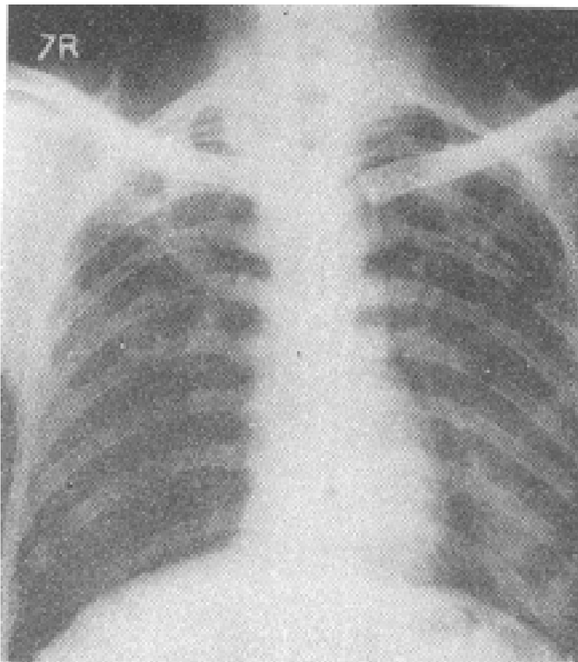


Fig. 2. Chest radiograph on presentation showing bilateral fibrocavitary disease along with infiltrative lesions in left lower /one

patient can be attributed to the erratic treatment by the treating physicians Unfortunately, single drug or inappropriate combinations were added each time without bacteriological confirmation which contributed to the development of *in vivo* resistance to other ATT which the patient received Inappropriate, incomplete or erratic treatment of active disease, as m our case, is a common cause of acquired drug resistance in tuberculosis

The cardinal rule followed for effective therapy of MDR-TB requires administration of multiple agents which the patient has not received earlier However, this rule has limitations as the number of effective drugs is limited and the choice of drugs must also be guided by the resistance pattern of the individual's strain It is suggested that anti-tuberculosis retreatment regimen should always include at least four but possibly as many as six or seven drugs depending on the extent of disease and potency of available agents[4] lavisw of the dtmtal and radiological deterioration m our patent along with persistent sputum positivity on direct smear we were compelled to use drugs which are not commonly used m tuberculosis and which the patient had not taken in the past viz Clofazimme, Ciprofloxacm, PAS and Amoxycillm-clavunalate, as all these drugs have anti-mycobactenal activity[45] PAS was also added to the regimen Although the patient had received Streptomycin and Pyrazmamide, these drugs were also added to the regimen as we felt that the patient had received these for a short duration and in an inappropriate combination However, based on the sensitivity report available after 3 months and the then direct smear report, we added Capreomycm, Ethionamide and Cycloserme after stopping Streptomycin Although the cost of the revised legime was prohibitive, the results were gratifying as evidenced by the clinical, bacteriological and radiological response in our patient

This report suggests that some of the currently available drugs which also have anti-tuberculosis activity may be useful in managing patients with drug resistance who have already received the conventional first line ATT and the reserve drugs commonly used against tuberculosis

ACKNOWLEDGEMENT

The authors are thankful to the New Delhi Tuberculosis Centre for the culture and sensitivity reports

REFERENCES

1 Cohn, D L , Bustreo, F , Ravighone, M C Drug-resistant tuberculosis Review of worldwide situation and the WHO/IUATLD Global Surveillance Project Clin Infect Dis 1997, 24 (Supl 1) SI21

2 Paramasivan CN An overview on drug resistant tuberculosis in India Lung India 1998, 16 21

3 Shah, A , Bhagat, R , Panchal, N Resistant tuberculosis Successful treatment with amikacin, ofloxacin, clofazimme and PAS *Tuberc Lung Dis* 1993,74 64

4 Iseman, M D Treatment of multidrug-resistant tuberculosis *NEnglJMed* 1993, 329 784

5 Home, N Ross and Home's Modern Drug Treatment of Tuberculosis, 7th ed (Indian ed) *Oxford Univ. Press,* Deffii, 1992, 25-27

Case Report

Ind. J. Tub., 1998, 45, 231

TUBERCULOSIS OF THE FLAT BONE OF THE VAULT OF SKULL - A CASE REPORT

K.B. Gupta, Sanjeev Tandon, Rajeev Sen and Rajnish Kalra*

(Received on 22.6.98; Accepted on 7.7.98)

Summary: **A rare manifestation of tuberculosis involving the vault of skull and presenting as» non-healing discharging wound over the parietal skull bone *is* reported.**

INTRODUCTION

Tuberculosis of the flat bones of the vault of skull is rare and is considered secondary to an active or latent tuberculous lesion elsewhere in the body. We are reporting a case of tuberculous osteomyelitis involving the parietal bone of the skull.

CASE REPORT

A 19 year old non smoker male presented with a non-healing wound, discharging yellowish pus over the right parietal bone of skull vault. Two months earlier, the patient sustained a minor trauma to his head followed by a swelling at the same site after six weeks, which was incised by a general practitioner, mistaking it for an infected hematoma. Initially, the wound healed but then it started discharging yellowish pus. There was no history of cough. The patient was anaemic without any lymphadenopathy. Systemic examination was normal.

Local examination revealed a 5 x 7 cms non-healing wound eroding the parietal skull bone with undermined edges, discharging yellowish pus, over the right parietal bone (Fig. 1). The pulsations of the dura synchronous with the radial pulse were clearly visible at the bottom of the wound.

