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**Editorial**

## **WORLD AIDS DAY**

Last December 1 was World AIDS Day.

It has been customary for long to observe a specific day each year for drawing people's attention to a particularly important disease or topic : holding of discussions, public meetings and rallies, wide media coverage and coining of slogans, etc. are the order of the day. Soon, there became so many days to observe that public attention got divided and their interest slackened. This was attended with gradual creeping in of a sense of "ritualism" among the organisers of such days. Enthusiasm and the intelligent use of innovative approaches went out the window, till, it would appear, the United Nations agencies, particularly WHO, popularized the practice once again. World AIDS Day is one such day.

The observance of World AIDS Day 1994, the seventh since 1988, was thoughtfully amalgamated with the United Nations theme of "International Year of the Family". On the occasion, WHO's Global Programme on AIDS came out with the banner "AIDS and the Family : Families take Care", marking it out as the "first line of defence against HIV..... and the best source of care for AIDS". The idea is to involve traditional as well as non-traditional families, of all kinds, in a social crusade against AIDS. Non-traditional families are people linked together by way of mutual love and friendship, trust, openness and support of various kinds, as if a part of common destiny. Traditional families, of course, have ties of blood, sexual partnership/marriage and adoption. Logically, both kinds of families could be enjoined to protect their members from acquiring HIV infection and taking care of those who fall ill with AIDS. According to a WHO estimate, 14 million men, women and children worldwide with one or more members having HIV/AIDS are living together as families. Of them, children's lot is the worst, since they get infected for no fault of their own, get less of food, love and care which are essential for proper development and, more frequently than not, lose parents untimely and become orphans. Attractive though the theme of family care is, there is a powerful social deterrent to deal with. Families, traditionally, reject what is perceived as a potential threat to the other members, instead of taking loving care of those afflicted. The centuries old "stigma" which attended those having tuberculosis or leprosy and the fate of the mentally deranged in our societies is mute

tuberculosis or leprosy and the fate of the mentally deranged in our societies is mute testimony to this traditional social behaviour.

All this notwithstanding, the HIV pandemic presses on needing urgent attention. The WHO Regional Committee for South East Asia reviewing the march of the pandemic, at Ulan Bator, Mongolia in August 1994, noted that the global estimate of AIDS cases, since it began, had gone up from 2.5 million in July 1993 to 4 million in July 1994, an increase of 60%. Ponder, as we may, over the scientific correctness of those estimates, the grimness of the situation remains inescapable. So is our helplessness in having to depend upon an uncertain family care programme to combat it. And yet, family care by its very nature has to be made an integral part of our efforts, even if it does not help very much in the final analysis.

In the absence of anything more substantial, there is perhaps good reason for adopting the "frail looking" family care programme to contain HIV/AIDS. Speaking at the Tenth International Conference on AIDS in Yokohama (Japan), in August 1994, Dr. William E. Paul, the Federal Co-ordinator of AIDS research in the U.S.A., ascribed the "current inadequacy of treatment for AIDS and lack of a protective vaccine as largely due to the wide gaps yet in our understanding of the disease". Therefore, in the U.S.A. at least, spending on clinical trials may be trimmed in the near future to heavily fund a revitalized and expanded programme of basic research to understand AIDS better.

The new agenda of AIDS research has the following main elements. How does HIV destroy body's immune system? Of particular interest in this connection are around 10 to 15% of the total HIV infected individuals who have now lived for 12 years and over after discovery of their HIV status and remained healthy. Studies are being aimed to find out if these individuals are immunologically different or were they infected with a different type of virus, or both. The development of a second generation of AIDS vaccines will take its cue from the mechanism of "virus reaction" with the immune system. It was believed all along that HIV infects and afterwards destroys the CD4 T cells in the system. However, it may not be happening in this simple way. Evidence has now become available that, at some stage after infection, the immune system gets into a state of "overdrive" which eventually, debilitates it. Therapy which can suppress and slow the "overdriving" system, perhaps, could, therefore, be more helpful. The CD/8 T cells also appear to be particularly effective in keeping the virus replication in check.

Till we can develop the higher technology needed to check the pandemic, we must perforce adopt and develop the social strategy against the ravages of AIDS and derive as much social benefit as is possible.

**D.R. NAGPAUL**



## GOAL OF TUBERCULOSIS CONTROL

In any game, a way has to be developed, by training, to win a match. The Goal is the objective and destination, and the Goal has to be visualised clearly to make a goal. So also, to reach tuberculosis control we should clearly define the control objective.

One morning, during a walk with my most respected "elder brother", Dr. B.K. Sikand, we discussed control and agreed that gradual diminution of the disease was control. But we did not fix the target.

Similarly, I had the great luck to discuss control with my very respected friend and colleague, Dr. K.N. Rao, a former Chairman of the Tuberculosis Association of India (TAI) and Director General of Health Services. He was going to preside over the 8th Expert Group meeting of WHO. We had a long discussion and decided that control should be defined by the infection rate as that is the mirror of infectious cases in a community. We could not firmly fix the target but agreed that this should be very low. We also agreed that the way to do it should be kept open as the development status, extent of tuberculosis and the development of anti-TB campaigns differ widely in different countries.

At that meeting of WHO, the Expert Committee took up the question of defining TB Control. The Committee agreed that: "Tuberculosis should be regarded as controlled when the infection rate has reached one percent at the age of 14 years in the community". The way to achieve it was not chalked out. I should like that TAI should take the initiative to form a committee of experts which will have power to take the steps, to be decided by this expert group. May I suggest that this group should draw its members from the Government, of India, National Tuberculosis Institute (NTI), Bangalore, TAI and include a competent statistician, an epidemiologist, and have the power to call upon any body else, preferably from the States, if necessary.

May I also have the privilege to suggest the way or the steps to reach the Goal. WHO had suggested that on reaching the target of one

percent infection rate at age 14 years, the separate anti - TB programme should be withdrawn and the few cases remaining in the population should be handed over to general public health care. Since there was no earlier elaboration of the needed processes. I shall try to suggest those steps here. I shall put them down according to priority. But, all of them can be started immediately, and together, if the committee can organise and execute them.

### 1. To determine how far we are from the target of control

The objective is to determine the rate of infection at the age of 14 years.

A cooperative study should be organised, requiring all the Training and Demonstration Centres to collect the data for the past 10 years or so and transmit them to the committee office. If needed, TAI or NTI should give the space for the committee office.

I apprehend difficulty regarding availability of past records; these data may be for the age group of 7-14 years. If so, the rate in this group should be estimated. But from now on, a direction should be given to make a separate group of age 13-15 years. The direction to be sent out to Training and Demonstration Centres should be to send 6 monthly or yearly reports from now on, till it is not required any more. As far as I can foresee, this direction will have to be continued for a long time till the rate is nearly 1 percent. This action should be made a routine practice for any clinic and the information should not be difficult to collect. A small sum may be allotted for clerical purposes, if voluntary service is not available.

### 2. To recognise and deal with the forces involved in control

#### Helpful Forces

#### (i) Herd Resistance

The National Sample Survey had revealed that

the morbidity rates of pulmonary tuberculosis are about equal in the urban and rural areas. This means that tuberculosis is equally distributed over the whole country. It may be reasonably expected from the natural history of contagious diseases that the disease had its maximal toll by killing those comparatively susceptible in the population leaving the comparatively resistant ones alive. As it affects all parts of a country, the disease becomes endemic and with time elapsing meets with more resistant people and the rate of morbidity falls. That is, the disease goes on the decline.

That we are on the falling limb of this phenomenon is indicated by :

- \* The start of diminution of the Infection rate in the younger age group, as shown by the record of 249 million tuberculin tests done as pre-BCG vaccination testing till 1960 before direct vaccination programme was adopted.
- \* The finding of a far higher morbidity in the older age-groups than in the younger ages which may be due to the former age groups having passed through much higher periods of infection than the younger ones now, indicating a decline of tuberculosis.

Around 1959, the disease rate was established by a very good Sample Survey. Another similar survey was planned around 1980, to find the progress or regress of the disease. However, it could not be carried out. But, this should not adversely affect our control programme. Herd resistance will continue to our benefit and I think tuberculosis will continue to be on the decline.

## **(ii) Improved standard of living**

Standard of living includes nutrition, housing, sanitation and many other aspects of living conditions. None of these is in our hands. So I will not discuss it but suffice it to say that wherever this improvement has happened, the disease has declined rapidly. And, I think tuberculosis cannot be controlled without improvement in the standard of living.

## **(iii) Impact of National Tuberculosis Programme (NTP)**

How much will the control programme contribute to the decline of the disease cannot be assessed separately, but the effect of chemotherapy must be a significant factor. Because, it not only cures but can be regarded as the most important preventive agent. An infectious case, after the start of chemotherapy, becomes non-infectious or sputum negative within a month or two. So, contacts become safe. Studies of the Madras Centre regarding home and hospital treatment showed this effect.

However, my studies in the urban and rural fields of the All India Institute of Hygiene and Public Health did show greater danger to the closest contacts, even after the start of chemotherapy. I, therefore, still practice segregation for this group of contacts.

It may be specially noted that in these studies a simple separation of the patient's bed in the same room afforded as much safety as separation in another room. Most of the patients in the study area were living in single room tenements. This finding is, therefore, a boon given by domiciliary chemotherapy.

## **Conditions Unfavourable to control**

These are: rapid increase of population and mass movement of population causing deterioration in living conditions. To me, the others are but minor conditions against control of the disease. Their remedial measures are in the hands of the national government. So, I shall not discuss them. I shall discuss those conditions where we are specifically involved. They are :

### **1. General practitioners' cooperation**

In my rough estimation, at least half of the known cases are in the hands of GPs. Among them, over and under diagnosis, irregular treatment, etc. are rampant. This is detrimental for control unless remedial measures are adequately established. In my previous publications, I had dealt with this subject and suggested :

- (a) Control orientation given during under-graduate teaching and training. This can be easily done by slightly modifying the present curriculum without adversely affecting the clinical teaching in medical colleges and universities because most of the GPs in the rural areas are almost directly drawn after their graduation. Some time ago, the Calcutta Medical Association made a short survey and found that GPs in their daily practice deal with about one-fourth respiratory diseases cases and among them about one-tenth have tuberculosis. I think, the management of these cases will improve and GPs' cooperation with the National Tuberculosis Programme will be better if this control orientation step is taken.

It will be unrealistic if we expect GPs' cooperation with financial loss to them. I had advocated pilot studies on this aspect.

- (b) Direct supply of drugs to GPs and responsibility for ensuring treatment regularity entrusted to them.

## 2. Provision for mobile clinics for diagnosis and drug supply for treatment in rural areas

The requirements are : A van equipped with X-ray and sputum examination facilities, simple recording schedules, a few technicians and home visitors (including female attendant). Starting from a static clinic in the morning, the mobile unit returns in the evening or even spends night out in a suitable place. As preparation, all the rural doctors on the mobile unit route are requested to send all their chest cases to a fixed place on a fixed day and time for making proper diagnosis and prescribing correct treatment. They should be assured of drugs for all the cases diagnosed as tuberculosis (because X-ray read by a competent person and sputum examined correctly) provided they accept the responsibility for referrals and send brief reports on regularity of drug intake and result of treatment.

The considerable expense on mobile units may even be less than that due to over- and under-diagnosis of tuberculosis and irregular chemotherapy.

I think a cooperative study on rural mobile units is justified and if found profitable and successful, the service may be expanded. In the vast rural areas, a mobile unit going to 10 places in a month and visiting these at 3 months interval, will be almost equal to setting up 30 clinics.

## 3. To step up Education

This step encompasses the following :

- a) Education of the public to improve people's participation.
- b) Not to be content with the tool of cure. The authorities seem to be so impressed with the prospect of cure that no more studies are considered necessary. They should be made to realise that cure and control are not the same. Cure can only partly help control.
- c) In addition to the existing educational efforts, we should start developing suitable literature for schools and other sectors of population and cooperate with the Health for All as the goal of other public health programmes.

## 4. Strengthen Domiciliary Chemotherapy

This is the main plank of our National Tuberculosis Programme as planned by the NTL. It is a very creditable plan, giving priority to the rural areas through its district tuberculosis programme and starting integration with, the general health services through peripheral health institutions.

But I still regret having accepted domiciliary treatment without providing adequate safeguards. I consider myself mainly responsible for this as I chaired the committee on domiciliary treatment of the International Union against Tuberculosis, at Paris, which critically evaluated contributions received from all over the world and accepted the concept. Again, at Istanbul, at the time of presentation of the Madras Chemotherapy Centre results domiciliary chemotherapy was stressed. All these studies were made among die cultured communities, in the practice field of research institutions. We forgot that the results may not

be the same everywhere, without ensuring home supervision. Three fourth of TB patients in India live in rural areas where home supervision service cannot be provided. We are still paying a high price for making the mistake of adopting domiciliary chemotherapy without proper supervision.

The remedial measure is to start pilot cooperative studies in unused or virgin rural areas using drug regimens which are in our financial capacity with special focus on regularity of treatment and cures achieved.

### **Approach towards control of Tuberculosis**

I repeat that the target of TB control is reaching one per cent infection rate at the age group of 14 years, when the special control programme should be withdrawn and the services are handed over entirely to the general public health measures. Under our conditions, to do so by a single step will be hazardous. We should proceed cautiously, under prior determined conditions, and stage by stage. May I suggest the following steps. While the suggested cooperative study of estimating infection rate at 14 years age should continue.

#### **Step 1 : of cooperation**

Around 10% closer cooperation could start yearly among all other health institutions, in addition to the Peripheral Health Centres, in measures of education, drug supply, home surveillance, and, if possible, regularity of chemotherapy.

#### **Step 2 : of integration**

Around 5% similar cooperation could start, gradually, handing over all the measures of the control programme to these institutions, keeping only specialist supervision in the hands of NTP.

#### **Step 3 : of restructuring**

A reduction in hospital beds, research centres etc. should be affected in the light of success of steps 1 and 2.

### **Collaborative studies**

A collaborative study may be defined as research done in cooperation with other faculties. All along, we had laid emphasis, rightly, on cooperative research. That is, studies, mainly operational, done in the same discipline i.e., in our case, the faculty of tuberculosis and chest diseases. I think, cooperative research should still continue as we have still to resolve many operational problems on chemotherapy and several other aspects. We may adopt this type of research as main policy. However, I have also seen, now and then, the presentation of many papers from my learned younger colleagues from other disciplines at our national conferences. We should encourage and help them. Also, TAI itself should undertake both cooperative as well as collaborative studies. There are vast unknown areas in the field of Immunology, etc. which remain unexplored. I have seen relapse cases in spite of adequate chemotherapy. I have also seen mothers spitting out millions of bacilli and yet sleeping in the same bed, under one cover with 3 or 4 children. Yet only one among them may develop the disease and others escape. We often do away with such fundamental problems by offering explanations which, to me, are not convincing enough. There is a great scope of collaborative studies to solve these, and many other fundamental problems which still have in complete answers.

### **Bibliography**

- Lyle Cummins. Primitive Tuberculosis' John Bale Medical Publications Ltd., London, 1939.
- Gangadharam, P.R.J. Proc. 21st Tuberculosis and Chest Disease Conference, Calcutta 1966.
- Garai, R. and Sen, P.K. Influence of home visits on tuberculosis chemotherapy in a rural community. *Ind. J Tub* 1976, 23, 74.
- Govt. of India. National Tuberculosis Programme of India. Vade-mecum, 1968.
- I.C.M.R. Tuberculosis in India - A Sample Survey, 1955-58; Special Report Series No. 34.
- I.C.M.R. Prevalence of drug resistance in patients with pulmonary tuberculosis presenting for the first time with symptoms, Part I, *Ind J Med* 1968. 56, 1617.
- I.C.M.R. Prevalence of drug resistance among all patients in urtjan clinics, Part II. *Ind J Med Res* 1969 57, 823.
- Saha, J.R. Drug resistance in tuberculosis, Proc. 23rd National Conf. on Tuberculosis and Chest Diseases, Bombay, 1968.

- Sen, P.K. Domiciliary treatment of pulmonary tuberculosis : record of 5,833 cases. Ind J Tub 1960, 7, 76.
- Sen, P.K. Presidential Address : 16th All India Tuberculosis and Chest Diseases Workers' Conference, Poona. 1960.
- Sen, P.K. Domiciliary Treatment of Pulmonary Tuberculosis in the Control Programme of Tuberculosis. Proc 10th Tuberculosis and Chest Diseases Workers' Conf. Mysore 1963.
- Sen, P.K. and Nandi, G.C. Fall outs and irregularities in domiciliary chemotherapy. Ind J Chest Diseases 1965.
- Sen, P.K. and Sil, A.K. Regularity of treatment in a rural clinic-influence of tape recoid exposure. Proc. 26th Nat and Chest Dis Conf. Bangalore, 1971.
- Sen, P.K. and Garai, R. Impact of tuberculosis control programme in a rural area. Ind J. Tub 1973 20, 125.
- Sen, P.K. and Roy, B.N. Bacillary resistance to drugs in tuberculosis. A trend over 13 years Ind J Tub 1975. 22, 68.
- Sen, P.K. Tuberculosis in home contacts : Tans. All India Tuberculosis Conf., Jaipur, 1959.
- Sen, P.K. Incidence of tuberculosis among home contacts. India J Tub. 1959. 6, 111.
- Sen, P.K. Influence of type and time of contact in pulmonary tuberculosis. Proc. 20th TB and Chest Diseases Workers Conf., 1965, Ahmedabad.
- Youmans, G.P. Tubeiculosis. Published by W.B. Saunders Company.