In the laboratory investigations, haemoglobin was 9.8 gm%, total and differential leucocyte counts were within normal limits, ESR was 68 mm/ 1st hour (Westergren's method). Pus smear was negative for acid fast bacilli. Repeated cultures of the discharge from the sinus were sterile. Skiagram chest PA view was normal. X-ray skull AP view revealed a lytic area in the parietal bone (Fig.2) Other radiological and imaging investigations did not reveal visceromegaly and lymphadenopathy anywhere else in the body. Mantoux test was strongly positive (26 x 26 mm). ELISA for HIV was negative and VDRL was non-reactive. Wedge biopsy from the skull wound revealed histological features compatible with tuberculous osteomyelitis (Fig. 3)

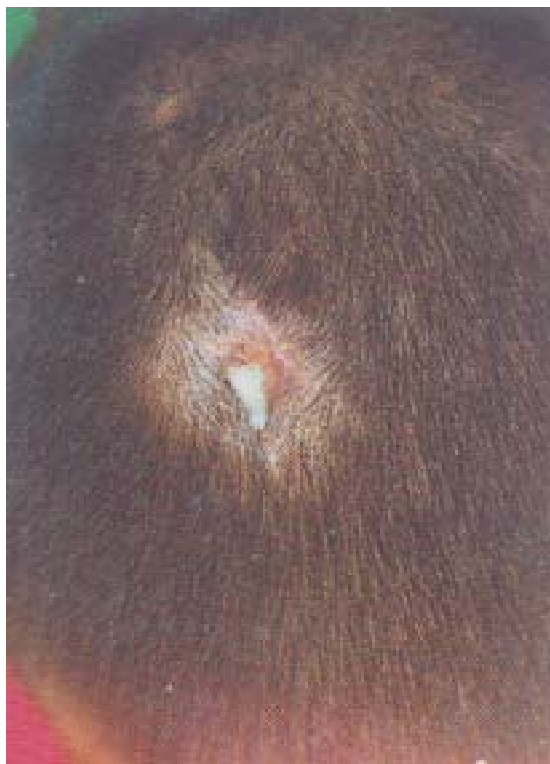


Fig. 1. Photograph showing discharging sinus over the right parietal skull bone

Departments of Chest & Tuberculosis and Pathology*, Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak.

Correspondence: Dr. Sanjeev Tandon, 68-B, Model Town, Rohtak - 124 001, (Haryana)

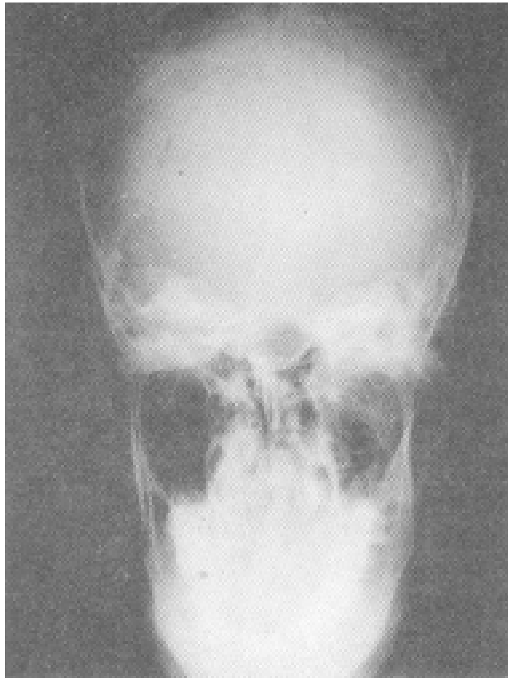


Fig. 2 X-ray skull AP view showing lytic area in the parietal bone

The patient was treated with standard short course chemotherapy (2HRZE/4HR) which was followed by complete healing of the skull wound with granulation tissue, without any discharge, after completion of 2 months of initial intensive phase of chemotherapy Subsequent follow-up in continuation phase is satisfactory

DISCUSSION

The first authentic case of tuberculosis of skull was repotted by Ried in 1842'' It is an extremely unusual site for skeletal tuberculosis, because of little cancellous bone in the flat bones since tuberculosis of the bone, in geneial, usually begins m the cancellous portion of the bone involved

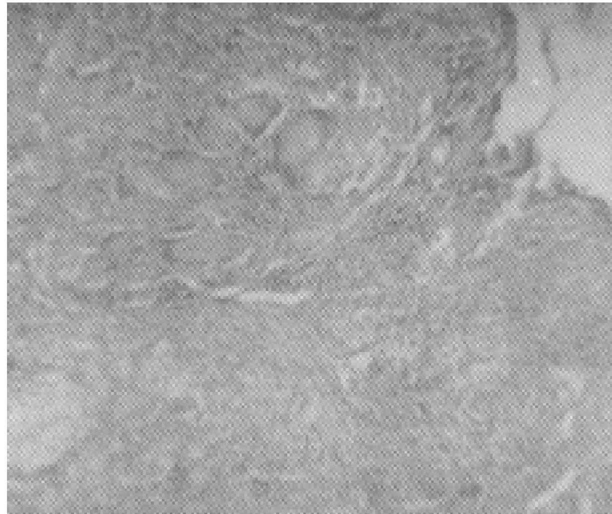


Fig. 3. Microphotograph showing caseatmg granuloma-tous inflammation involving skin and underlyingstructures, in the biopsy taken from the edge of the discharging sinus (H & E stain x 200)

This case is a rare presentation of tuberculous osteomyelitis of the flat bone of the skull and the importanc e of histology in making the correct diagnosis of a non-healmg wound overlying a lytic bony lesion No active tuberculous focus elsewhere, suggestive of primary focus, could be located in the present case To illustrates the role of hematogenous dissemination from a primary tuberculous focus, subsequently becoming active aftei minor trauma.