**P.K. Sen,**  
President,  
Tuberculosis Association of India;  
Editor Emeritus  
The Indian Journal of Tuberculosis; and  
Director,  
B.C. Roy  
TB & Chest Research Institute,  
Calcutta.



## CARCINOMATOUS PULMONARY CONSOLIDATIONS\*

T.G. Manickam<sup>1</sup> S. Rajasekaran<sup>2</sup> and P.J. Vasanthan<sup>3</sup>

**Summary ; Resolution of pulmonary (lobar/segmental) consolidations depends on the causative factor. Bronchial obstruction, resulting either from intraluminal occlusion or from extraluminal compression, is an important diagnostic problem in patients with unresolved or incompletely resolved lobar/segmental consolidations. In all, 218 such adult patients, selected consecutively during a period of two years were subjected to fiberoptic bronchoscopy at the Endoscopy Clinic of Government General Hospital, Madras, Of these, 72 patients were found to have bronchogenic carcinoma and in 3 patients foreign bodies were removed, Squamous cell carcinoma was the predominant cell type in this series. As many as 60 (83.3%) of 72 bronchogenic carcinoma patients were male smokers and 75 per cent of primary lung cancers were detected in the right lung. Unresolved consolidations accompanying hilar enlargement (37.5%) and mediastinal widening (5.6%) were invariably malignant**

### Introduction

Bronchogenic carcinoma is one of the most important challenges facing the medical world today. Primary lung cancer has been recognised as the most common malignancy in males. Approximately, over 125000 individuals die annually from this entity<sup>1</sup>. Cigarette/beedi smoking and environmental pollution are the twin major reasons for the ever increasing incidence of lung cancer. Enhanced awareness among the physicians and the advent of fiberoptic bronchoscopy have

contributed to its increased detection. However, bronchogenic carcinoma presents itself in various forms roentgenographically resembling many other non-carcinomatous pulmonary lesions and continues to pose many problems in its early diagnosis. Unresolved, incompletely resolved and slowly resolving pulmonary consolidations fall in this category.

### Material and Methods

Patients attending the Endoscopy Unit, Institute of Otorhinolaryngology, Government General Hospital were selected serially during 1990-1992, if they fulfilled the following selection criteria.

1. They should be adult patients with unresolved or incompletely resolved lobar or segmental consolidations.
2. They should be negative by sputum smear microscopy for AFB at least on two occasions.
3. They should be willing to undergo fiberoptic bronchoscopy.

All the 218 selected patients were interrogated and the details of clinical history, smoking habits, physical examination and the routine investigation results were recorded. Postero-anterior and lateral view chest skiagrams of each patient were studied to localise the lobar/segmental lesions.

All the patients were subjected to flexible fiberoptic bronchoscopy. Bronchial biopsies were obtained from the intraluminal growths, widened carina (main and secondary), distorted bronchi, narrowed bronchial lumen or thickened mucosa. In the absence of any definite bronchoscopically visible abnormalities, random bronchial mucosal

1. Civil Surgeon, Endoscopy Clinic, Institute of Otorhinolaryngology,

2. Assistant Professor,

3. Post-graduate student, Dept. of Thoracic Medicine, Government General Hospital, Madras 600 003.

\* Paper presented at 49th National Conference on Tuberculosis and Chest Diseases at Pondicherry, 6-9, October, 1994

Correspondence : Dr. T.G. Manickam, 2/1, Muthuvel Naicken Street, Dr. Raghavan Colony, Kodambakkam, Madras-600 024.

biopsies were resorted to from the affected lobar and segmental bronchi. Biopsied specimens were examined histologically and cytopathologically at the Institute of Pathology and Electron Microscopy, Madras Medical College, Madras.

For the purpose of this study, the smoking pattern of each patient was obtained and the smoking index was calculated. It was the product of average number of cigarettes and/or beedis smoked per day and the total duration of smoking in years<sup>2</sup>.

## Results

### 1. Age and Sex distribution

One hundred and ninety two (88.1%) of the total 218 patients with unresolved consolidations were males; 156 patients (71.5%) were aged above 40 years, with the average age of study population being 49 years.

### 2. Radiological pattern of consolidations

There were various forms of consolidations with or without associated features among the 218 selected patients. The break up particulars are as follows:

Lobar consolidation	116 (53.2%)
Segmental consolidation with or without hilar enlargement	51 (23.4%)
Hilar prominence with consolidation and collapse	27 (12.4%)
Lobar consolidation with pleural effusion	20 (9.2%)
Lobar consolidation with mediastinal widening	4 (1.8%)

### 3. Bronchoscopic findings

Observations made with flexible fiberoptic bronchoscopy in 218 patients were :

Intra-luminal growth	34 (15.6%)
Widened carina & distorted Bronchi	27 (12.4%)
Bronchial narrowing	25 (11.5%)
Thick secretion	86 (39.4%)
Inflamed mucosa	26 (11.9%)
Pale mucosa	16 (7.3%)
Foreign body	3 (1.4%)
Normal	1 (0.5%)

### 4. Histo/Cyto-pathological findings

Of the 218 patients, 126 (57.8%) were having inflammatory lesions. Primary lung cancers were found in 72 patients (33%). Squamous cell metaplasia and dysplastic changes were observed in 16 patients (4.6%).

### 5. Bronchogenic carcinoma : Cell types

Among the 72 malignant lesions, squamous cell carcinoma was the predominant cell type in 47 patients (65.3%). Large cell carcinoma and small cell carcinoma were detected in 17 (23.6%) and 4 patients (5.5%) respectively. The least detected cell type was adenocarcinoma (2 patients only) and the remaining two malignant lesions were beyond classification.

### 6. Factors related to carcinomatous consolidations

#### a) Age and sex

Sixty three patients (87.5%) with primary lung cancers were aged more than 40 years. On the other hand, inflammatory lesions accounted for 61.9% of patients in this age group. A very high proportion of malignant lesions (93.1%) was in males.

#### b) Smoking Index

Non-smokers were predominant (49.2%) among 126 patients with inflammatory lesions (Table 1). Sixty patients (83.3%) with primary lung cancers were smokers, of whom 50 were having smoking index of more than 300. The risk of malignancy increased with increasing smoking index. Of the 47 squamous cell carcinoma patients, 83% were smokers.

#### c) Radiological pattern of consolidations

All the 27 patients (12.4%) with hilar prominence and accompanying consolidation and collapse were found to be primary lung carcinomas and 20 (74.1%) among them were squamous cell carcinomas (Table 2). Of the 126 lobar consolidations without apparent hilar mass or adenitis, only 23 (19.8%) were malignant and the majority (67.2%) turned out to be inflammatory

lesions. Segmental malignant consolidations were noticed in 9 patients. Of the 9 patients with accompanying malignant pleural effusion, 6 had haemorrhagic pleural aspirate. Whenever mediastinal nodes accompanied lobar consolidation (4 patients), detection of malignant lesions was invariable and they were either small cell carcinoma (50%) or squamous cell carcinoma (50%).

d) *Lung and lobar predilection*

Fifty four patients (75%) with primary lung cancer had lesions in their right lung. Both the upper lobes accounted for 45.8% of the malignant lesions. Significantly, 17 (70.8%) of 24 patients with consolidation of both right middle and lower lobes had malignant lesion at the intermediate

**Table 1.** *Pathological lesions in relation to Smoking Index*

Smoking Index	Malignancy		Inflammation		Metaplasia/ Dysplasia		Others		Total	
	PTS.	%	PTS.	%	PTS.	%	PTS.	%	PTS.	%
0	12	16.7	62	49.2	5	31.25	4	100	83	38.1
≤ 300	10	13.9	36	28.6	2	12.5	0	0	48	22.0
301 - 600	31	43.0	12	9.5	5	31.25	0	0	48	22.0
> 600	19	26.4	16	12.7	4	25.0	0	0	39	17.9
Total	72	100	126	100	16	100	4	100	218	100

**Table 2.** *Histo/Cytopathological findings in relation to radiological pattern of pulmonary lesions*

Radiological Pattern	Malignancy				Inflammation		Metaplasia/ Dysplasia		Others		Total	
	Pts.	%	Pts.	%	Pts.	%	Pts.	%	Pts.	%	Pts.	%
Hilar Mass/adenitis with consolidation & collapse	27	37.5	0	0	0	0	0	0	0	0	27	12.4
Lobar consolidation	23	31.9	79	62.7	11	68.8	3	75	116	53.2		
Lobar consolidation with pleural effusion	9	12.5	9	7.1	1	6.2	1	1	25	20	9.2	
Segmental consolidation with or without hilar glands	9	12.5	38	30.2	4	25.0	0	0	0	51	23.4	
Lobar consolidation with mediastinal widening	4	5.6	0	0	0	0	0	0	0	4	1.8	
Total	72	100	126	100	16	100	4	100	218	100		

**Table 3. Lobar Predilection**

Lung-lobes/ segments	Malignancy		Inflammation		Metaplasia/ Dysplasia		Others		Total	
	Pts.	%	Pts.	%	Pts.	%	Pts.	%	Pts.	%
Rt. UL	21	29.2	19	15.1	0	0	0	0	40	18.3
Rt. ML	5	6.9	20	15.9	4	25.0	0	0	29	13.3
Rt. LL	11	15.3	32	25.4	4	25.0	2	50	49	22.5
Rt. ML & Rt. LL	17	23.6	6	4.7	1	6.2	0	0	24	11.0
Lt. UL	12	16.7	17	13.5	5	31.3	0	0	34	15.6
Lt. LL	6	8.3	32	25.4	2	12.5	2	50	42	19.3
Total	72	100	126	100	16	100	4	100	218	100

bronchus (Table 3). Of the 126 inflammatory lesions, 64 (50.8%) had lower lobe (right and left) predilection, 32 (76.2%) of 42 left lower lobe consolidations were inflammatory and only 14.3% lesions were malignant. There was no specific lobar predilection for a particular malignant (cell type) lesion.

#### *e) Bronchoscopic findings*

All the 34 patients (15.6%) with intra-luminal growth were primary lung cancers and 55.8% of them were squamous cell type. All the four small cell carcinomas had bronchoscopically visible growth. Bronchoscopy in 18 patients revealed bronchial narrowing and in another 14 patients carinal (main/secondary) widening and bronchial distortion were observed. Thus, 66 (91.7%) of 72 carcinomatous consolidations had either direct or indirect bronchoscopic evidence of malignancy. Among the 126 inflammatory lesions, thick secretion in 75 patients (59.5%) and inflamed mucosa in 24 patients (19%) were the predominant bronchoscopic findings.

#### *7. Foreign bodies*

Three foreign bodies were responsible for the unresolved lobar consolidations in as many patients. They were: a molar tooth, 'Chitharalhai' piece (a root used in ayurvedic medicine for 'curing' cough) and cotton-plug. While the molar tooth

had to be removed through rigid bronchoscope, the other two foreign bodies were removed through the flexible bronchoscope itself.

#### **Discussion**

Primary lung cancer is now being increasingly diagnosed in India and is one of the important causes of death due to malignant diseases. Most of the lung cancers, when detected are inoperable. Since lung cancer mimics other respiratory disorders—acute respiratory infection, bronchial asthma, pneumonic consolidation, pleurisy with effusion—the physicians generally delay the diagnosis by attempting to clear up the symptoms with different and/or repeated courses of antibiotics<sup>3</sup>.

Failure of pneumonia to resolve should be regarded as either indicative of carcinoma or a chronic process until proved otherwise<sup>4</sup>. Lobar or segmental consolidations accounted for 15.9% of 232 bronchogenic carcinomas in our earlier study<sup>5</sup> and squamous cell carcinoma alone was found to 'be responsible in 75.7 per cent 'malignant consolidations'. Being the predominant carcinoma arising from central bronchi in 65% of cases,<sup>1</sup> bronchial obstruction and post-obstructive consolidation and collapse have been reported in almost 17% of all cases of squamous cell carcinoma<sup>6</sup>.

Squamous and small cell carcinomas are the

most common central masses<sup>7</sup> and the resultant unilateral hilar enlargement may be the earliest radiographic manifestation of bronchogenic carcinoma<sup>8</sup>. The hilar origin of a carcinomatous lesion is usually the result of a tumour arising in one of the major (hilar) bronchi, extended into the peribronchial tissues<sup>4</sup>, besides enlarged bronchopulmonary lymph nodes that are the site of metastases from a very small primary lesion in adjacent or peripheral parenchyma. Such hilar masses or lymph glands often produce sufficient bronchial obstruction<sup>9</sup>.

A study of resected specimens of bronchogenic carcinomas showed that 84 per cent of tumours originated from segmental or sub-segmental bronchi<sup>10</sup>. The bronchial obstruction is most often segmental but may be lobar or, infrequently, involves the entire hemithorax. The degree of obstruction and resulting collapse depends on the specific bronchial location of the primary tumour. The central mass may be obscured by the collapsed lung<sup>1</sup>. In this study, lobar consolidation was observed along with hilar prominence/enlargement in 27 (37.5%) of 72 carcinomatous consolidations. Segmental consolidations were observed in only 9 patients (12.5%). Lower detection level of segmental carcinomatous consolidations could be due to much delay in the diagnosis of bronchogenic carcinoma, as 64 (89%) patients were inoperable.

Infection may develop in the peripheral lung due to the partial or complete obstruction of the bronchus. This process, called post-obstructive pneumonitis, results from filling of alveolar spaces with inflammatory debris. This debris prevents the collapse of segment or lobe of the lung, as occurs in a simple atelectasis<sup>1</sup>. However, some degree of atelectasis is almost invariable<sup>9</sup>. Since air cannot pass the obstruction, an air-bronchogram is absent, which is virtually pathognomonic of an endobronchial obstruction and of utmost importance in differential diagnosis. Clinically, these patients may present with signs and symptoms of acute pneumonia and subsidence of the acute inflammation with antibiotic therapy may open the airway so that air-bronchogram may become visible in distorted channels in the obstructed segment<sup>19</sup>. In these circumstances, pneumonia may resolve partially, in which case,

the lesion may be diagnosed as a 'slowly resolving pneumonia'. For these reasons, all pneumonias should be followed to their complete disappearance, especially in adults, at the risk of missing development of lung cancer.

Recurrent pneumonias and slowly or inadequately resolved pneumonias should require bronchoscopy to rule out malignant lesions. This study has clearly established that 72 (33%) of such consolidations had primary lung tumours. Radiologically, of these 72 patients only 27 (37.5%) had hilar enlargement and 4 more patients (5.6%) had mediastinal widening pointing to possible malignancy. Thus, even in the absence of definite radiographic evidence of any mass lesion, all the pneumonias in patients in the cancer age group should be investigated bronchoscopically. In this study, bronchoscopy had provided direct or indirect evidence of malignancy in 91.7% of 72 primary lung cancers.

In general, there is a 6 to 4 ratio of involvement of the right versus the left lung in the occurrence of primary lung cancers<sup>1</sup>. In this study, 54 patients (75%) had malignant tumours in their right lung. Predictably, the upper lobe malignant lesions were common to the extent of 45.8%. However, the most significant finding of this study was the highest detection (70.8%) of bronchogenic carcinoma from 24 patients with unresolved consolidations involving both the right middle and lower lobes.

Largest proportion (65.3%) of 72 carcinomatous consolidations was the squamous cell type. It usually originates from the central bronchi (hilar bronchi) causing bronchial obstruction more frequently. Moreover, frequency of detection of squamous cell carcinoma depended on the percentage of smokers: 83.3 per cent of patients with carcinomatous consolidations were smokers, with 76.4% of patients having smoking index of more than 300. Squamous cell carcinoma was also found to occur exclusively among smokers in a study<sup>11</sup> where it was found to be 83.5% in male smokers.

In conclusion, a high index of suspicion of carcinomatous consolidation should be the vital factor in detecting primary lung malignancy in

elderly patients (>40 years) and chronic smokers (Smoking Index > 300). Fiberoptic bronchoscopy is an essential investigative procedure in patients with unresolved or incompletely resolved or slowly resolving lobar or segmental consolidation of the lung.

#### References

1. Sider L. Radiographic manifestations of primary bronchogenic carcinoma. *Rad. Clin. North Am.* 1990, 28, 583.
2. Jindal S.K and Malik S.K. Smoking Index-a measure to quantify cumulative smoking exposure. *Lung India* 1988, 6, 195.
3. Vyas J.J., Desai P.B. and Rao D.N. Lung Cancer. *Ind. J. Tub.* 1981, 28 164.
4. Rigler L.G. The roentgen signs of carcinoma of the lung. *Am. J. Roent.* 1955, 74, 415.
5. Rajasekaran S, Manickam T.G., Vasanthan P.J., Jayachandran C.S., Subbaraman R, Bhanumathy V, Vijayalakshmi C.S. and Oelha Prakash. Pattern of primary lung cancer-A Madras study. *Lung India* 1993, 11, 7.
6. Byrd R.B., Miller W.E. and Carr D.T. Radiographic appearance of squamous cell carcinoma of the bronchus. *Mayo Clin. Proc.* 1968, 43, 327.
7. McFarlane J.C.W., Doughty B.I. and Crosbie W.A. Carcinoma of the lung: An analysis of 362 cases diagnosed and treated in one year. *Brit. J. Dis. Chest* 1962, 56, 57.
8. Cohen S and Hossain M.S. Primary carcinoma of lung. A review of 417 histologically proved cases. *Dis. Chest* 1966, 49, 67.
9. Pare, J.A.P. and Fraser R.G. *Synopsis of Diseases, of the Chest.* WB Saunders, Philadelphia. 1983; pp 410.
10. Lisa J.R., Trinidad S and Rosenblatt B. Site of origin, histogenesis and cytohistology of bronchogenic carcinoma. *Am. j. Clin. Path.* 1965, 44. 375.
11. Jindal S.K., Malik S.K., Dhami R. Gujral S., Malik A.K. and Datta BN. Bronchogenic carcinoma in Northern India *Thorax* 1982. 37. 343.



## IgG ANTIBODIES AGAINST ANTIGENS OF VARIOUS MYCOBACTERIAL SPECIES IN CHILDREN AND IN PRE- AND POST-BCG YOUNG ADULTS

Daniel Herbert<sup>1</sup>, C.N. Paramasivan<sup>2</sup>, Manjula Datta<sup>3</sup>, R.S. Vallishayee<sup>4</sup> and R. Prabhakar<sup>5</sup>

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*Summary:* IgG antibodies against of various mycobacteria were estimated by ELISA in serum samples collected. (a) from 36 children (mean age 4.4 years) belonging to Koppur village in the south Indian BCG trial area, (b) before and after BCG vaccination of 13 young individuals (mean age 16.5 years) belonging to Trivellore in the same area and (c) before and after BCG vaccination from 20 young British subjects (mean age 14.5 years). In the Koppur children, the antibody levels were highest against *M. scrofulaceum* and *M. avium* and lowest against *M. bovis* and *M. tuberculosis* H37Rv. In these children, there was no correlation between antibody levels and tuberculin reactivity. In the Trivellore subjects, antibody levels were highest against *M. bovis* BCG and *M. gardoniae*, and lowest against PPD RT22 and *M. terrae* and none of the differences in the antibody levels against individual antigens between the pre- and post-BCG serum samples was statistically significant ( $p > .05$ ). The British subjects had the highest levels against *M. tuberculosis* 7219 while the lowest levels were against *M. kansasii* and *M. tuberculosis* 51; after BCG Vaccination the antibody levels were selectively increased against *M. tuberculosis* 7219, *M. flavescens* and *M. gordonae* ( $p < 0.05$ ).

### Introduction

The protective effect of BCG in controlled trials has ranged from none in a south Indian trial to almost 80 per cent in a British trial<sup>1</sup>. It is likely that the low protective effect in south India compared to Britain is at least partly due to greater prior sensitisation to environmental mycobacteria in south India which may obviate or block the effect of subsequent vaccination<sup>2-4</sup>. The degree of sensitisation to mycobacterial antigens varies from country to country probably because of the relative prevalences of non-tuberculous mycobacteria (NTM) in the environment and genetic factors, or even within the same area due to differences in age and social behaviour patterns<sup>5</sup>. Presumably, in south India there is a widespread infection with NTM in children from very early age, and it has been reported that among the NTM, *M. avium intracellulare*, *M. terrae* and *M. scrofulaceum* are the species most frequently isolated from the sputum of subjects belonging to this area<sup>6</sup>.

Although it is generally accepted that humoral immune response resulting from this sensitisation does not provide adequate protection against tuberculosis, the antimycobacterial antibodies may be of importance in modulating the host's delayed type hypersensitivity and protective immune response through various mechanisms<sup>7-9</sup> and in the development of diagnostic methods based on antibody detection. We have measured the IgG

<sup>1</sup>Research Officer (Bacteriology), <sup>2</sup>Deputy Director (Bacteriology), <sup>3</sup>Deputy Director (Epidemiology), <sup>4</sup>Deputy Director (CJIL Field Unit), <sup>5</sup>Director.

Tuberculosis Research Centre (ICMR) Spurtank Road, Chetput, Madras-600 031

Reprint request: Dr. R. Prabhakar, Director, Tuberculosis Research Centre (ICMR) Spurtank Road, Chetput, Madras-600 031

Correspondence: Dr. C.N. Paramasivan, Deputy Director (Bacteriology), Tuberculosis Research Centre (ICMR)-Spurtank Road, Chetput, Madras-600 031

antibody levels to various mycobacterial species by ELISA in serum samples from a group of children and young individuals belonging to the south Indian BCG trial area and from a group of young British subjects to obtain information on the sensitisation patterns to mycobacterial antigens in these three groups, to find out if there is any association between antibody levels and tuberculin reactivity status in children belonging to this area, and to compare the changes, if any, and the differences in changes in the antibody levels after BCG vaccination in young individuals belonging to this area and Britain.

#### Material and Methods

**Serum samples :** Serum samples collected from 36 children from Koppur village in the south Indian BCG trial area were used. The age of these children ranged from 2 to 6 years and the mean was 4.4 years. The tuberculin reactivity to PPD-S ranged from 0 to 30mm and the mean was 7.5mm. The children could be divided into three different tuberculin reactivity groups; 18 had 0-3mm reactivity, 8 had 4-10mm reactivity and 10 had >10mm reactivity, representing low, intermediate and high level of reactivity to PPD-S.

Serum samples, collected before as well as 8 weeks after BCG vaccination and tuberculin conversion, from 13 young individuals from Trivellore in the same geographic area (mean age 16.5 yrs) and 20 young British subjects (mean age, 14.5 yrs) were also included in the present study. The pre-BCG Mantoux reaction to PPD-S was <8mm to 3TU in the young Indians and <4mm to 4TU in the young British subjects. The post-BCG/tuberculin conversion reaction was >12 mm to 1 TU in these individuals.

Serum samples from the young British subjects were provided by D.B. Lowrie, National Institute of Medical Research, Mill Hill, London.

**Antigens :** The IgG antibody levels in the serum samples were estimated by ELISA against PPD-RT 22 and mycobacterial sonicate supernatant antigens listed in Tables 1 and 2.

The sonicate antigens were prepared by C.N.

Paramasivan in the Royal Postgraduate Medical School, London, as described earlier<sup>10</sup>. PPD-RT 22 was obtained from the BCG Laboratory, Madras.

**ELISA procedure :** ELISA to estimate the antimycobacterial antibodies of class IgG in the serum samples was done as described by Narayanan et al<sup>11</sup>. Briefly, antigen coating of microwell plates (Gibco/Nunc Cat. No. 439454) was carried out using 0.1ml of 5mcg/ml solution of the antigen in carbonate buffer (0.06M, pH 9.6) per well. Each serum sample was divided into two aliquots and given different code numbers. Each coded serum sample was tested at 1/40 and 1/80 dilutions on 15 plates, each plate coated with a different mycobacterial antigen. A 1/100 dilution of anti-human IgG peroxidase conjugate (Sigma Cat. No. A-6029) was used as the secondary antibody and orthophenylene diamine (OPD) was used as the substrate. The optical density (OD) of the resultant reaction in each well was read at 490nm in a Biotek ELISA plate reader.

**Statistical analysis:** From the OD values from duplicate samples tested, average values were calculated for each dilution of the serum. The mean antibody levels against individual antigens for the different tuberculin reactivity groups among the children were compared by unpaired t-test. Mean antibody levels against individual antigens for the pre- and post-vaccination samples were compared by paired t-test. A one-way ANOVA was carried out for all the antigens in the three tuberculin reactivity groups, and the means were tested for increasing trend after adjusting for the antigens as covariant.

#### Results

The mean IgG antibody levels in OD units at 1/40 dilutions of serum samples from the 36 Koppur children belonging to the three different tuberculin reactivity groups are presented in Table 1. Antibody levels were highest against *M.scrofulaceum* and *M.avium* serotype 8 while the lowest levels were against *M.tuberculosis* H37Rv in all the three groups. The ranking of antibody levels (from highest to lowest) was also similar in these three groups: it was *M.scrofulaceum* followed by *M.avium intracellulare* serotype 8,

**Table 1.** Mean antibody levels and standard deviations in OD units at 1/40 dilution

Serum samples from children (mean age 4.4 years) belonging to different tuberculin reactivity groups																	
Tuberculin reactivity Group mean dia.		Mtb H	Mtb 37Rv	Mtb 51	Mtb 7219	Mbo	BCG	Mkan	Mscr	Antigen Mai 8	Antigen Mai 16	Mter	Mfla	Mgor	Mfor	Mche	PPD
0-3mm 0.33 (n=18)	Mean	.128	.284	.222	.175	.216	.199	.488	.386	.218	.234	.200	.218	.230	.232	.234	
	SD	.050	.127	.096	.069	.091	.070	.133	.069	.045	.068	.036	.040	.042	.042	.044	
p<.001																	
4-10mm. 8.62 (n=8)	Mean	.138	.265	.220	.172	.194	.194	.425	.370	.217	.225	.184	.201	.218	.222	.222	
	SD	.059	.159	.110	.076	.079	.088	.153	.091	.038	.078	.026	.027	.033	.038	.035	
p<.001																	
>10mm 19.5 (n=10)	Mean	.150	.300	.251	.186	.227	.201	.476	.358	.215	.259	.189	.202	.204	.223	.218	
	SD	.068	.172	.105	.095	.106	.096	.135	.084	.061	.050	.038	.044	.027	.038	.024	
All Children (n=36)	Mean	.136	.284	.229	.177	.214	.198	.471	.375	.217	.239	.193	.210	.220	.227	.227	
	SD	.056	.144	.100	.076	.091	.079	.137	.077	.047	.065	.035	.039	.037	.040	.038	

Mtb H37Rv = *M.tuberculosis* H37Rv (laboratory strain), Mtb 51 = *M.tuberculosis* 51 (British strain), Mtb 7219 = *M.tuberculosis* 7219 (South Indian strain), Mbo = *M.bovis* (NCTC 5693), BCG = *M.bovis* BCG (Glaxo), Mkan = *M. Kansasii* (NCTC 10268), Mscr = *M. Scrofulaceum* (NCTC 10803) Mai8 = *M. avium intracellulare* serotype 8 (NCTC 10610), Mail6 = *M.avium intracellulare* serotype 16 (NCTC 10425), Mter = *M. terrae* (NCTC 10856), Mfla = *M.flavescens* (NCTC 10271), Mgor = *M.gordonae* (NCTC 10267), Mfor = *M.fortuiturn* (NCTC 10394), Mche = *M.chelowi* (NCTC 10882), PPD = PPD RT22.

Table 2. Mean antibody levels and standard deviations in OD units at 1/40 dilution

## Pre- and post-BCG serum samples from young Indian and British subjects

BCG status		Mtb H37Rv	Mtb 51	Mtb 7219	Mbo	BC G	Mkan	Antigen Mscr	* Mai 8	Mai 16	Mter	Mfla	Mgor	Mfor	Mche	PPD
Young Indian Subjects (n=13)																
Pre-BCG	Mean	.320	.378	.346	.364	.468	.342	.348	.368	.306	.245	.273	.456	.408	.396	.260
BCG	SD	.090	.109	.136	.139	.065	.076	.088	.052	.108	.058	.067	.094	.094	.102	.082
POST-BCG	Mean	.321	.379	.340	.374	.469	.323	.361	.375	.301	.236	.262	.454	.405	.401	.265
BCG	SD	.029	.034	.120	.125	.055	.052	.085	.053	.074	.055	.044	.087	.079	.095	.074
Young British Subjects (n=20)																
PRE-BCG	Mean	.334	.262	.483	.392	.432	.283	.296	.374	.434	.406	.358	.437	.369	.447	.442
BCG	SD	.090	.075	.112	.065	.083	.083	.076	.053	.077	.079	.060	.070	.071	.100	.095
				p<.05								p<.01		rx.O1		
POST-BCG	Mean	.343	.267	.510	.397	.429	.290	.315	.375	.449	.417	.394	.465	.364	.429	.406
BCG	SD	.087	.075	.107	.052	.084	.068	.076	.052	.082	.076	.080	.073	.061	.095	.076

\* For the full names of antigens see footnote under Table 1

*M.tuberculosis* 51, *M.terrae*. PPD-RT 22, *M.chelonae*, *M.fortuitum*, *M.tuberculosis* 7219, *M.avium intracellulare* serotype 16, *M.gordonae*, BCG, *M.flavescens*, *M.kansasii*, *M.bovis* and *M.tuberculosis* H37Rv in the 0-3mm group; the same pattern with only the positions of *M.tuberculosis* 7219 and *M.fortuitum*, and *M.kansasii* and *M.flavescens* interchanged in the 4-10mm group; and, again, a similar pattern with *M.tuberculosis* 7219 and BCG moving up in the order and the positions of *M.chelonae*, PPD-RT 22, *M.fortuitum* and *M.gordonae* changed in the >10mm group. Similar results were obtained with 1/80 dilutions of the serum samples (data not presented). The mean tuberculin reactivity in the three groups of children were 0.33, 8.62 and 19.5mm. Unpaired t-test showed that there were no significant differences in the mean antibody levels against individual antigens between the three tuberculin reactivity groups ( $p>0.05$ ). In one-way ANOVA, no significant variation was seen, and there was no statistically significant increasing trend.

Of the Koppur children, 24 were male and 12 were female. The mean tuberculin reactivities in the male and female children were 6.70 and 9.08mm, respectively. The difference in the tuberculin reactivities of the two groups was not statistically significant ( $p>0.05$ ). The differences between the males and females in the mean antibody levels against individual mycobacterial antigens were also not statistically significant ( $p>0.05$ ).

The pattern of antibody levels at 1/40 dilution of serum samples from the young individuals from Trivellore were different from those in the Koppur children (Table 2). In the pre-BCG young individuals from Trivellore, the antibody levels were highest against *M. bovis* BCG and *M.gordonae*. The lowest levels at this dilution were seen against PPD-RT22 and *M.terrae*. At 1/80 dilution also, similar results were obtained (data not presented). In the young Indian subjects, the mean antibody levels against individual antigens in post-BCG serum samples were similar to the levels in pre-BCG samples; the order of antibody levels to the 15 antigens was also the same in post-BCG samples except that *M.flavescens* and PPD-RT22 had interchanged their positions. Results

with 1/80 dilutions (data not shown) were very little different from those with 1/40 dilutions. Paired t-test revealed that none of the differences in the mean antibody levels against individual antigens between the pre- and post-BCG serum samples at 1/40 or 1/80 dilution was statistically significant ( $p>0.05$ ).

The pattern of antibody levels was different in the young British subjects. The highest levels of antibodies at 1/40 dilution of both pre- and post-BCG/tuberculin conversion serum samples were found against *M.tuberculosis* 7219. The lowest levels were seen against *M.kansasii* and *M.tuberculosis* 51. Essentially, identical patterns were obtained with 1/80 dilutions of the serum samples also (data not shown).

In the young British subjects, the post-BCG serum samples had significantly higher mean antibody levels than pre-BCG samples against *M.tuberculosis* 7219, *M.flavescens* and *M.gordonae* at 1/40 dilution (Table 2) and to *M.gordonae* (.282 and .313 in the pre- and post-BCG samples, respectively) at 1/80 dilution also ( $p<0.05$ ). The mean antibody levels against the other antigens, individually, were similar (differences not statistically significant,  $p>0.05$ ) in the pre- and post-BCG samples.

## Discussion

Even though the sample size is perhaps too small to permit generalization, several interesting observations are evident from this study. It has been reported earlier that *M.avium intracellulare* and *M.scrofulaceum* are among the NTM species most frequently isolated from the sputum of subjects belonging to the south Indian BCG trial area<sup>6</sup>. The prominence of antibody response to *M.avium intracellulare* and *M.scrofulaceum* in subjects from this area in the present study also suggests that these NTM species are most likely to be the ones responsible for the early appearance and wide prevalence of DTH to PPD-B in this area.

The pattern of antimycobacterial antibodies in the young individuals (mean age 16.5 yrs) from Trivellore was different from that in the Koppur children (mean age 4.4 years). Age, along with

any differences in the profile of environmental mycobacteria, could probably account for the difference in the patterns of antibody levels between the two groups of subjects.

An interesting observation in the present study was the relatively low levels of antibodies seen against the antigens to which the older subjects were likely to have had more exposure as in the case of *M. tuberculosis* 7219 (prepared from a south Indian low virulence strain) and *M. tuberculosis* 51 (prepared from a British strain) in the Indian and British subjects, respectively.

The present study showed that in the Koppur children there were no significant differences in the mean antibody levels against individual antigens including PPD-RT 22 between the three tuberculin reactivity groups (0-3,4-10 and >10mm) indicating that tuberculin reactivity may be independent of the antimycobacterial antibody levels in these children. Many earlier studies by others have examined the relationship between tuberculin reactivity status and antimycobacterial antibody levels with similar findings<sup>12-15</sup>. Correlation between tuberculin reactivity and antibody levels have also been reported by others<sup>16-17</sup>.