REFERENCES

1 Valentine, S J Tuberculosis of the flat bones of the skull *Br J Surg* 1921,228
2 Straus, C D Tuberculosis of the flat bones of the vault of the skull *Surg Gynec Obstei* 1933 57 384
3 Meng C M , Wu Y K Pubciculosis of the flat bones of the skull *JBJ Surg* 1942 24 341

Ind. J. Tub., 1998, 45, 233

IVORY VERTEBRAE-A RARE MANIFESTATION OF VERTEBRAL TUBERCULOSIS

Dhiraj Kapoor[1] and R.K. Patial[2]

(Received on 26.2.98; Accepted on 7.5.98)

Summary; **Occurrence of ivory vertebrae In an untreated case of vertebral tuberculosis Is presented because of its rarity.**

INTRODUCTION

Tuberculosis is known not to spare any system of the body. Tuberculosis of the spine, first described by Sir Percival Pott in 1779, accounts for approximately 50% of skeletal tuberculosis. Ivory' Vertebrae (isolated hyperdense vertebrae) occurrence in tuberculosis is very uncotnmon. Infrequently, it develops after anti-tuberculosis treatment[1]. However, its common causes are Paget's disease, multiple myeloma, Hodgkin's lymphoma, chordoma, Ewing's sarcoma, lipoma, chronic osteomyelitis and osteoblastic metastasis[2].

CASE REPORT

A fifty year old male was admitted to I.G. Medical College Hospital, Shimla with five months history of fever, high grade, continuous and associated with chills and rigors. There was an associated history of increased frequency of micturition without burning sensation. He had lost 6 kg of weight in the last five months. There was no history of cough, haemoptysis, headache or abdominal pain. Patient was being treated for urinary tract infection for the last 2 weeks prior to admission, without any improvement. On examination, the patient looked ill, with a hypoasthenic build and below average nutritional status, and temperature of 103°F. Rest of the physical and systemic examination was normal. Haemogram showed Hb-10g%, TLC 5,600/cmm, and ESR 80 mm, 1st hr. Biochemical investigations including liver and renal functions and serum electrolytes were normal. Blood and urine cultures were sterile. Urine tested for AFB by smear was negative. Peripheral blood smear was negative for malarial parasite. Widal and serology for HIV were negative. Chest X-ray and ECG were normal. Ultrasouind of abdomen suggested a retroperitoneal mass pushing the kidneys upward. X-ray of lumbar spine (AP view), showed a hyperdense L3 vertebra with sclerotic osteophytes, normal disc space but without any evidence of destruction. CT scan of abdomen revealed bilateral multioculated psoas abscess and hyperdense L3 vertebra (Fig. 1) The axial view of this vertebra showed the central and anterior parts of the body hyperdense as compared to rest

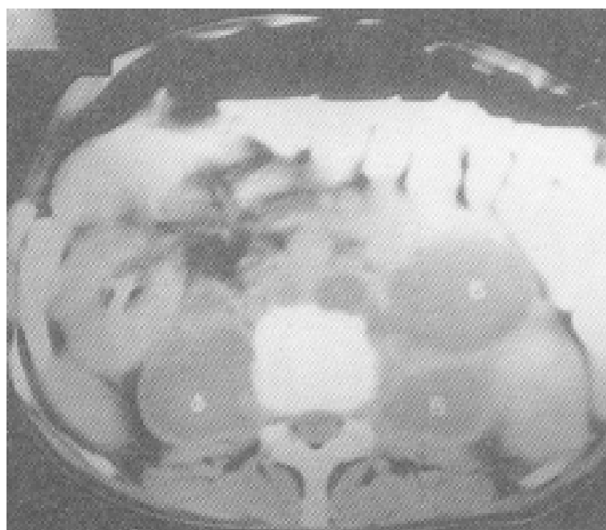


Fig.l. CT scan of abdomen showing bilateral multiloculated psoas abscess; hyperdense L 3 vertebrae and irregular vertebral erosions

1. Ex-Registrar, 2. Assistant Professor

Department of Medicine, Indira Gandhi Medical College, Shimla

Correspondence : Dr. Dhiraj Kapoor, Assistant Professor, Department of Medicine, R.P.Medical College Hospital, Dharamshala, District Kangra - 176 215

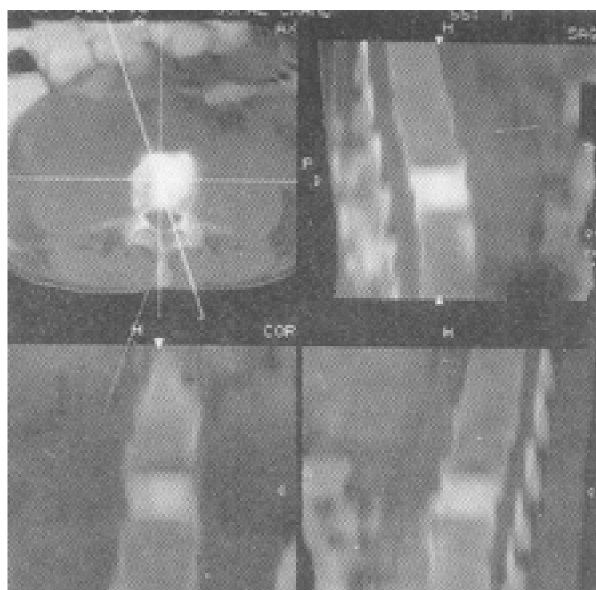


Fig.2. Sagittal and coronal reformatting showing a solitary hyperdense vertebra. Axial view shows hyperdensity in the anterior and central parts.