The relationship between BCG vaccination and antibody levels has been examined by many workers. Raheman et al<sup>13</sup> in India did not find any correlation. Some of the studies conducted abroad have also reported similar findings<sup>15,17,20</sup>. On the other hand, positive correlation between BCG vaccination status and antibody levels have been reported by others<sup>21-24</sup>. Based on such evidence from literature, it has been concluded by Grange<sup>7</sup> that BCG vaccination appeared to induce only a transient antibody response.

The differences seen in the present study between the Indian and British subjects in the humoral immune response to BCG vaccination could be due to the differences in the pre-existing sensitisation patterns between these two groups<sup>4,5</sup>. Prior contact with shared mycobacterial antigens could accelerate subsequent responses to these antigens and may also suppress the formation of antibodies to newly introduced specific antigens by the phenomenon of antigenic competition<sup>7</sup>. Genetic differences between the two groups

studied could also be involved acting through the HLA class 2 immune response genes<sup>25</sup>.

The differences in the patterns of antibodies observed in the present study between the Indian and British subjects could be due to differences in the degree of exposure and in the mycobacterial antigens encountered by these two groups<sup>5</sup>. According to Grange<sup>7</sup>, differences in antibody levels between individuals could be due to differences in prior exposure of antigens, different antigens being processed differently by macrophages, the amount of antigens, local tissue reactions to the antigens, formation of immune complex, general state of nutrition, interaction of other immune responses, presence of immunosuppressive factors and genetic factors. The relevance of the differences seen between the British subjects and Indian subjects from the BCG trial area in the humoral immune response to BCG vaccination and pattern of antibodies is not clear. Stanford et al<sup>26</sup> examined the value of multiple skin testing, lymphocyte transformation test and ELISA of antibodies to mycobacterial antigens as correlates of protection. Of the three types of tests assessed, only skin testing appeared to be of any value as a measure of protection. The question whether the differences in the antibody patterns and response to BCG vaccination in the Indian and British subjects seen in the present study have any such prognostic significance needs to be addressed further.

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#### References

1. Luelmo, F. : BCG vaccination: *Am. Rev. Respir. Dis.*; 1982, 125, 70.
2. Raj Narain, Krishnamurthy, M.S. and Anantharaman, D.S. : Prevalence of nonspecific sensitivity in some parts of India; *Ind. J. Med. Res.*; 1975, 63, 1098.
3. Tuberculosis Prevention Trial, Madras.: Trial of BCG vaccines in south India for tuberculosis prevention; *Ind.*

- J Med Res, 1980, 72 Suppl, 1
- 4 Abrahams, EW Ougmal mycobacterial sin, Tubercle, 1970, 51, 316
  - 5 Stanford, J L, Cunningham, F, Pilkington, A, Sargeant, A, Bhatt, N, Bennet, E and Mehrotra, M L A prospective study of BCG given to young children in Agra, India a region of high contact with environmental mycobacteria, Tubercle: 1987, 68, 39
  - 6 Paramasivan, C N, Govmdan, D, Piabhakar, R, Somasundaram, P R, Subbammal, S and Tupathy, S P Species level identification of non tuberculous mycobacteria from South India BCG trial area during 1981, Tubercle, 1985, 66 9
  - 7 Grange, J M The humoral immune response in tuberculosis Its nature, biological role and diagnostic usefulness, Adv Tuberc Res 1984, 21, 1
  - 8 Lowrie, D B and Andrew, P W Maciophage antimycobacterial mechanisms Br Med, Bull, 1988, 44, 624
  - 9 Om Parkash, Ramanathan, V D Singh, D P and Sengupta, U Effect of anti mycobacterial antibodies on activation of the alternative pathway of the human complement system, FEMS Lett 1988 55 255
  - 10 Paiamasivan, C N Jackett, P S Coates A R M Lowne D B and Mitchison D A Monoclonal antibodies against *Mycobacterium avium-intracellulare* Ind J Med Res 1988, 88, 13
  - 11 Natayanan, S, Paiamasivan C N, Abdul Ravoof, Narayanan, P R and Piabhakar, R Sensitisation pattern of healthy volunteers and tuberculosis patients to various mycobacterial antigens by ELISA, Ind J Tub, 1987, 34, 132
  - 12 Gupta, A K Jamil, Z, Snavastava, V K, Tandon, A and Saxena, K C Antibodies to purified tuberculin (PPD) in pulmonary tuberculosis and their correlation with PPD skin sensitivity, Ind J Med Res 1983 78, 484
  - 13 Raheman SF Vasudeva, ND Ingole D L, Wagner S, Maudi H, Pathak, M C and Mazumdar R D ELISA A potential screening procedure in epidemiological surveys of tuberculosis, Ind J Tub 1988 35 8
  - 14 Benjamin, R G, Debanne, S M Ma, Y and Daniel T M Evaluation of mycobacterial antigens in an enzyme-linked immunosorbent assay (ELISA) for the serodiagnosis of tuberculosis, J Med Microbiol 1984, 18, 309
  - 15 Balestino, E A, Daniel T M, de Latim M D S Latim, O A, Ma, Y and Sococoza I B Serodiagnosis of pulmonary tuberculosis in Argentina by enzyme linked immunosorbent assay (ELISA) of IgG antibody to *Mycobacterium tuberculosis* antigen 5 and tuberculin purified protein derivative, Bull WHO, 1984, 62 755
  - 16 Pitchappan, R M, Biahmajothi, V, Rajaiam, K, Thirumalaikolundu, S, Balakrishnan, K Muthuveelialakshmi, P Spectrum of immune reactivity to mycobacterial (BCG) antigens in healthy hospital contacts in south India, Tubercle, 1991, 72, 133
  - 17 Kardjito, T, Handoyo, I and Grange, J M Diagnosis of active tuberculosis by immunological methods I The effect of tuberculin reactivity and previous BCG vaccination on the antibody levels determined by ELISA, Tubercle, 1982, 63 269
  - 18 Neveu, P J, Buscot, N and Soullim, J P Dissociation between humoral and cellular responses to PPD after BCG vaccination, Int Arch Allergy Appl Immunol, 1980, 62, 409
  - 19 Kahsh S B, Radm, R C, Phair, J P, Levitz, D Zeiss, C R and Metzger E Use of an enzyme-linked immunosorbent assay technique in the differential diagnosis of active pulmonary tuberculosis in humans, J Infect Dis 1983, 147, 523
  - 20 Krambovitis, E Detection of antibodies to Mycobacterium tuberculosis plasma membrane antigen by enzyme-linked immunosorbent assay, J Med Microbiol 1986, 21 257
  - 21 Wallace, R Dena, B B, Jessamine, A G and Greenberg, L Circulating antibody response in BCG vaccination, tuberculous infection and sarcoidosis, Can Med Assoc J, 1967, 96, 585
  - 22 Bardana, E J Jr, McClatchy, J K, Farr, R S and Menden, P Universal occurrence of antibodies to tubercle bacillus sera from non-tuberculous and tuberculous individuals, Clin Exp Immunol 1973 13, 65
  - 23 Wmteis, W D and Lamm, D L Antibody response to Bacillus Calmette Guern during immunotherapy in bladder cancer patients, Cancer Res, 1981, 41, 2672
  - 24 Tuineer, M Van Vooren J P, Nyabenda, J, Legios F Lecomte, A Thinaux I, Seuuys E and Yernault I C The humoral immune response after BCG vaccination in humans Consequences for the serodiagnosis of tuberculosis Em Respir 1, 1988 1 589
  - 25 de Vries, R R P Regulation of T cell responsiveness against mycobacterial antigens by HLA class 2 response genes, Rev Infect Dis, 1989, 11 Suppl 2 5400
  - 26 Stanford, I L Rook, G A W Samuel, N, Madlenei F Khamemi, A A, Nemati, T Modabbei F and Rets R J W Preliminary immunological studies in search of correlates of protective immunity carried out on some Iranian leprosy patients and their families, Lept Rev 1980, 51, 303



## ETHIONAMIDE, CYCLOSERINE, ISONIAZID, SODIUM PAS AND KANAMYCIN IN RETREATMENT OF DRUG FAILURE PULMONARY TUBERCULOSIS PATIENTS

Rupak Singla<sup>1</sup>, V.P. Myneedu<sup>2</sup>, A. Jaiswal<sup>1</sup>, M.M. Puri<sup>1</sup> and R.C. Jain<sup>3</sup>

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**Summary:** Since drug failure-patients of pulmonary tuberculosis are difficult to retreat, a study was carried out, to see the efficacy and acceptability of a regimen consisting of Cycloserine, Ethionamide, Isoniazid and Sodium PAS for 12 months supplemented with injection Kanamycin in the initial three months (3 KCEHP/9 CEHP) in 80 such patients. They had already taken antituberculosis drugs – Streptomycin, Isoniazid, Rifampicin, Ethambutol and Pyrazinamide in various combinations for at least 6 months and were still Sputum smear and culture positive. Sputum examinations for *M.tuberculosis* by smear and culture were done every month for one year during re-treatment.

Forty patients (50%) completed full chemotherapy. Among, these, 78% patients achieved bacteriological quiescence. On follow up, for 24-36 months (average 28 months), 26% relapsed bacteriologically. There were few side effects and no need to interrupt/change the regimen. However, poor treatment adherence was mainly due to high cost of the drugs.

### Introduction

In the last few years, many patients of pulmonary tuberculosis are being identified who fail to respond to various regimens using antituberculosis drugs such as Streptomycin, Isoniazid, Ethambutol, Rifampicin or

Pyrazinamide<sup>1-3</sup>. These drug failure cases pose many difficulties for the physician. Strangely, the literature gives inadequate guidance about the proper treatment of such cases. A few regimens using second line drugs have been tried in the management of such drug failure cases with varying results.

In this study, the efficacy and acceptability of a regimen consisting of Cycloserine, Ethionamide, Isoniazid and Sodium PAS for 12 months with injection Kanamycin in the initial three months has been investigated.

### Material and Methods

Patients of pulmonary tuberculosis who had taken a minimum of six months' therapy with Streptomycin, Isoniazid, Ethambutol, Pyrazinamide and Rifampicin in various combinations and were still sputum smear and culture positive for *M.tuberculosis* were included in the study. To make sure that the patients under study were drug failure cases and to avoid unnecessary use of second line drugs, all were first given Streptomycin, Isoniazid, Ethambutol, Pyrazinamide and Rifampicin for 3 months followed by Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for 3 months. If they were still sputum positive they were included in the study. In all, 80 patients were taken. There were 61 males and 19 females. Mean age of the patients was 32.4 years, ranging from 18 to 59 years. Patients with concomitant diabetes mellitus, hepatic failure or renal insufficiency were excluded.

The regimen prescribed to all the patients was

1 Chest Physician, 2 Bacteriologist, 3 Consultant Surgeon and Director

L.R.S. Institute of Tuberculosis and Allied Diseases, Sri Aurobindo Marg, New Delhi-110030.

Correspondence: Dr. Rupak Singla, Chest Physician, L.R.S. Institute of Tuberculosis and Allied Diseases, Sri Aurobindo Marg, New Delhi-110030,

Ethionamide (750 mg/day for <50 Kg weight; 1000mg/day for >50 Kg weight), Cycloserine (500 mg/day for <50 Kg weight; 750 mg/day for >50 Kg weight), Sodium<sup>®</sup> PAS 200 mg/Kg/day, alHn two divided doses; and Isoniazid (300 mg/day) once daily for 12 months. This was supplemented with injection Kanamycin (0.75gm/day for <50 Kg weight; 1 gm/day for >50 Kg weight) in the initial three months. Initially, the patients were admitted for 3 months and given the medication under direct supervision. During the hospital stay the medicines were supplied from the hospital. After discharge, the patients were asked to purchase medicines from the market. They were followed up in the out-patient department on monthly basis by a team of doctors in a separate room. At each visit the medicines and their purchase slips were physically checked.

Sputum examinations for *M.tuberculosis* by smear and culture were done every month. Skiagram of the chest was done at 0, 3, 6, 9 and 12 months of therapy, or in-between if required. The criteria for a favourable bacteriological response were that sputum smear and culture for *M.tuberculosis* should become negative by nine months and remain negative for at least six months. The drug sensitivity study could not be done due to lack of facilities.

### Observations

The analysis of the past treatment of the patients showed that the average duration of the past treatment was 20 months ranging from 8 months to 10 years. Ninety one percent (73/80) of the patients had moderate to advanced bilateral disease. Seven patients had unilateral disease. Cavitation was present in 87% (70/80) of the patients.

### Treatment Completion

Out of the 80 patients, 40 (50%) completed the full course of 12 months of chemotherapy. Three patients died due to respiratory failure and toxemia. All the three patients died during the first two and a half months of therapy and remained sputum positive. The remaining 37 patients (46%) dropped out before completion of treatment (Table 1). The main reason for poor

treatment adherence was the high cost of the drugs. None of the patients stopped treatment due to intolerance to the drugs.

**Table I :** *Treatment adherence and sputum conversion*

	Treatment completed	Treatment not completed
Sputum converted	31(78%)	21(53%)
Sputum not converted	9(22%)	19(47%)
Total	40	40(3 died)

### Sputum Conversion

Out of 40 patients who completed the therapy, 31 (78%) became sputum smear and culture negative for *M.tuberculosis* (Table 1). Among these 84% (26/31) patients converted within the first 3 months and 96% (30/31) converted within the first 5 months (Table 2) of therapy.

**Table 2 :** *Time taken for sputum conversion in patients who completed the treatment and achieved sputum conversion*

Months of therapy	1	2	3	4	5	6	7	8
No. achieving sputum conversion	6	14	26	29	30	30	30	31
Percentage	19	45	84	93	96	96	96	100

Among 40 patients who did not complete full treatment, 53% (21/40) still achieved sputum smear and culture negativity (Table 1). Analysis of these patients showed that longer the duration of treatment taken before dropping out, greater the chance of sputum conversion (Table 3).

### Follow up and Relapses

The 31 patients who completed full treatment were followed up for an average period of 28 months, ranging from 24 to 36 months. Eight (26%) patients showed bacteriological relapse. And 88% (7/8) of these patients relapsed between

**Table 3 :** Relationship of duration of treatment taken to sputum conversion in patients who took incomplete treatment

Duration of treatment taken (months)	Number of Patients	Patients with sputum conversion (percentage)
1-3	18	4(22%)
4-6	10	6(60%)
7-9	9	8(89%)
9-11	3	3(100%)

4 to 6 months after stopping treatment. One patient relapsed 12 months after completing therapy.

Analysis of the relapsed cases for possible high risk factors revealed that relapse was more common in patients who converted late during chemotherapy. Two patients converted after 5 months of chemotherapy and both of them relapsed. There was no correlation between relapse and age of the patient or duration of past treatment.

#### Radiological response

Among 40 patients who completed the treatment, cavity persisted in all the 31 patients who had cavitation. But 75% (23/31) patients showed shrinkage in the size of the cavity and 26% (8/31) showed thinning of the wall of the cavity.

#### Side effects

The commonest side effect was altered taste in 75% of the patients. Other side effects were nausea (25%), vomiting (10%), mild depression (9%), giddiness (9%) and deafness (3%). But all of these side effects, except deafness, responded to conservative treatment and the anti-tuberculosis treatment was continued. In two patients with deafness, injection Kanamycin had to be discontinued. Three patients developed severe psychosis with violent behaviour and Cycloserine had to be discontinued. None of the patients developed jaundice.

#### Discussion

In developing countries like India where adequate funds to treat even freshly diagnosed cases of tuberculosis are lacking, the increasing number of treatment failures due to drug resistant bacilli is posing a real problem. The factors which contribute to acquired drug resistance and treatment failure include irregular drug treatment, sub-therapeutic dosage of drugs, improper regimens, drug default, non-availability of drugs at the clinics, and addition of only one drug to an already failing regimen.

The treatment failure cases require the use of second line drugs which, however, are less potent, more expensive and potentially toxic. Compared to the magnitude of the problem of treatment failure, little work has been done in this field in this country. Various regimens have been tried with varying results<sup>4,8</sup>. In these regimens, the second line drugs have been given for a period varying from 18 months to 2 years. Longer duration leads to poor treatment adherence, increased cost and more toxic effects. In the present study, a 12 months' regimen of Cycloserine, Ethionamide, Isoniazid and Sodium PAS supplemented with injection Kanamycin for first 3 months has been investigated. Each patient in the study group was first given Streptomycin, Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for three months followed by Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for three months. Only the patients still remaining sputum positive were included in the study. So each patient was its own control.

Only 50% of the patients completed the full course of 12 months' chemotherapy indicating high default rate. High cost of the drugs was the major cause of default. In this regimen the cost of drugs was more than rupees 100 per day. In the study by Purohit et. al<sup>17</sup> also, only 44% patients completed the 18 months' therapy. In the present study, the bacteriological quiescence was achieved in 78% of the patients who completed the full therapy. Khanna<sup>6</sup> investigated Kanamycin (6 months), Cycloserine, Ethionamide and Sodium PAS for 18 months in hospitalized patients and observed bacteriological conversion in 10 out of 14 patients (71%). Purohit et. al<sup>17</sup> used Kanamycin

(6 months), Ethionamide, Sodium PAS and Isoniazid for 18 months on domiciliary basis and bacteriological conversion was achieved in 73% of the patients.

Among those who achieved bacteriological conversion, 84% of the patients in the study converted in the first 3 months and 96% within the first five months of therapy. Even among patients who took incomplete treatment (average 4.8 months), sputum converted in 53% of the patients. Sputum conversion was directly related to the duration of treatment taken before dropping out.

Patients who completed treatment were followed up for 24 to 36 months (average 28 months). Eight (26%) of these patients relapsed bacteriologically. Most of the relapses (88%) occurred between 3 to 6 months after stopping treatment. Relapse was more common in patients who converted late during chemotherapy. Whether increasing the duration of treatment in such cases to more than 12 months will reduce the relapse rate needs further observation and evaluation.

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#### References

1. Jain, N.K. : Drug resistance in India. A tragedy in the making. *Ind. J. Tub.*; 1992, 39: 145.
2. Jain, N.K., Chopra, K.K. and Prasad, G.: Initial and acquired isoniazid and rifampicin resistance to *tycobacterium tuberculosis* and its implications for treatment. *Ind. J. Tub.*; 1992, 39: 121.
3. Trivedi, S.S. and Desai, S.G. : Primary anti-tuberculosis drug resistance and acquired Rifampicin resistance in Gujrat. *Ind. J. Tub.*; 1988, 69: 37.
4. Sommer, A.R.: Ethionamide, Pyrizinamide and Cycloserine used successfully in the treatment of chronic pulmonary tuberculosis. *Tubercle*; 1962, 43:345.
5. East Africa/British Medical Research Council Retreatment Investigation 2nd Report. Streptomycin plus PAS plus Pyrazinamide in the retreatment of pulmonary tuberculosis in East Africa. *Tubercle*; 1973, 54: 283.
6. Khanna, B.K. : Treatment of long-term tuberculosis treatment failures. *Ind. J. Tub.*; 1985, 32: 171.
7. Purohit, S.D. Gupta, M., Agnihotri, S.P. Madan, A. and Gupta, P.R.: Management of chemotherapy failures. *Ind. J. Tub.*; 1991, 38: 3.
8. Zierski M. : The treatment of drug resistant chronic pulmonary tuberculosis with new tuberculostatics. *Bull I.U.A.T.*; 1968, 41: 195.

## EXTRAPULMONARY INVOLVEMENT IN HIV WITH SPECIAL REFERENCE TO TUBERCULOUS CASES\*

V.K. Arora<sup>1</sup>, K. Gowrinath<sup>2</sup> and R. Sambasiva Rao<sup>3</sup>

**Summary:** Forty out of two hundred and seventy (14.81%) cases of extrapulmonary involvement who were positive for HIV antibodies confirmed by immunocomb or immunoblot test constituted the study group. Twentyeight out of 40 (70%) had extrapulmonary tuberculosis and the rest were nontuberculous and/or of undetermined aetiology. Thirteen out of 28 (46.5%) with tuberculous lymphadenitis involving upto 2 groups' of glands and subjects with pleural effusion without concurrent pulmonary involvement showed excellent response to 2EHR3/4HR therapy, comparable to HIV seronegative subjects. The fatality rate in the remaining subjects was around 90% during the period of follow up of 6-18 months.

### Introduction

Extrapulmonary involvement occurs frequently and earlier than other opportunistic infections, especially in individuals dually infected with human immunodeficiency virus (HIV) and tubercle bacillus and is more difficult to diagnose than pulmonary tuberculosis<sup>1,2,3</sup>. Documentation of extrapulmonary tuberculosis is important because the condition constitutes AIDS-defining illness<sup>4</sup>. According to a recent report<sup>5</sup>, the occurrence of extrapulmonary tuberculosis has increased by 20% as compared to 3% increase in cases of pulmonary tuberculosis and is believed to be due

to more severe immunodeficiency. A few reports of HIV and extrapulmonary involvement are available from India<sup>6,7,8</sup> too. Information on extrapulmonary tuberculous involvement and response to chemotherapy are available, with varying results from USA, Europe and Africa.

We report here our experience with 40 consecutive cases infected with HIV-1 and having extrapulmonary involvement attending the Tuberculosis and Chest Diseases Department, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry between March 1991 and July 1994.

### Aims

1. To observe the distribution of disease in extrapulmonary sites in HIV infected individuals.
2. To assess the response to chemotherapy in tuberculous cases with HIV infection and to compare the results with those of seronegative individuals.
3. To identify other extrapulmonary non-tuberculous involvement in HIV subjects.

### Material and Methods

One thousand two hundred and ninety one patients attending the department were tested for HIV antibodies by ELISA, and confirmed by immunocomb or immunoblot test, after taking informed consent; of them, 270 subjects had

1. Director-Professor, 2. Senior Resident, 3. Dean

Departments of Tuberculosis & Chest Diseases, & Microbiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry 605006.

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Correspondence : Dr. V.K. Arora, Director-Professor, Dept of Tuberculosis & Chest Diseases, JIPMER, Pondicherry 605006

extrapulmonary involvement. All cases of concurrent immunodeficiency with diabetes mellitus, malignancy, steroid therapy and chronic alcoholism were excluded from the study. Forty of the 270 (14.8%) subjects who were positive for HIV-1 infection constituted the study group.

All these subjects were assessed clinically for their presenting signs and symptoms. FNAC, pleural biopsy, lymph node biopsy and direct smear examination of aspirate were done after taking adequate precautions. The material was sent for culture for tubercle bacillus, fungus and pyogenic organisms. All HIV subjects with extrapulmonary tuberculosis (EPT) were put on 2EHRZ/4HR in conventional doses. The results were compared with 180 seronegative cases of extrapulmonary tuberculosis who completed short course chemotherapy during the study period.

## Results

Out of 1291 subjects in whom sera were tested for HIV infection, 74, (5.73%) were positive for HIV-1 antibodies. Analysed yearwise, the trend was : 7/264 (2.65%) in 1991, 10/248 (4.03%) in 1992, 41/394 (10.40) in 1993.

The break up of the 40 cases studied showed only extrapulmonary site involvement in 19 and concurrent pulmonary involvement in 21 subjects. The ratio between male and female was 3:1. The mean age was 31.6 years.

All the subjects except two belonged to poor socio-economic group (Income <Rs. 1000/month) and majority had rural (<5000 population) background. Majority of the subjects were married (29 out of 40) and in all men except one history of heterosexual promiscuity could be elicited. All females except two had no high risk behaviour for HIV infection. Out of the 40 subjects, 28 were diagnosed as having tuberculous etiology. Extrapulmonary involvement with respiratory symptoms included invasive candidiasis with pleural effusion (1), oral candidiasis with lymphadenitis (1), cryptococcal meningitis with tuberculous abdomen (1), suspected interstitial pneumonitis with genital herpes (2), generalised

lymphadenopathy (2) and pleural effusion of undetermined aetiology (5).

Thirteen of the subjects with tuberculous lymphadenitis had upto 2 groups of lymph gland involvement (cervical, axillary or both). The distribution of break up of subjects with tuberculous aetiology is shown in Table 1. Subjects of disseminated tuberculosis(4), pleural effusion with pulmonary involvement (3), abdominal tuberculosis (1), tuberculous lymphadenitis (1), and genital tuberculosis (1) died within 1-4 months (mean 2.2 months) of diagnosis even when on 2EHRZ/4HR therapy. Fourteen of the subjects, 10 with tuberculous lymphadenitis, 2 with genital tuberculosis, and 2 with isolated pleural effusion Showed excellent response to chemotherapy and these were similar to the results of seronegative cases with extrapulmonary tuberculosis and are under follow up for more than 6-18 months. Four subjects were lost during follow up. Of the subjects with extrapulmonary tuberculosis, nine were diagnosed by demonstration of acid fast bacilli in aspirate from lymph node and the rest by biopsy or cytological examination showing typical granulomatous lesions.

Table 1 : *HIV and extrapulmonary involvement*

	Males	Females	Total
Genital	-	3	3
Lymph node	13	2	15
Pleural	4	1	5
Abdominal	.	1	1
Disseminated	3	1	4
	20	8	28

Ten of the subjects with extrapulmonary tuberculosis and 11 of the 12 cases with non-tubercular extrapulmonary involvement died. (Fig. 1 & 2).

## Discussion

The Regional Surveillance Centre for HIV infection established in JIPMER, Pondicherry, has screened 42,795 subjects upto July 1994 with HIV positivity in 947 subjects giving a rate of 2.21%. On the other hand, out of 1291 subjects

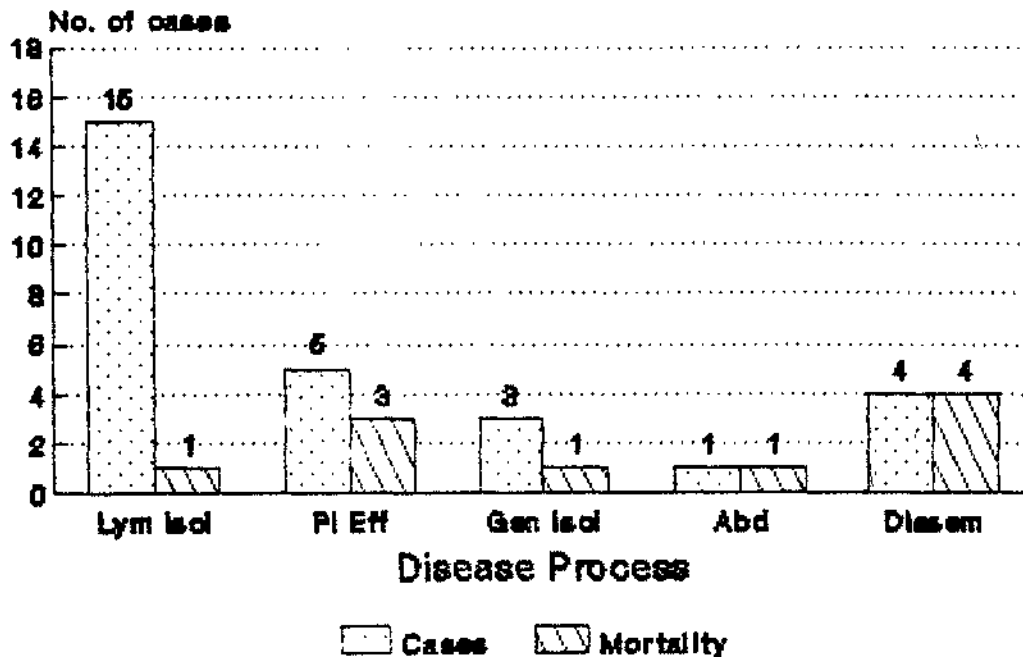


Fig. 1 Extrapulmonary involvement in HIV (fatality) - Tuberculous Cases

ED C«»M ESS Mortality

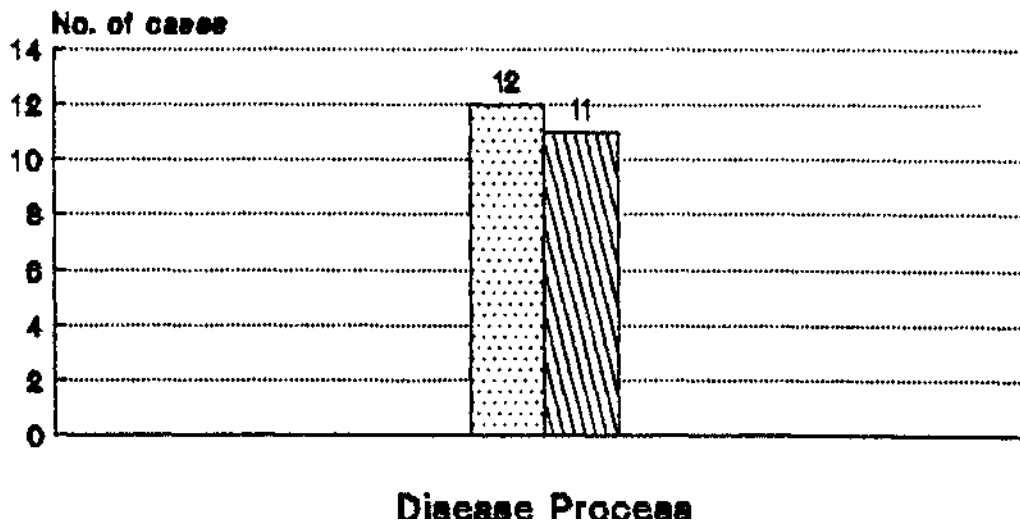


Fig. 2 Extrapulmonary involvement in HIV (fatality) - Non-tuberculous Cases

screened in the department upto July 1994, HIV positivity was found in 74 subjects giving a rate of 5.73% which is 8 times more than the national average of 7.1/1000. When the number of cases per year from March 1991 to July 1994 was analysed, the trend was: 2.65% (7/264) in 1991,

4.03% (10/248) in 1992, 10.40% (41/394) in 1993 which is higher than the incidence reported from Bombay<sup>9</sup>.

The mean ages was 31.6 years and the ages in both sexes were more or less similar which

finding differs from an earlier report from our country<sup>6</sup> as well as from African countries where young female patients (< 25 years) were more often infected with HIV than their male counterparts<sup>10</sup>.

History of heterosexual promiscuity was elicited in (29/40) subjects which conforms to Mann's Pattern 2<sup>11</sup>. No risk factor could be identified in all but two female patients. All the females were housewives and probably acquired the infection from their spouses, implying that they constitute a source of vertical transmission.

Extrapulmonary involvement among HIV infected coincides or precedes that of AIDS probably as a result of defect in cell mediated immunity occurring at an earlier stage<sup>12,13</sup>. Tuberculous cases showed extrapulmonary involvement up to 70% in USA<sup>14,15</sup> and 65% in French citizens<sup>16</sup>. The present study shows extrapulmonary tuberculous (EPT) involvement in 28/74 (37.8%) which is less than in earlier studies from USA and France but in agreement with African studies<sup>17,18</sup>, where pulmonary involvement is as frequent as extrapulmonary involvement. Further, 10.8% (28/270) subjects of EPT were HIV positive. No comparable data from Indian studies is available in this regard.

Disseminated tuberculosis was reported to occur commonly and to the extent of 55%<sup>19</sup>. However, present study found disseminated tuberculosis only in 4/28 cases, and all of them died.

Isolated genital tuberculosis occurred in 3/28 cases in our study (vault of vagina-1 vaginal tuberculosis-1 & cervicitis-1)<sup>20</sup>.

Direct smear examination of aspirates was positive for AFB in over 60% of lymphadenitis cases. This is in agreement with an earlier finding from Zimbabwe<sup>21</sup>.

Thirteen subjects who completed short course chemotherapy (9 lymphadenitis + 2 genital + 2 pleura) showed excellent response at the end of 4th month of treatment and in only 1 case treatment had to be prolonged to nine months before achieving complete regression of lymph nodes. The median relapse-free post-treatment

follow-up time in 13 subjects, who responded excellently, was 9 months; range 7-18 months), and results are comparable with HIV seronegative subjects, who had median relapse free period of 13 months, the range being 9-26 months.

Isolated tuberculous pleural effusion was found in two cases (diagnosed by pleural biopsy) and both showed excellent response to chemotherapy. However, the presence of pleural effusion with pulmonary tuberculosis and with concurrent pulmonary involvement/associated complications had grave prognosis as all the 3 cases died within three weeks of diagnosis and only 1 case of idiopathic pleural effusion (tubercular) survived. The short history in these patients is indicative of extensive spread of the disease because of immunodeficiency, due to HIV infection.

The Centres for Disease Control (CDC)'s new AIDS classification and proposed 1992 definition containing AIDS defining conditions now includes tuberculosis (disseminated or extrapulmonary). AIDS patients with pleural effusion are known to have significantly lower serum albumin levels and CD4 counts than those without pleural effusion<sup>22</sup> indicating deteriorating immunological status. The short history and high mortality (72%) in the present series confirms the late stage of the disease. In pleura, cellular immune response is known to play a part producing a local activation of T cells and macrophages with high fluid Isozyme concentrations in immunocompetent subjects. Contrary to this, in immunodeficient subjects, pleural effusion may occur as a result of direct involvement, rather than due to immunological mechanism. Whether pleural involvement should also be considered as AIDS defining criterion is debatable.

One subject showed Ethambutol induced Steven Johnson's syndrome. However, in the rest, no major side effects compelling withdrawal of therapy were noticed. This differs from earlier studies from Italy where drug toxicity was found to be very high<sup>23</sup>.

Eleven of the 12 (92%) subjects with HIV and non-tuberculous extrapulmonary involvement died in the present series whereas with extrapulmonary tubercular involvement, the fatality rate was

10/28 (35.7%). Even though CDC classification includes extrapulmonary tuberculosis as AIDS defining illness, yet in the present series, there has been excellent response in solitary genital involvement or lymphadenitis (upto 2 groups), and pleural effusion subjects without concurrent pulmonary involvement. In India, the prevalence of tuberculosis infection varies from 30 to 65% in different age groups, and, therefore, it appears that the breakdown into tuberculosis occurs in an early phase of HIV infection. It is the relatively immunocompetent subjects, who showed an excellent response to chemotherapy. Since the fatality rate in seronegative extra pulmonary tuberculosis in our study is 1/180 as compared to seropositive cases with a fatality of 10/28, therefore, the chances of dying in a HIV seropositive individual with extrapulmonary tuberculosis is much higher than in HIV seronegative cases with extrapulmonary tuberculosis and this finding is in agreement with earlier reports<sup>24</sup>.