of the vertebra. The sagittal and coronal reformatting also showed a solitary hyperdense vertebra (Fig.2). About 100 cc of greyish pus was aspirated from the psoas abscess. The pus was sterile but showed AFB on Ziehl-Neelsen staining. The patient was put on Isoniazid 300 mg, Rifampicin 450 mg, Pyrazinamide 1200 mg, Ethambutol 800 mg daily. His general condition improved and he became afebrile on the 14th day of therapy. He was discharged on anti-tuberculosis therapy and is doing well on follow up, without developing any new symptoms.

DISCUSSION

Tuberculosis is a common cause of prolonged pyrexia. Skeletal involvement occurs in appromixately 1 to 3% of patients with tuberculosis. It is always secondary and the infection reaches through the haematogenous route. The paravertebral venous plexus of Batson is the favoured vascular system for the spread, though lymphatic drainage from pleura or kidney can play this role via the periaortic lymph nodes with subsequent erosion into the spine[3]. The lower thoracic and upper lumbar vertebrae are commonly involved because of the relationship of these vertebrae with the cisternae chyli, kidneys, increased stress and mobility, and increased vascularity[4].

Single vertebral involvement is uncommon. An ivory vertebra (increased density) is rare and may be seen after specific therapy . However, sclerotic changes may occur without treatment[3] on account of decreased blood supply to vertebra due to thrombosis, endarteritis, occlusion or destruction of blood vessels by a dissecting abscess. Pathologically, these vertebrae have intact trabeculae and the sclerotic changes are caused by the granulation tissue and caseous material filling the marrow spaces rather than an increase in the density. Our patient had an ivory vertebra along with a psoas abscess. The urinary symptoms were probably due to irritation of the urinary tract The combination of caseating and productive sclerosis may coexist in one-fourth of the patients with tuberculosis of spine. Paravertebral abscess had been met with in around 58% of the patients of vertebral tuberculosis'. In the lumbar spine, pus may collect beneath the fascia and extend along the psoas muscle.

Demonstration of AFB in the pus from the abscess in unusual but its presence excludes the other causes of ivory vertebrae, further supported by the patient's response to antituberculosis therapy.

REFERENCES

1. Tuli, S.M. Tuberculosis of the skeletal system. 1st edn., Jaypee Brothers, New Delhi, 1991; 138.
2. Mohan, V., Gupta, S.K. Univertebral sclerosis (Ivory vertebrae). *Indian J of Radiology and Imaging,* 1991; 1 (SII): 775.
3. Epstein, B.S. The spine- A Radiological Text and Atlas 4th edn., Lea and Febiger, Philadelphia, 1976; 362.
4. Duthie, R.B., Bentley, G. Mercer's Orthopaedic Surgery 8th edn., Edward Arnold, London, 1983; 528.

Ind. J Tub , 1998, 45, 235

DOCTORS TO RE-LEARN BESIDE MANNERS

Around 18,000 doctors in the USA have been asked by their Health Maintenance Organisations (HMOs) to attend institutions like the "Bayer Institute for Health Care" to relearn -their bedside manners and polish their ways to interact with patients. It is recognised that the present day brusque and even rough conversation doctors have with their patients is due to pressure of work and less time and the unreasonable expectations of some patients. Nevertheless, there is no justification whatsoever for patients and their doctors to have widely different perceptions and expectations while receiving treatment.

Doctors in India have perhaps even greater need to attend to this emerging cancer in their professional ethics. The opening chapter of this "re-learning gambit" in the U.S.A. is for doctors to learn how to put up a smiling face and keep quiet till the patient has old all about the ailment in own words. This is followed by asking some leading questions by the doctor before starting a physical examination, attended with the requisite concern expressed about patients' welfare.

CIGARETTES MADE MORE LETHAL THAN PURE TOBACCO

Over 39,000 secret tobacco-industry documents, made public recently in the USA, have revealed that while the major manufacturers of cigarettes were fully knowledgeable quite early about the adverse health effects of tobacco smoking, and were knowingly soft-pedalling the danger to health by projecting a "smoke-screen" of efforts aimed at reducing the nicotine content of their cigarettes as well as putting in "filters" to reduce the tar content, they were secretly making their cigarettes more addictive for profit/commercial reasons.

Thus, the documents show, hundreds of different chemicals were being added, of which the most damaging was Etorphine, known to be 10,000 times more addictive than morphine. Another culpable additive was ammonia which enhanced the delivery of nicotine into the system even from the reduced tobacco nicotine content of the "safer" cigarette.

Secret documents, dated as early as the sixties had duly noted that nicotine was as addictive as cocaine, though quite effective in the release of stress mechanisms; that "young adult males, should be specially made the target of encouraging the smoking habit", and that "when consumers ask whether cigarette smoking caused cancer, the answer should always be that the effect of smoking on human health is still a controversial and inconclusive matter".

Determined to keep published reports about the dangers of "second-hand smoking" from mushrooming, the industry adopted a two track strategy, in the mid-1980s. The major step was to directly attack the credibility of scientists who chose to publish their results and indirectly pressurize them, through their bosses, not to do so on the peril of losing their jobs. The other step was for the major companies to divide their own individual universes of opponents and "battle" them though litigation, media disgrace, government pressure, employers' and insurers' downgrading, as found feasible and practicable.