We conclude that since there will be an estimated 5 million people infected with HIV and about 1 million cases of AIDS in India by 2000 A.D., the impact of HIV infection with tuberculosis may become alarming. We may prevent significant number of HIV infected individuals from dying early of tuberculosis if tuberculosis is detected early and treated promptly. This will ensure prolongation of median life of patients with tuberculosis, as HIV & TB are known to modify the clinical characteristics of each other<sup>25</sup>.

## References

1. Leading Article : The Global Tuberculosis Situation and the new control strategy of the World Health Organization. *Tubercle* 1991; 72:1.
2. Pitchenik A.E., Fertel D, Bloch A.B. Mycobacterial Disease: Epidemiology, diagnosis, treatment and prevention. *Clin Chest Med* 1988; 9:425.
3. Murray J.F. The White Plague: Down and out or up and coming. *Am Rev Respir Dis* 1989; 140:1788.
4. Centers for Disease Control. Revision of the surveillance definition for AIDS. *MMWR (Suppl)* 1987; 36:1S-5S.
5. David H. Has, Roger M. Des Perez; Tuberculosis and acquired immunodeficiency syndrome: A historical perspective on recent developments. *Am J. Med.* 1994; 96:439.
6. Arora V.K. Seetharaman M.L. Gowrinath K, Sambasiva Rao R. Lung and HIV infection with special reference to Tuberculosis: Preliminary report on 20 HIV-1 seropositive cases. *Indian J Chest Dis Allied Sci* 1993; 35:103.
7. Mohanty K.C. Sundrani R.M. and Sudhir Nair. HIV infection in patients with respiratory diseases. *Ind. J. Tub.* 1993; 40:5.
8. V.K. Arora, A. Johri. Reactivation of Tuberculosis and leprosy in HIV positive cases. *Tubercle & Lung Dis* 1994; 75:237.
9. K.C. Mohanty, Sudhir Nair, Tushar Sahasrabudhe. Changing trend of HIV infection in patients with respiratory diseases in Bombay since 1988. *Ind J. Tub.* 1994; 41:147.
10. Simooya O.O. Maboshe M.N. Kaoma R.B. Chimfwembe B.C. Thurairajah A, Mukunyandela M. HIV infection in newly diagnosed tuberculosis patients in Nafola, Zambia. *Central African J. of Med* 1991; 37:4.
11. Mann J. *Global AIDS: Epidemiology, impact, projections, global strategy in AIDS prevention and control.* Pergamon Press, Oxford 1988; 3.
12. Harrison W. Farber, Thomas W. Barber: Mycobacterial infections. *In* Howard Libman & Robert A. Witsberg eds *HIV infection. A clinical manual* 2nd edition. Boston, Little Brown and Company 1993; 263.
13. Small P.M. Schechter G.F. Goodman P.C. Sande M.A. Chaissan RE, Hopewell PC. Treatment of Tuberculosis in patients with advanced human immunodeficiency virus infection. *N. Eng. J. Med.* 1991; 324:289.
14. Pitchenik A.E. Cole C. Russell B.W. Fischl M.A. Spira T.J. Snider D.E. Tuberculosis, a typical mycobacteriosis, and the acquired immunodeficiency syndrome among Haitian and non Haitian patients in South Florida. *Ann Intern Med* 1984; 101:641.
15. Rieder H.L. Snider D.E. Cauthen G.M. Extrapulmonary Tuberculosis in the United States. *Am Rev Respir Dis* 1990; 141:347.
16. Perrone C, Ghouboutni A, Lepout C, Salmon Ceron D, et al. Should pulmonary tuberculosis be an AIDS defining diagnosis in patients infected with HIV? *Tubercle & Lung Dis* 1992; 73:39.
17. Loemba Hughes, Makuwa M, Bnzit Y. Tuberculosis associated HIV in Congo: A Four Years retrospective hospital and ambulatory study (Conference Abstracts). VIII International Conference on AIDS/III STD World Congress. Amsterdam 1992; 19.
18. Alsu T, Raviglione Mario C, Narain J.P., Eriki P, et al. Monitoring HIV associated tuberculosis in Uganda: seroprevalance and clinical features. VIII International Conference on AIDS/III STD World Congress. Amsterdam 1992; 19.
19. Sunderam G, Mcdonald R.J. Maniatis T, Oleske J, Kapila R, Reichman Lb. Tuberculosis as a manifestation of the acquired immunodeficiency syndrome (AIDS) *JAMA* 1986; 256:362.

20. Arora V.K. Raksha Arora, Rajaram, P : Tuberculosis of the Vagina in an HIV Seropositive Case; *Tubercle and Lung disease*; 1994, 75, 239.
21. Pitchie A.D. Chicksen B. Fine needle extrathoracic lymph node aspiration in HIV associated sputm negative tuberculosis. *Lancet* 1992; 1504.
22. Joseph J, Strange C, Sahu S.A. Pleural effusions in hospitalized patients with AIDS. *Ann. Intern. Med.* 1993; 118:856.
23. Monno L, Angarano O, Carbouara S, Infante G, Coppolaz D. Costa S, Quarto M, Pastore G, Current problems in treating tuberculosis in Italian HIV infected patients. *Tubercle & Lung Dis* 1993; 74:280.
24. Nunn P.P. Brindle R, Caipenter L. Odhiambo J, Wasunna K, Newham R. Cohort study of HIV infection in Tuberculosis patients, Nairobi, Kenya. Analysis of early (6 months) mortality. *Am Rev. Respir. Dis.* 1992;.146:849.
25. Wallis R, Vjecha M, Amir Tahmasseb M, Okwera A, Byekwaso F, Nyole S. Influence of Tuberculosis on HIV-1 cytokine expression and elevated B<sub>2</sub> - microglobulin in HIV-1 associated tuberculosis. *J Infect Dis.* 1993; 167:43.



## PULMONARY FUNCTION TESTS IN PATIENTS OF TUBERCULOUS PLEURAL EFFUSION BEFORE, DURING AND AFTER CHEMOTHERAPY\*

Rupak Singla

**Summary :** Pulmonary function tests were carried out in patients of tuberculous pleural effusion under treatment, to study the initial lung function impairment, effect of severity of pleural effusion, changes over time and residual abnormalities, if any, at the end of chemotherapy. Correlation of lung function with radiological improvement was also studied,

In 46 patients of untreated and uncomplicated tuberculous pleural effusion, spirometry was done pretreatment and after 1, 2 and 6 months of treatment. Lung volume and diffusion capacity were measured pretreatment and after 2 and 6 months of treatment.

Pulmonary function tests (PFT) in pleural effusion show moderate restrictive abnormalities with mildly reduced diffusion capacity with mild hypoxaemia and hypocapnia and mild respiratory alkalosis. The derangements in PFT are proportional to the severity of pleural effusion, after institution of antituberculosis therapy, radiological improvements occur much earlier but the lung functions continue to improve upto six months after treatment is over. Even at the end of six months of therapy, some residual restrictive abnormalities are left which are directly proportional to the severity of pleural effusion prior to the start of treatment.

### Introduction

In patients with pleural effusion, the alteration in physiological states leading to restrictive lung functions and hypoxaemia have been recognized<sup>1,2,3</sup> Studies have been done regarding acute changes in pulmonary functions within 24 hours or so after thoracocentesis. But very few studies are available about the course of recovery of lung functions over time after institution of therapy. These studies have limitations either due to very small number of patients or, lack of periodic follow up, over time. Yoo et al<sup>2</sup> studied only 3 patients; Alschule et al.<sup>2</sup> studied 8 patients and Estenne<sup>4</sup> studied 9 patients.

The present study was done in patients of tuberculous pleural effusion to study the initial lung function impairment, changes over time after the institution of anti-tuberculosis therapy and the residual abnormalities left at the end of 6 months of treatment. The effect of severity of pleural effusion on lung functions has also been studied. The correlation between improvement in X-Ray and improvement in lung functions has also been studied. To our knowledge this is the first report of its kind.

### Material and Methods

Forty six previously untreated patients of uncomplicated tuberculous pleural effusion were included in the study. There were 35 male and 11 female patients. Mean age of the patients was 26 years (range 13 to 70 years) (Table 1). The diagnosis of tuberculosis was confirmed by the

L.R.S. Institute of Tuberculosis and Allied Diseases, Sri Aurobindo Marg, New Delhi

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Correspondence: Dr. Rupak Singla, Chest Physician, L.R.S. Institute of Tuberculosis and Allied Diseases, Sri Aurobindo Marg, New Delhi-110 030,

**Table 1** : Age, height and sex distribution of patients according to category of pleural effusion.

Patients	Total	Male	Female	Age (years)	Height (meters)
All	46	35	11	26.6 ± 11.0 (13-70)	1.60 ± 0.08
Mild	20	17	3	24.2 ± 11.0 (13-55)	1.60 ± 0.07
Moderate	18	13	5	29.0 ± 11.2 (17-70)	1.60 ± 0.07
Severe	8	5	3	27.0 ± 9.1 (15.45)	1.60 ± 0.09

Values are expressed as Mean ± S.D. (Range)

presence of granuloma in histopathological examination, after pleural biopsy or demonstration of acid fast bacilli in pleural fluid/biopsy associated with exudative pleural effusion. Patients with encysted pleural effusion were excluded from the study. There were 4 male smokers in the study group.

A detailed clinical examination was done in all the patients along with X-Ray of the chest and routine investigation of blood and urine. X-Ray chest was done every month for 6 months. All patients were given the regimen of 2 months Isoniazid, Rifampicin, Ethambutol and Pyrazinamide followed by 4 months of Isoniazid and Rifampicin.

Pulmonary function tests were evaluated in all the patients. Spirometry was done using dry rolling seal spirometer of Morgan Transfer Test machine. Minimum 3 forced expiratory manoeuvres were performed and the best value was recorded. Lung volumes were estimated by multiple breath closed circuit helium dilution method. Two tests were done and the mean value was recorded. Diffusion capacity was measured by single breath technique and the values were corrected for hemoglobin. Arterial blood gas was collected by heparinised arterial blood sampler disposable syringe with patient in supine position, from radial artery. The blood was analyzed immediately

using Radiometer ABL 330 machine. Spirometry was done pre-treatment and after 1, 2 and 6 months of treatment. Lung volumes were done pre-treatment and after 2 and 6 months of treatment. The values of Spirometry and static lung volume were expressed as percentage of predicted values for Indians of same age, sex and height<sup>6,7</sup>.

However, the values for DL<sub>co</sub> were expressed as percentage of predicted normal for Caucasians due to lack of Indian data. Impairment of static lung volume and DL<sub>co</sub> (<80% of predicted normal value) were evaluated as per arbitrary criteria of Ries and Clausen<sup>8</sup> and Ayres<sup>9</sup>.

Based on X-Ray chest, patients were classified as mild, moderate and severe types. Patients with pleural fluid level upto lower border of fifth rib anteriorly were classified as mild, upto lower border of third rib as moderate and above the third rib as severe pleural effusion.

The data were analyzed by analysis of variance using multiple range test.

## Results

*Pulmonary function test abnormalities before starting treatment:* Pre-treatment PFT in all patients and in patients with mild, moderate and severe

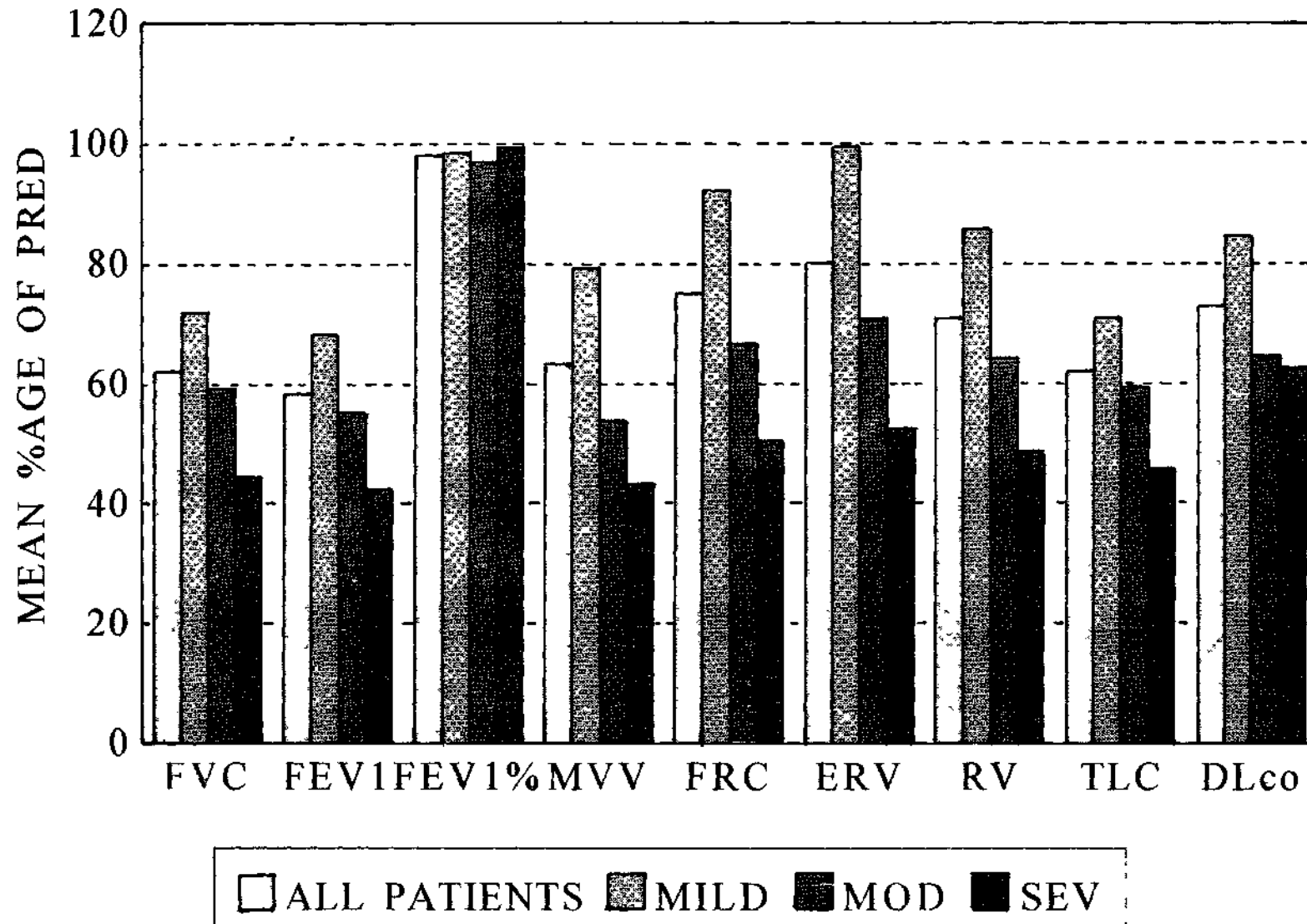


Fig.1 PFT BEFORE STARTING TREATMENT

pleural effusion are shown in Fig 1 and Table 2. Spirometry showed FVC and FEV<sub>1</sub> to be moderately reduced in total patients. The reduction increased with increasing severity of pleural effusion and the differences between the three group were statistically significant. The FEV<sub>1</sub>% was normal. FEF<sub>25-75</sub> was mildly reduced in total patients. This reduction increased significantly with increasing severity of pleural effusion. MVV was moderately reduced in total patients. This reduction also increased significantly with increasing severity of pleural effusion. Static lung

volume showed TLC to be moderately reduced in total patients. This reduction increased with increasing severity of pleural effusion. The differences between the three groups were statistically significant. FRC, ERV and RV were within normal range in total patients and in mild pleural effusion. In moderate and severe groups FRC, ERV and RV were reduced mildly and moderately, respectively.

Diffusion capacity was mildly reduced in total patients. DL<sub>co</sub> was within normal limits in mild

**Table 2.** PFT parameters before starting treatment (values are percentage of predicted normal) expressed as Mean (S.D.)

PFT Parameters	All (46)	Mild (20)	Mod (18)	Sev (8)	Mild vs Mod	Mod vs Sev	Mild vs Sev
FVC	62.3 (11.9)	72.1 (7.7)	59.4 (6.0)	44.7 (4.4)	NS	***	***
FEV <sub>1</sub>	58.5 (12.0)	68.5 (8.2)	54.4 (7.0)	42.7 (3.8)	*	**	***
FEV <sub>1</sub> %	98.0 (8.3)	98.6 (9.3)	96.9 (8.7)	99.5 (4.7)	NS	NS	NS
FEF <sub>25-75</sub>	51.0 (19.9)	61.6 (20.7)	44.5 (15.1)	39.0 (15.4)	**	*	** *
MVV	63.4 (23.0)	79.4 (23.3)	53.9 (11.9)	43.6 (13.7)	NS	*	***
FRC	75.1 (25.0)	92.4 (21.1)	66.8 (19.8)	50.6 (13.0)	*	NS	***
ERV	80.2 (30.5)	99.6 (24.0)	71.0 (26.2)	52.6 (23.8)	*	NS	***
RV	71.2 (28.7)	86.1 (28.6)	64.4 (25.6)	48.9 (12.9)	NS	NS	**
TLC	62.2 (12.3)	71.0 (8.9)	59.7 (8.2)	46.0 (8.0)	*	*	** *
DL <sub>co</sub>	73.2 (16.9)	84.7 (14.3)	65.0 (14.7)	62.9 (9.5)	*	NS	***

\*\*\* = P < .001

\*\* = P < .01

\* = P < .05

NS = P > .05

List of Abbreviations used

FVC - Forced Vital capacity

FEV<sub>1</sub> - Forced Expiratory Volume 1 second

FEV<sub>1</sub>% - Ratio of Forced Vital capacity to Forced Expiratory Volume 1 second

FEF<sub>25-75</sub> - Forced Expiratory Flow at 25 to 75 % Vital Capacity

MVV - Maximum Ventilation Volume

TLC - Total Lung capacity

FRC - Functional Residual Capacity

RV - Residual Volume

ERV - Expiratory Reserve Volume

DL<sub>co</sub> - Diffusion Capacity for Carbon Monoxide

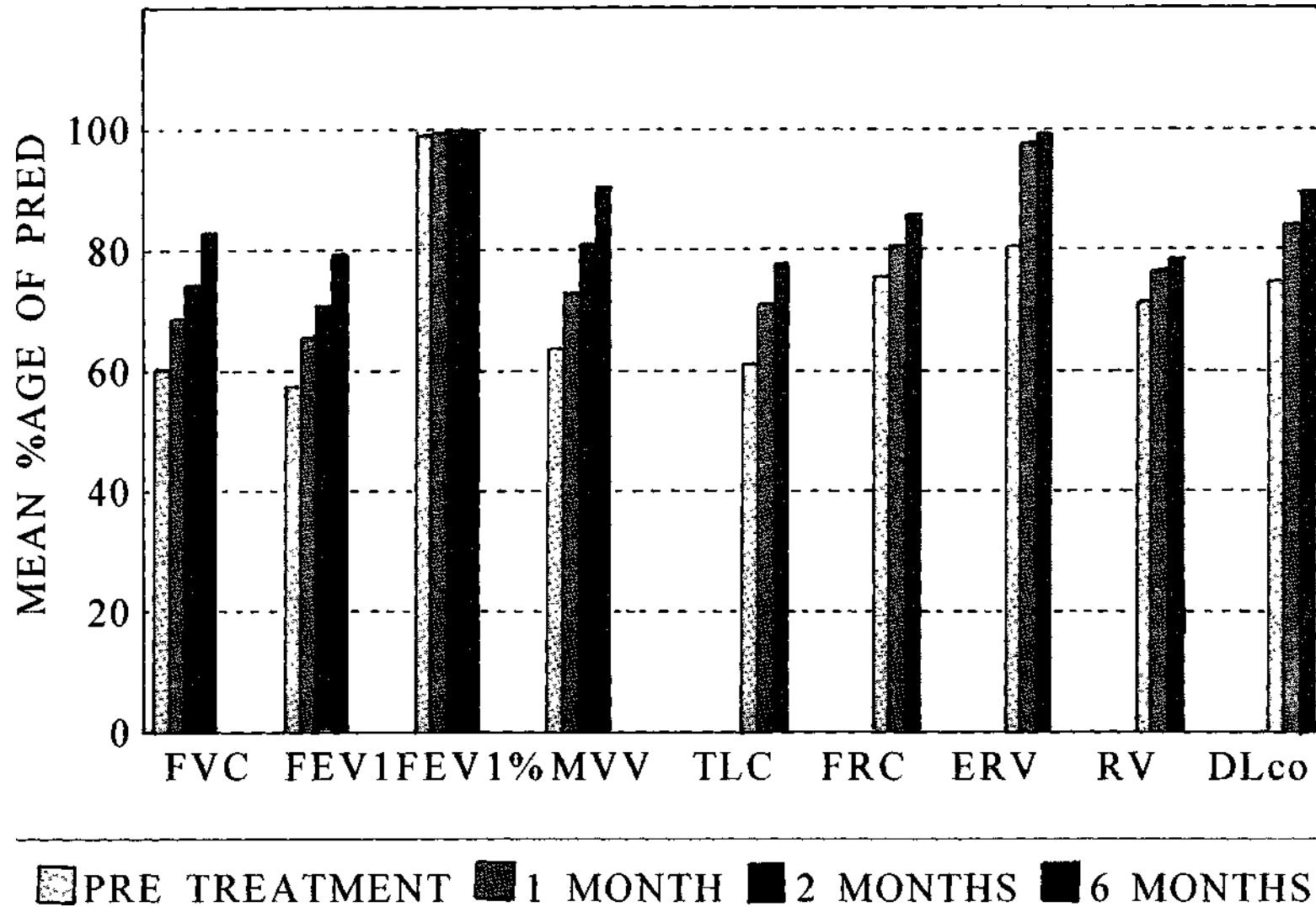


Fig. 2 PFT PARAMETERS DURING TREATMENT

**TABLE 3** : Arterial Blood Gas analysis in patients before starting treatment

ABG Parameters	All PT (38)	Mild (17)	Mod (13)	Sev (8)	Mild vs Mod	Mod vs Sev	Mild vs Sev
pH	7.45 (0.03)	7.43 (0.02)	7.47 (0.03)	7.40 (0.01)	**	*	NS
PaO <sub>2</sub>	7.67 (11.0)	83.4 (6.8)	77.0 (9.6)	61.8 (3.7)	NS	**	***
PaCO <sub>2</sub>	33.1 (4.3)	34.5 (3.9)	30.4 (4.8)	34.4 (2.2)	*	NS	NS
SaO <sub>2</sub>	95.1 (2.0)	96.3 (0.8)	95.6 (1.4)	91.9 (1.5)			
HCO <sub>3</sub>	23.1 (2.3)	23.1 (1.9)	22.3 (3.0)	24.2 (1.0)			
ABE	-2.0 (1.8)	-0.5 (1.6)	-0.6 (2.4)	0.87 (0.71)			

Values are expressed as Mean (S.D.).

\*\*\* =  $p < .001$

\*\* =  $p < .01$

\* =  $p < .05$

NS =  $p > .05$

pleural effusion while it was mildly reduced in moderate and severe pleural effusion. This reduction was statistically significant as compared to the mild group. Arterial blood gas analysis (ABG) at room air showed findings suggestive of mild hypoxaemia and hypocapnia and mild respiratory alkalosis (Table 3). Patients with severe pleural effusion had statistically significant low mean PaO<sub>2</sub> as compared to mild and moderate pleural effusion patients. In moderate pleural effusion, PaO<sub>2</sub> was lower as compared to the mild group but the difference was not statistically significant. Mean PaCO<sub>2</sub> and pH values did not show any relation with the severity of pleural effusion.

*PFT during the course of treatment:* Out of total 46 patients, 31 (14 mild, 9 moderate and 8 severe pleural effusion patients) returned for assessment as required at 1,2 and 6 months after treatment. Rest of the patients were excluded from the study for follow up. The percentage of

predicted normal for each PFT parameter at each month is shown in table 4 and Fig. 2.

**Table 4** : PFT parameters during treatment

PFT Parameter	Pre-treatment	1 Month	2 Months	6 Months
FVC	60.57	68.87	74.59	82.97
FEV <sub>1</sub>	57.69	65.65	71.13	79.51
FEV <sub>1</sub> %	99.14	99.33	99.91	99.77
FEF <sub>25-75</sub>	51.89	58.79	63.29	69.74
MVV	63.98	73.19	81.19	90.52
TLC	61.31	71.40	77.87	
FRC	75.84	80.76	86.00	
ERV	80.74	97.70	99.37	
RV	71.51	76.99	78.70	
Dlco	75.02	84.18	89.83	

Values are percentage of predicted normal expressed as mean.

Spirometry showed statistically significant improvement in FVC, FEV<sub>1</sub>, FEF<sub>25-75</sub> and MVV after 1,2 and 6 months of therapy. FEV<sub>1</sub>% remained same during treatment. Lung volume showed statistically significant improvement in TLC after 2 and 6 months, FRC, ERV and RV also improved but the improvement was not statistically significant. Diffusion capacity showed statistically significant improvement after 2 and 6 months of treatment.

X-Ray chest done every month showed near complete clearing of pleural fluid with only minimal pleural thickening, as costophrenic angle blunting only, in 28 out of 31 patients. The average time taken to achieve maximum radiological clearing in mild, moderate and severe pleural effusion was 2.8, 3.6 and 4.8 months respectively. Three patients, 2 with severe and 1 with moderate pleural effusion had significant pleural thickening radiologically even at the end of six months of therapy.

*PFT at the end of six months of treatment:* After completion of 6 months of treatment the PFT parameters (Table 5) showed improvement and mean values of FVC, FEV<sub>1</sub>, FEF<sub>25-75</sub>, MVV, FRC, ERV, RV and DL<sub>co</sub> were within normal range although towards lower side. Mean TLC was mildly low.

Comparison between the mild, moderate and severe pleural effusion patients showed that mean FVC and FEV<sub>1</sub> were lowest in severe, intermediate in moderate and maximum in mild pleural effusion, although the difference was not statistically significant. TLC, FRC and RV were significantly low in severe pleural effusion as compared to mild and moderate pleural effusion. DL<sub>co</sub> was significantly lower in moderate and severe pleural effusion as compared to mild pleural effusion.

**Discussion**

In our study, the pulmonary functions in pleural effusion patients showed moderate restrictive lung functions with maintained FEV<sub>1</sub>%. Mean FEF<sub>25-75</sub> was mildly reduced indicating

**Table 5 : PFT parameters at the end of 6 months of treatment**

PFT Parameters	Mild (14)	Mod (9)	Severe (8)	All PT
FVC	87.37 ±8.05	82.33 ±8.10	76.00 ±12.31	82.97 ±10.13
FEV <sub>1</sub>	83.31 ±12.10	78.03 ±6.90	74.53 ±9.90	79.51 ±10.62
FEV <sub>1</sub> %	98.43 ±9.5	100.27 ±6.27	101.54 ±9.05	99.77 ±8.41
FEF <sub>25-75</sub>	73.84 ±27.7	65.84 ±11.51	66.93 ±29.47	69.74 ±24.20
MVV	109.44 ±21.03	74.92 ±13.03	74.97 ±15.28	90.52 ±24.42
TLC	84.04 ±8.94	76.76 ±7.17	68.31 ±8.81	77.87 ±10.44
FRC	97.39 ±19.64	77.37 ±25.00	75.76 ±12.49	86.0 ±21.94
ERV	116.75 ±24.31	88.42 ±22.55	81.28 ±25.14	99.37 ±28.34
RV	99.44 ±99.44	66.81 ±31.80	68.01 ±22.58	78.7 ±31.4
DL <sub>co</sub>	95.76 ±8.93	86.15 ±7.06	83.60 ±4.23	89.83 ±9.11

Values are percentage of predicted normal expressed as Mean ± S.D.

small airway obstruction. Mean FRC, ERV and RV were towards lower side of normal range. TLC was moderately reduced. Diffusion capacity was mildly reduced. Arterial blood gas analysis showed mild hypoxaemia and hypocapnia and mild respiratory alkalosis.

Earlier studies have found restrictive lung functions in pleural effusion patients, 5,0. Altschule et al<sup>1</sup> observed ERV to be slightly reduced and RV was slightly affected. Regarding arterial blood gas analysis, a number of studies have been done<sup>1,3,10,11,12</sup>. Most of these have studied the change in PO<sub>2</sub> before and after thoracentesis. Before thoracentesis hypoxaemia has been observed<sup>3,11,12</sup>. But Altschule et al<sup>1</sup> and Anthonisen Et al<sup>10</sup> observed no arterial blood gas abnormality

Hypoxaemia in pleural effusion could be due to pleural effusion producing collapsed, non-ventilated but perfused alveoli leading to ventilation-perfusion mismatch<sup>11</sup>. Very few studies have reported diffusion capacity in pleural effusion patients<sup>2,11</sup>. These studies found  $DL_{CO}$  to be reduced. Fall in  $DL_{CO}$  could be due to reduced surface area available for gas exchange due to ventilation perfusion mismatch.

The effect of severity of pleural effusion on lung functions has not been studied earlier. In the current study based on X-Ray chest, the patients were divided in three groups: mild, moderate and severe. The restrictive lung function abnormality indicated by reduced FVC, FEV<sub>1</sub> and TLC increased with increasing severity of pleural effusion and the difference was statistically significant. FEF<sub>25-75</sub> significantly reduced with increasing severity of pleural effusion indicating closure of small airways. Mean FRC, ERV and RV were within normal range in mild pleural effusion. In moderate and severe pleural effusion these parameters were reduced mildly and moderately respectively.

Diffusion capacity was within normal range in mild pleural effusion. In moderate and severe pleural effusion the  $DL_{CO}$  was mildly reduced and the reduction was statistically significant.

Arterial blood gas analysis showed mean  $P_{AO_2}$  within normal range ( $83.4 \pm 6.8$ ) in mild pleural effusion. Patients with moderate pleural effusion had slight fall in  $P_{AO_2}$  ( $77 \pm 9.6$ ) as compared to mild but was not significant statistically. Patient with severe pleural effusion had statistically significant low  $P_{AO_2}$  ( $61.8 \pm 3.7$ ). pH and  $P_{ACO_2}$  did not show any correlation with increasing severity of pleural effusion.

*PFT during the course of treatment:* There was statistically significant improvement in FVC, FEV<sub>1</sub>, FEF<sub>25-75</sub> after 1, 2 and 6 months of treatment. Lung volumes showed statistically significant improvement after 2 and 6 months of treatment. FRC, ERV and RV also improved after 2 and 6 months but the improvement was not significant statistically. Significant improvement was observed in DL after 2 and 6 months.

Earlier studies on pleural effusion have not mentioned the course of recovery of lung functions after starting treatment. Brown et al<sup>3</sup> mentioned that pleural effusion produce restrictive pulmonary volume and reduced pulmonary compliance. The recovery of lung functions after treatment depends upon the balance between increase in pulmonary volume and/or fall in the size of thoracic cavity after resorption of pleural fluid. The duration of pleural effusion may also affect the pulmonary functions.

*PFT at the end of 6 months of treatment:* After completion of 6 months of treatment, TLC was mildly low indicating mild restrictive abnormality. All other parameters studied i.e. FVC, FEV<sub>1</sub>, FEF<sub>25-75</sub>, FRC, RV, ERV and  $DL_{CO}$  had improved to be within predicted normal range of values though at lower side of the range.

On comparing the three groups of pleural effusion it was observed that the maximum radiological improvement had occurred by 2.8, 3.6 and 4.8 months in mild, moderate and severe pleural effusions respectively. But lung function showed that some residual restrictive abnormalities were still persisting despite radiological clearing. The residual abnormalities, were directly proportional to the severity of pleural effusion prior to the onset of treatment.

#### Acknowledgements

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#### References

1. Altschule M.D., Zamcheck N. Effect of pleural effusion on respiration and circulation in man. *J Clin Invest* 1944, 23 325.
2. Yoo O.H., Ting E.Y. Effect of pleural effusion on pulmonary function. *Am Rev Resp Dis*, 1964, 89 55.
3. Blown N.E., Zamel N., Aberman A. Change and pulmonary mechanics and gas exchange following thoracocentesis. *Chest* 1978, 74(5) 540.
4. Estenne R. - Mechanism of relief of dyspnoea after thoracocentesis in patients with large pleural effusion. *Am J Med* 1983, 74, 813.
5. Jain S.K., Ramiah T.J. Spirometric studies in healthy women 15-40 year of age. *Ind J Chest Dis*, 1967, 9, 1.

Jain S.K., Gupta C.K. Lung function studies in healthy men and women over forty years of age. *Ind .1 Med Res*, 1967, 55, 612.

Jain S.K., Ramiah T.J. Normal standards of pulmonary function test for healthy Indian men 15-40 years old : comparison of different regression equations (prediction formulae). *Ind .1 Med Res*, 1969, 57, 1453.

Reis A.I. Clausen J.L. Lung volume In : Wilson AF ed. *Pulmonary Function Testing - Indications and Interpretation*. Orlamlo Florida : Grune and Station Inc. 1985, 69.

9. Ayres L.N. Carbon monoxide diffusion capacity, *ibid*, 137.

10. Anthonisen N.R., Martin R.R. Regional lung functions in pleural effusion. *Am Rev Resp Dis*, 1977, 116, 201.

11. Perpina M, Benlloch E, Marco V, Abod F, Nauffal D. Effect of thoracocentesis on pulmonary gas exchange. *Thorax* 1983, 38, 747.

12. Karetzky M.S., Kothari G.A., Fourre J.A., Khan A.U. Effect of thoracocentesis on arterial oxygen tension. *Respiration*, 1978, 36, 96.

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## NORTH AMERICAN BLASTOMYCOSIS IN A SOUTH INDIAN GIRL - REPORT OF A CASE

Debidas Ray, P.S. Jairaj and Anand Date

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**Summary: A case of blastomyeosis of the North American variety in a young girl from Tamil Nadu in southern India is reported.**

### Introduction

Unlike bacterial infections which spread from person to person, fungal infections usually emanate from spores found among vegetables and animals. However, *Blastomyces dermatidis* are rarely isolated from soil. Blastomycosis occurs characteristically in North America. It is frequent in south eastern United States. It is especially noteworthy and perhaps of historical importance that the microorganisms were later grown in culture in markedly scattered areas in Africa<sup>1</sup>. Because of its rarity in non-endemic areas outside America, we present a case of blastomycosis of the North American variety occurring in a young Tamilian girl. To our knowledge, no such case report is available in the Indian literature.