"EXOIC TUBERCULOSIS"

A case of severe mitral : regurgitation due to perforation of anterior valve leaflet by tuberculous endocarditis in a patient who had no other tuberculous lesions has been reported. *M tuberculosis* were cultured from the vegetations on the leaflet. There was no immune-compromise *(Int. J. Tuberc. Lung Dis.* 1998, 2, 435).

In a letter to the Editor, *Int. J. Tub. Lung Dis.;* (1998, 2, 439) Richards M.J. and Angus D. speculate that one of their patients, who had genito-urinary tuberculosis, passed on the infection to his wife, who was diagnosed to be having tuberculosis of the uterus and its adnexa. Neither of them had any evidence of pulmonary tuberculosis and both were immuno-competent.

AIDS VACCINE READY FOR CLINICAL TRIALS

After completing preliminary trials successfully in Phases I and II at the Vaxgen Inc. laboratories, the Federal Drugs Administration (U.S.A.) has permitted large scale human trials (in the U.S.A. and Thailand) of an anti-AIDS vaccine developed by Dr. Donald Francis, a viroloeist noted for his

contribution to the fight against smallpox in India and Ebola in Sudan. The phase III trial will now involve 5,000 volunteers in the U.S.A. and 2,500 in Thailand and will take at least 3 years to complete.

Consensus of opinions among the researchers concerned so far is that protective immunity against AIDS, through generating antibodies against HIV, alone cannot help protect against AIDS. The preliminary trials have shown that "AIDSVAX" is safe and produces antibodies strongly against HIV among 90% of the vaccinated subjects. Its efficacy will now be scientifically tested. That the basic interaction between HIV and the human immune system is still incompletely understood needs to be underlined.

ANTI-AIRS DRUGS FOR WIBIR USE

The 12th International Conference, held in Geneva in June 1998 focused, also, on the use of multidrug therapy for AIDS sufferers, on a scale much wider than has been possible so far. There are an.estimated 30 million HIV infected people worldwide of whom approximately one tenth may be in need of multi-drug therapy. A very large majority of such sufferers are in the third world countries where the use of such expensive drugs is just not thinkable. Nowadays, a "cocktail" of 3 drugs is being used to get good results from AIDS therapy. Of about a dozen anti-AIDS drugs in use for AIDS and other infectious diseases that exist concurrently with AIDS, the most used are AZT, 3TC and the "Protease inhibitor" antiviral drug Crixivan. The United Nations AIDS Programme (UNAIDS) has persuaded the giant pharmaceutical firms of Glaxo-Welcome, Bristol-Myers Squibb, Abbot Laboratories and Roche Holdings to agree to sell these drugs at around 60% of the market price in the U.S.A., (where a year's treatment of a patient may cost $ 10,000 to $ 20,000) to the consumers in poor countries. It is quite obvious that these multinationals have agreed to discount their prices not out of compassion but on business sense because they are insisting on certain terms of procurement and distribution of their discounted drugs in the developing countries. The prospect of entering a huge market is attractive enough to permit slashing of prices but there is no guarantee of how long UN interest and funding will last, nor is there any assurance that the discounted stocks will not fall into wrong hands and be resold at higher prices in the rich countries. It is apparent that an experimental phase of the agreement will decide the future of the wider application of anti-AIDS chemotherapy in the AIDS 'hot spots' of the third world.

There is also a new anti-AIDS drug on the horizon-Duponts' Sustiva- which is a non-nucleoside reverse transcriptase inhibitor and works in a way different from the Protease inhibitors. Sustiva may reduce the number of tablets to be taken daily, from the present 10-12 (2 x 300 mg AZT + 2 x 150 mg 3TC + C x 200 mg Crixivan) to just 3-one each of AZT (450 mg), 3TC (450 mg) and Sustiva (600 mg) daily. Besides, Protease inhibitors have the troubling long term side effect of excessive fat deposits in the gut and along the back. The newer multi-drug combination may prove useful to the rising number of patients found resistant to AZT, etc., probably because of poor adherence to drug regimens. However, Sustiva is known to have caused congenital anomalies in animal models and emotional problems in subjects undergoing clinical trials.

PREVENTING NEONATAL HIV INFECTION

Recent studies, reported from France have confirmed that a combination of Caeserian Section and AZT chemotherapy of sero-positive mothers lowers the risk of transmitting HIV infection during vaginal delivery from 25% to less than 3%. Caeserian section alone lowers the risk to 8%. Dr. Laurent Mendelbrot, the leader of the French research group has reported on 2,834 mother-infant pairs. Of the, 1,917 mothers who did not receive AZT, 17.2% transmitted HIV to their infants compared with 6.6% who had AZT. Of the mothers who took AZT before delivery and chose to get C. Section, transmitted the infection to their new-borns to the extent of 0.8%.

NEWS AND NOTES

SAARC TB Centre

The SAARC TB Centre held a training programme for strengthening IEC activities among Member Countries with special emphasis on TB and HIV infection, in Delhi, during February, 1998.

A 5 day training programme for "TB Programme Managers" was held in Maldives, in April 1998.

A Seminar on "Socio-anthropological Research Studies in the Field of Tuberculosis" was held in Kathmandu in May-June, 1998.

The 2 day workshop on "Research inTuberculosis and HIV Infection in the SAARC Member Countries", held in Kathmandu in October 1997, made the following recommendations : "To make holistic approach, advocacy, training, community based service delivery and research as the identified major areas of collaboration, both at intra and inter country levels:

1. Advocacy

A strategy aiming at politicians, administrators and technocrats needs to be developed so that the management activities receive adequate political commitment as well as technical and administrative support including funding. How both the epidemics interact and the rational steps that can be taken for more effective HIV/TB prevention and treatment need to be emphasised.

2. Training

Basic training programmes for both AIDS and Tuberculosis health workers need to be developed, i.e. AIDS workers need to be trained in TB control programme and TB workers in the important facets of the AIDS programme, preparing an army of workers who are well equipped to manage the cases of HIV/TB dual infection.

3. Community Based Service

Tuberculosis remains the most important opportunistic infection in HIV cases. TB services are required to be taken to the door step of the community, at a place convenient to both, health providers and users.

4. Research

(a) Research in TB and HIV is a priority. It must be linked to programme needs and coordinated between National AIDS and TB programmes. All TB and HIV research activities should be officially approved through the national health research council or its equivalent. Joint research projects conducted by SAARC member states should be developed by the respective programmes.

(b) Many countires have limited capability to plan and conduct research. NTP and AIDS programmes may benefit from assistance given for development of protocols and supervision of research staff and financial support. For this purpose, inter/intra country and international agencies' collaboration may be useful. SAARC TB Centre will provide support to TB-HIV research initiatives in the following ways :

(i) Providing a platform for interaction.

(ii) Collection of information and diseminating the same.

(*iii*) Preparation and review of research protocols.

(c) TB-HIV research needs to vary from country to country. Priorites should be developed jointly by the two programmes. Testing of TB patients for HIV/AIDS is a highly sensitive issue. Routine mandatory testing of TB patients for HIV is not recommended, unless a specific beneficial intervention is sought for. Voluntary testing must include pre- and post counselling, with assurance of confidentiality.

(d) Possible TB-HIV research priorities include :

(*i*) Strengthening of surveillance activities (sentinel surveillance of HIV in TB patients, if undertaken by any member country, should be done only by unlinked anonymous testing)

(ii) Longitudinal cohort studies of the outcome of tuberculosis infection/disease amongst people infected with HIV.

(iii) Assessing the efficacy of DOTS

diagnostic routine in dual infection cases of HIV/TB.

(*iv*) Testing the efficiency of the treatment regimens of DOTS in cases of HIV-TB.

(*v*) Developing models of community based care of people with HIV and TB.

(*vi*) Assessing the impact of the TB/HIV epidemics.

NATIONAL POLICY ON VOLUNTARY BLOOD DONATION

The draft National Policy on Blood Donations, issued in August 1998 aims at increasing the voluntary blood donations in order to enusure safety and adequacy of blood needed for surgery and medical emergencies. Professional donors will be discouraged and no new commerical blood banks will be issued a license. Vigorous campaigns will be started to promote voluntary blood donation.

Besides, guidelines have been issued regarding re-organisation of blood transfusion services, proper use of blood components, single unit transfusion and service charges levied on account of handling blood.

A post-graduate degree course in transfusion medicine may be started in each state, in place of only 2 colleges giving such a degree, as at present.

There are at present 603 government and 130 vountary blood banks, 245 banks linked to private hospitals and 245 commerical blood banks. Most of these depend on professional donors for their supplies.

53RD NATIONAL CONFERENCE ON TUBERCULOSIS AND CHEST DISEASES

The 53rd National Conference on Tuberculosis and Chest Diseases will be held under the auspices of the Tuberculosis Association of India and the Orissa State TB Association at Ravindra Mandap, Bhubaneswar, (Orissa) from 27th to 30th December, 1998. Those who wish to attend the conference can obtain the Registration form from the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi - 110 001.

TB HEALTH VISITORS' COURSE

The Health Visitors' Course for 1998-99 conducted by the Tuberculosis Association of India at the New Delhi TB Centre commenced from 1st July, 1998.

SILVER JUBILEE CONFERENCE ON TB AND CHEST DISEASES

The Tuberculosis Association of Andhra Pradesh held its Silver Jubilee Conference on Tuberculosis and Chest Diseases from 11th to 13th September, 1998 at Hyderabad. The conference was co-sponsored by the Department of International Development (U.K.).

Ind. J. Tub., 1998, 45, 239

BOOK REVIEW

Summaries of NTI studies : compiled by P. Jagota and M.N. Srikantaramu, 1997published by the National Tuberculosis Institute, 8, Bellary Road, Bangalore-560 003. Pages 128, Price not stated.

The National Tuberculosis Institute, Bangalore is too well known to need any introduction, being a leader in research on Tuberculosis, specially the operational and community aspects of tuberculosis control.

Over the almost thirty years of its working, the Institute has published various monumental research papers, and developed the National Tuberculosis Programme which, in turn, has served as the model for the NTPs of many countries wordwide. Of particular importance has been the fact that this institute has worked towards developing practical and feasible programmes rather than idealistic ones, a fact which is adequately illustrated in the summaries of papers chosen for this collection.

One would only wish that more of such collections are issued by this prestigious institution and that they are made available to all tuberculosis workers. If the other prestigious research institution on tuberculosis, the Tuberculosis Research Centre, also publishes a similar collection, then indeed Indian research and contribution to the fight against tuberculosis will come into full focus.

S.C. Kapoor

The Indian Journal of Tuberculosis

ABSTRACTS

Vol. 45, No. 4 **October, 1998**

A controlled clinical trial of oral short-course regimens in the treatment of sputum-positive pulmonary tuberculosis. Tuberculosis Research Centre, Chennai. Int. J. Tuberc. Lung Dis. 1997, 1: 509.

A total of 1203 out-patients were randomly allotted to three oral SCC regimens. I /12EHRZ,/ $6EH_7$); II ($2/EHRZ_2/4EHR_2$ $III/2HRS_2/4HR_2$ in Chennai and Madurai. Only 1091 were analysed and others had to be dropped from the trial for various reasons such as intercurrent disease, wrong diagnosis, drug toxicity and non compliance. Regimen I patients, i.e. those on 8 months daily chemotherapy collected drugs weekly during first 2 months and fortnightly after that (20 visits). Those under Regimens II & III were further divided into two groups each, one attending for every drug day, i.e. twice weekly and the other collected two doses every week one being taken under supervision and the other self administered. Sputa were examined by smear and culture before start of chemotherapy and every month for the duration of treatment, and every two months after that until 24th month. Radiographs were taken at 1,2,6,8,12 and 24 months for all patients.

Drug sensitivity tests were performed on all positive cultures.

825 patients had bacilli initially sensitive to H and R. After two months of the regimen, 88% of those under Regimen I were culture negative, compared to 73% in Regimen II and 75% in III. At the end of chemotherapy, 11/305 in 1, (ie. 3.6%) I/ 263 (.0.4%) in II and 24/257 (9.3%) in III had unfavourable response, defined as two or more cultures positive at end of treatment. In other, response of Regimen II was significantly better than to I and III and I better than III.

Follow up results could be assessed in 777 patients, 5% in I, 11% in II and 10% in III showed bacteriological relapse during the 24 month follow up. Most of the relapses occurred during the first 3 months in I but upto 12 months in II & III.

In the cases of initial INH resistance, unfavourable response was noticed in 17% in I, 20% in II and 62% in III. It is concluded that Regimen I and to some extent Regimen II, ie. those containing Ethambutol, could feasibly be used under programme and that semi supervised SCC could well succeed where DOTS is not possible.

S.C. Kapoor

Preventability of incident cases of tuberculosis in recently exposed cases. C.R. Maclntyre and A.J Plant Int. J. Tuberc. Lung Dis. 1998; 2 : 56.

In a retrospective cohort study of 783 contacts screened in Victoria, Australia in 1992, a two year follow up revealed eight cases of incident tuberculosis, ranging in age from 2 years to 49 years, i.e. an incidence of 511/100,000, as against 6/ 100,000 in the general population. The authors conclude that, in six out of the eight cases, active disease could have been prevented if adequate measures had been taken. Another conclusion that emerges is that close contacts of infections cases are at high risk, compared to general population.

S.C. Kapoor

A randomised placebo-controlled trial of the efficacy of beta-sitosteril and its glucoside as adjuvants in the treatment of pulmonary tuberculosis. P.R. Donald et al Int. J. Tuberc. Lung Dis. 1997; 1: 518.

Beta-sitosterol (BSS) and its glucoside (BSSG) are abundant in plants but cannot be synthesized by the human body. These sterols have, in experimental animals been shown to lower cholesterol and stimulate lymphocytes proliferation, apart from their immunomodulating effects.

As, inspite of good chemotherapy, over 25% of tuberculosis patients in developing countries may fail to benefit, a pilot study, randomised and placebo-controlled, was undertaken on sputum positive tuberculosis patients under chemotherapy by administering 0.2 mg and BSSG 20 mg BSS thrice daily along with ATT (HRZ) for 6 months.

There was no difference in bacteriological response among the trial and placebo groups. However, lymphocytes showed statistically significant improvement in the study group.

Further studies, about the effect of BSS/BSSG on T_4/T_8 ratio are indicated.

S.C. Kapoor

Intracramal Tuberculoma in Kuwait; Nuama Abdul Ghaffar, M.R. El-Sonbaty, N.A. Rahman; Int. J. TubercuLungDis.; 1998, 2, 413

Tuberculoma constituted 1.4% (13/925) of all intracranial space occupying lesions seen in two hospitals in Kuwait in 9 years (1987-1995). Seizures was the frequent presenting symptom; 9/13 responded well to medical treatment with anti-tuberculosis drugs and six did not require surgery. Those with good response to ATT showed considerable radiological improvement at 6 weeks and almost complete clearing at 12 weeks. The authors recommend a six week therapeutic trial with ATT, especially in places where sophisticated neurosurgical facilities are not available.

S.C. Kapoor

Adrenal function during tuberculosis infection and effects of anti-tuberculosis treatment on endogenous and exogenous steroids; K. Keven, AR, Uysal, G. Erdogan; Int. J. Tuberc. LungDis.; 1998, 2,419

Basal hormone levels and synacthen stimulation tests were carried out on 22 patients of active tuberculosis before and after 3 weeks of ATT including Riframpicin. No significant differences were found in the basal plasma cortisol or ATCH levels, but basal dehydroepiandrosterone sulfate, and urinary free cortisol levels rose significantly after treatment. 1 mgm overnight dexamethosone suppression test was positive before treatment in nine patients but negative in all patients after ATT. Rifampicin may have some effect on steroid metabolism.

S.C. Kapoor

Pulmonary tuberculosis treated with directly observed therapy. Serial changes in lung structure and function. Richard Long; Bruce Maycher; Anil Dhar; Jure Manfreda; Earl Hershfield and Nicholas Anthonisen. Chest 1998; 113 : 933.

Structural changes as evidenced by C.T findings and functional abnormalities were assessed prospectively in 25 patients with drug susceptible pulmonary tuberculosis. Conventional CT and pulmonary function testing were performed at baseline and after one and six months of directly observed therapy in 15 cavitary patients and 10 patients with non-cavitary disease. All but one patient with non-cavitary miliary TB had CT evidence of endobronchial disease, and all patients with cavitary disease had coexistent reduced lung attenuation. Functional impairment was minimal and in proportion to the number of diseased segments and cavitary volume. Bronchiectasis was significantly more likely to complicate cavitary than non cavitary disease (64 vs 11%; $P < 0.05$).

CT findings correlated well with function in pulmonary TB. Physiologic data were consistent with the concept .that pulmonary TB is an endobronchial disease that causes parallel reductions in ventilation and perfusion. This concurrent involvement of both airways and contiguous pulmonary blood supply offers an explanation for the minimal respiratory limitation experienced by these patients despite often extensive lung disease. Supervised therapy of drag-susceptible disease results in minimal structural and functional residue.

Ashok Shah

Sleep disturbances in clinically stable young asthmatic adults. Ravinder Vir, MD; Rajesh Bhagat, MD; and Ashok Shah, MD, Ann Allergy Asthma Immunol 1997; 79 : 251.

A study was conducted to determine the occurrence and nature of sleep disturbances in 30 young adult unmarried university students with clinically stable bronchial asthma. The patients and a similar group of 30 normal subjects were asked to respond to a questionnaire and were required to maintain a sleep diary for one week. The questionnaire revealed that 28 (93%) of the 30 patients experienced sleep disturbances (average 2.7/subject) as com-

pared to 10 (33%) subjects in the control group) average 0.4/subject). The sleep diary confirmed that 27(90%) of the 30 patients had sleep disturbances (2.4/subject/wk) as compared with 8(27%) subjects (0.3/subject/wk) in the control group. These differences were statistically significant. Day time sleepiness arid tiredness (63%) and difficulty in maintaining sleep (60%) along with early morning awakening (46%) were more frequently seen. The asthmatic patients also had a shorter duration of sleep (427 min) as compared with the controls (474 min). These Findings were significantly different from the control group. Increased daytime sleepiness and tiredness was perhaps a reflection of the poor quality of sleep experienced by patients with clinically stable asthma. This, consequently, may lead to impaired daytime performance which can have a potentially serious effect on the patient and society.

Ashok Shah

Pneumothorax in HIV-infected patients : role of Pneumocystis carinii *pneumonia and pulmonary tuberculosis. M. Tumbarello, E. Tacconelli, T. Pirronti, R. Cauda, L. Ortona, Eur Respir J1997; 10:1332-1335.*

Patients with acquired immune deficiency syndrome (AIDS), are at increased risk of pneumothorax, which usually occurs in the setting of *Pneumocystis carinii* pneumonia. A case control study was carried out comprising 140 HIV-infected patients grouped as follows : 35 patients with pnuumothorax and 105 matched controls without pneumothorax.

Univariate anlaysis identified four risk factors' for pneumothorax: 1) previous P *carinii* pneumonia (P = 0.01); (2) current *P. carinii* pneumonia (P = 0.02); (3) pulmonary tuberculosis (P = 0.01); and (4) cysts, pneumatocles or bullae on chest radiographs (P < 0.001). Multivariate analysis indicated that current *P. carinii* pneumonia (P = 0.001) and pulmonary tuberculosis (P = 0.04) were both independent risk factors for pneumothorax. This study demonstrates that, in addition to *Pneumocystis carinii* pneumonia, pulmonary tuberculosis enhances the risk of pneumothorax in patients with acquired immune deficiency syndrome.

Ashok Shah

Tuberculosis of the central airways : CTfindings of active andfibrotic disease. Woo Kyung Moonl Jung-Gi Im Kyung Mo Yeon, Man Chung Han. AJR 1997, 169, 649.

The purpose of the study was to analyze CT findings of active and fibrotic disease in patients with central airways tuberculosis. As confirmed by bronchoscopic findings and biopsy. 41 patients with tuberculosis of the trachea and main bronchi were categorized as having active disease *(n* - 30) or fibrotic disease (*n* = 11). Follow-up CT scans were obtained after anti-tuberculosis therapy in 11 patients with active disease and two patients with fibrotic disease.

Active disease in 30 patients involved the trachea *(n* = 20), the right main bronchus *(n* = 14), or the left main bronchus *(n* = 13). Seventeen patients had multiple lesions. On CT scan, these airways showed irregular *(n* = 24) or smooth *(n* = 4) narrowing in 28 patients; minimal *(n* = 5) or marked *(n* = 18) wall thickening with contrast enhancement in 23 patients; and obstruction with peribronchial cuffing in 9 patients. Enlarged mediastinal lymph nodes were seen in 26 patients. Fibrotic disease in 11 patients involved the trachea *(n* = 6), the right main bronchus *(n* = 2), or the left main bronchus *(n* = 9). Six patients had multiple lesions. On CT scan, the airways showed smooth *(n* = 7) or irregular *(n* = 2) narrowing without *(n* = 5) or with minimal *(n* = 4) wall thickening in nine patients and obstruction without peribronchial cuffing in four patients. On follow-up CT scan, the findings for the airway lesions were almost normal in nine patients who had initial active disease. However, the findings for airway narrowing did not change in Iwo patients with fibrotic disease after 6 months of follow-up.

Central airways narrowing was seen in both active and fibrotic cases. However, in patients with active disease, CT scan showed irregular and thick-walled airways, a pattern that was reversible, whereas patients with fibrotic disease generally had smooth narrowing of airways and minimal wall thickening, a pattern that was not reversed during the follow-up period.

Ashok Shah