### Case Report

A 15 year old female from the city of Madras was admitted to the Christian Medical College Hospital, Vellore with history of swelling of the face and neck which was noticed one year earlier and was initially thought to be due to allergy. But the swelling of the face persisted and increased steadily and the patient started experiencing gradually increasing breathlessness on exertion. She had occasional cough, very little sputum and no fever. There was no history of

loss of weight. Before she visited us, she had been empirically put on antituberculosis therapy (ATT) at Madras for 3 months. As she had no relief, ATT was discontinued.

On examination, there were distended veins in the neck, more noticeable on the right side. Trachea was shifted to the right side. On percussion, there was dull note in right infraclavicular region. On auscultation, there was diminished air entry and vocal resonance; bronchial breath sounds were heard over the same region.

Examination showed haemoglobin 11.2 Gm%, total leucocyte count 11,600 per cumm with 53% neutrophils, 41% lymphocytes, 5% eosinophils and 1% monocytes. The ESR was elevated to 122 mm/hour. Other haematological and biochemical investigations were normal. Sputum examinations for acid fast bacilli were negative. Chest radiography showed right hilar mass with collapse and consolidation of right upper lobe (Figure 1)

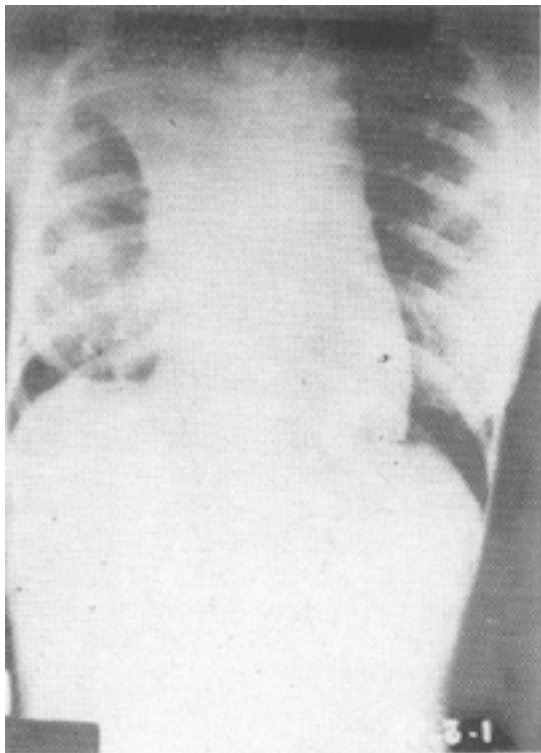
The diagnosis of superior venacaval obstruction due to an intrathoracic mass was made and the patient was taken up for right thoracotomy. At operation, the right upper lobe was found to be collapsed with partial collapse of right middle lobe which was riddled with suspected tumour deposits extending over superior venacava and the entire right hilum. As this was thought to be inoperable, biopsy from the same site was obtained. Histological examination revealed a granuloma consistent with blastomycosis (Figure 2). As the patient was having pain and swelling of right shoulder and elbow, X-ray was taken which showed rarified areas in right humerus

Department of Chest Diseases, Thoracic Surgery and Pathology, Christian Medical College, Vellore

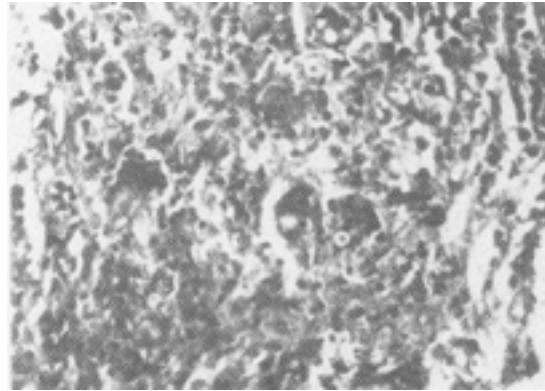
Correspondence : Di. Debidas Ray, Lmeitus Medical Scientist, Indian Council of Medical Reseach. Tuberculosis Reseach Centie Spin Tank Road, Chetput, Madias 600 031

(Figure 3) The patient later developed fever and swellings in the neck. There were palpable enlarged lymph glands and left axillary lymph node biopsy showed granulomatous mass with budding fungus consistent with North American variety of blastomycosis. She was treated with parenteral Amphotericin B, initially starting with 1 mg in 250 ml of 5% dextrose intravenously. The dosage was increased gradually and administered intravenously in 500 ml of 5% dextrose. Administration of a total dosage of 3 gm of Amphotericin B was planned but as the patient started improving, she insisted on going home. Before she took discharge a total dose of 2375 mg had been given.

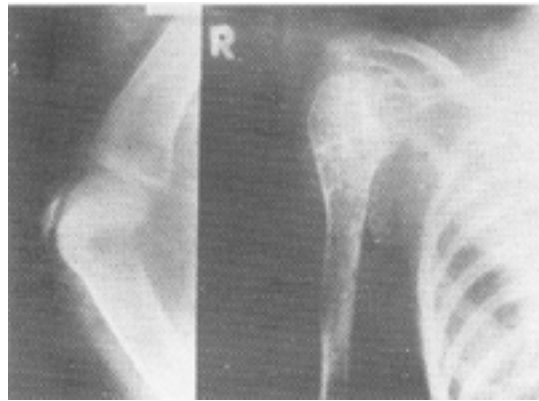
Two years later, she was readmitted with abdominal pain and passing of turbid white urine. While in the ward, she passed a white clotted mass, microscopic examination identified blastomyces in the clot. Repeat blood counts showed leucocytosis of 11000 per cumm with eosinophilia of 21%, urea and creatinine were



**Fig 1. Chest x-ray reveals right hilar mass with collapse and consolidation of upper lobe of the right lung**



**Fig. 2. Microphotography showing granuloma with numerous Blastomyces, some in giant cells: The morphology is consistent with North American variety**



**Fig. 3. Radiography of right shoulder and elbow showing areas of rarefaction more noticeable in humerus**

normal. Bone marrow examination showed hypercellularity with normoblastic erythroid hyperplasia, myeloid hyperplasia, eosinophilia and plasmocytosis. Plain X-ray of abdomen showed enlarged kidneys. Intravenous pyelography showed non-functioning right kidney. Renal scan showed patchy areas of diminished pickup in right kidney and upper part of left kidney. While in hospital, she slowly developed headache, vomiting and blurring of vision. There was papilloedema but no other focal signs. Electroencephalogram showed bilateral slow wave disturbance, brain scan was normal. She was suspected to have developed fungal meningitis and was restarted on

Amphotericin B. However, her condition continued to deteriorate and she developed left hemiparesis. As her condition was moribund, her parents decided to take her home.

### Discussion

Because of its endemicity in the United States the entity itself has been named as blastomycosis of North American and South American varieties. After years of searching, blastomycosis has finally been found in a natural reservoir<sup>2</sup>. Opportunistic infection with blastomyces is said to be rare. Characteristic of this infection is dissemination to other organs from lung. Metastatic dissemination occurs frequently to skin, bone, male genitourinary tract, kidney and brain. Adrenal gland involvement has also been reported<sup>3</sup>. In our patient, beside lung and lymph nodes, involvement of bones and kidneys occurred and involvement of brain was suspected in the final stage.

Methods for diagnosis include sputum culture, biopsy material from skin, aspirate from prostatic fluid and, with involvement of CNS, culture of cerebrospinal fluid<sup>3</sup>. Various serological tests like radio-immunoassay, radio-immunodiffusion for blastomyces have been recommended and the significance of false positive serologic tests has also been discussed<sup>4</sup>. Concurrent pulmonary blastomycosis and tuberculosis in an HIV seropositive man has recently been reported and unreliability of serodiagnosis and necessity of culture or tissue confirmation has been highlighted<sup>5</sup>. Pulmonary blastomycosis may mimic malignancy and differentiation may prove to be a challenging task<sup>6</sup>. In our case, the suspicion of malignancy was the main reason for thoracotomy and biopsy. The diagnosis of North American variety of blastomycosis was supported by histology.

Until recently, Amphotericin B has been the

mainstay of chemotherapy for blastomycosis and response rate has been 80-90%<sup>7</sup>. Success with ketokonazole in a dosage of 200-400 mg/day for upto 6 months<sup>8</sup> as well as failure<sup>9</sup> and both success and failure with ketokonazole<sup>10</sup> in treatment of blastomycosis have recently been reported.

### References

1. Utz J.P. The pulmonary mycosis in bronchopulmonary diseases and related disorders. Cranston W Wolman, Carl Muschenheim eds. Harper & Row Publishers, Maryland, New York. 1st edition 1972, p 418.
2. Klein B.S., Vergeront J.M., Weeks RRJ, Kumar U.N., Mathai O, Varkey B, et al. Isolation of *Blastomyces dermatidis* associated with a large outbreak of blastomycosis in Wisconsin. N Engl J Med., 1986, 314, 529.
3. Sarosi G.A., Davies S.T. Blastomycosis. Am Rev Respir Dis.; 1979, 120, 911.
4. Jordan M.M., Chawla J, Ownes M.W. George R.E. Significance of false positive serologic tests for histoplasmosis and blastomycosis in an endemic area. Am Rev Respir Dis.; 1990, 141: 1487.
5. Kitchen L.W., Clerk R.A., Hoadley D.J., Wisniewski T.L., Janney F.A., Green D.L. Concurrent pulmonary blastomycosis dermatidis and mycobacterium tuberculosis infection in an HIV seropositive man. J Infect Dis., 1989, 60, 911.
6. Poc R.H., Vasalo C.L., Plessingar V.A. Pulmonary blastomycosis versus carcinoma - a challenging differential. Am J Med Sci.; 1972, 265, 145.
7. Parker J.D., Dole I.L., Tose P.E. A decade of experience with blastomycosis and its treatment with amphotericin B. Am Rev Respir Dis., 1969, 99, 895.
8. Bradsher R.W., Rice D.C., Abernathy R.S. Ketokonazole in endemic blastomycosis. Ann Intern Med., 1985, 103, 872.
9. Thicle J.S., Buechner H.A, Cook E.W. Failure of ketokonazole in two patients with blastomycosis. Am Rev Respir Dis.; 1983, 128, 763.
10. McManus E.J., Jones J.M. The use of ketokonazole in the treatment of blastomycosis. Am Rev Respir Dis.; 1984, 133; 141.



## HERNIATION OF LUNG: A CASE REPORT

A.S. Bagga, U.C. Kakadkar, D.J. Lawande and R. Chatterjee

(Received on 15.7.94, Accepted on 20.9.94)

Summary: A case of spontaneous acquired intercostal lung hernia is presented in view of the rarity of the condition. The pathogenesis and classification of lung hernias along with clinical features, roentgenological findings and management are discussed.

### Introduction

Lung hernia is defined<sup>1</sup> as the protrusion of lung tissue covered by parietal and visceral pleurae, beyond the confines of thoracic cavity through an abnormal opening in the thoracic wall.

Not many cases of herniation of lung have been reported in literature

Lung hernia is classified<sup>2</sup> according to the anatomic location such as cervical, thoracic, diaphragmatic or mediastinal. According to etiology classification<sup>2,3,4</sup> it can be congenital or acquired. Acquired hernias are further classified as traumatic, consecutive, spontaneous or pathological. Review of current literature shows that nearly 82% of lung hernias are acquired and the rest congenital.

Spontaneous lung herniation occurs in the presence of a local impairment of the thoracic wall in association with increased intra-thoracic pressure produced by protracted coughing<sup>1,2</sup>.

We present a case of thoracic spontaneous acquired herniation of lung associated with fibrocavitary pulmonary tuberculosis.

### Case Report

S.Y., a 50 year old male, dock labourer by occupation, was admitted to Goa Medical College complaining of cough with expectoration, low grade fever with evening rise for three months. Cough had gradually increased in intensity and, during the week preceding admission, the patient had started getting intractable cough, and moderate fever. Patient also complained of dull aching pain around the right mammary area. Patient also had anorexia with loss of weight of three months' duration.

Four days prior to admission, the patient experienced a sudden severe chest pain above the right mammary area, followed by appearance of a swelling over the right upper anterior chest wall. The swelling had reddish discoloration in its lower part

Patient did not give a history of trauma or surgical intervention on the chest wall. However, the patient noticed that the swelling over the chest wall increased with coughing. This was the first time when such a swelling had developed on his chest.

The patient had been admitted to our hospital five months prior to this admission as a case of smear positive pulmonary tuberculosis. X-ray chest had shown fibromfiltrative lesions in left upper zone with a large cavity in the right upper zone. Patient was administered Isoniazid, Ethambutol and Rifampicin in standard doses, which he continued for two months regularly with good radiological response and conversion

of sputum. At this stage, the patient discontinued anti-tuberculosis treatment. Since the patient developed the symptoms again, he reported to us for the present admission.

The patient had smoked 10-15 beedies per day for the last twenty-five years but was not an alcoholic. Physical examination revealed an elderly male of thin build, pulse and blood pressure were normal and respiratory rate was 24 per minute. Axillary temperature was 100°F. There was marked pallor and grade II clubbing of fingers. Chest was emphysematous in shape. There was a soft, crepitant, non-tender swelling, 10 x 10 cms in size occupying the right infraclavicular, mammary and infra axillary areas, overlying the third, fourth and fifth intercostal spaces (Figures 1 and 2). The swelling increased in size on coughing and on performing Valsalva's manoeuvre. The swelling could be reduced partially by pressure, but appeared again when the pressure was released.

There was a chest wall abscess overlying the lower part of the above swelling just below the right nipple. This abscess was 4 cms in size, pinkish red in colour, warm with diffuse borders, and tender to touch. Cough impulse was present over the abscess (Figure 1).

Bronchial breath sounds were heard over the right infraclavicular and mammary areas with inspiratory crepitations over the left suprascapular area. The hemogram, urinalysis, and blood sugar level were normal. Sputum smear was positive



**Fig. 1 : Lung herniation on right side seen as swelling in the antero-lateral aspect of chest with chest wall abscess below the right nipple**



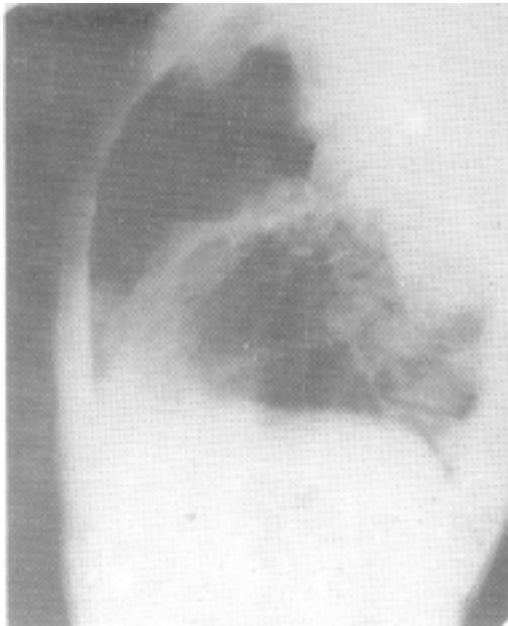
**Fig. 2 : Right lateral aspect of the swelling extending upto infra axillary area**



**Fig. 3 : X-ray chest PA view showing bilateral pulmonary tuberculosis with large "cavity on (R) side occupying upper and mid-zone which herniated**

for AFB. Chest x-ray showed a large cavity in the right upper and midzones with fibromfiltrative shadows in both the upper zones. There was hyperlucency of left lung fields due to emphysema (Figures 3 and 4). There was a definite radiological deterioration over the period of last three months.

Fluoroscopy of chest revealed a radiolucent



**Fig. 4 : X-ray chest lateral view showing hyperlucency of left lung due to emphysema**

swelling overlying the anterolateral aspect of right upper lung with increase in its size on coughing. The part of the right lung which contained the cavity had herniated. Patient was given conservative management in the form of bed rest, antitussives, oxygen inhalations along with anti-tuberculosis drugs i.e. Streptomycin, Rifampicin, Isoniazid and Pyrazinamide in standard doses. Adhesive plaster with a pressure bandage was applied over the chest wall swelling. Patient was also administered Ampicillin 250 mg. every six hours for the chest wall abscess.

The abscess over the chest wall, near the nipple, burst on the third day with a thin purulent discharge. Culture of this pus was sterile. On the fifth day temperature came down to 99° F. The swelling over the chest reduced in size considerably with this conservative management, but a vague chest pain still continued. Patient took premature discharge on the eleventh day after admission but collected medicines from {TB Clinic over the next two months, through his son who informed us that the patient had a draining sinus over the site of rupture of the abscess. The chest wall swelling had reduced in size

considerably. At this stage, patient was lost to follow-up.

### Discussion

Congenital hernia of the lung is due to development defects in the thoracic wall, most frequently in the supraclavicular fossa or anteriorly at the junction of rib and costal cartilage<sup>1</sup>.

Acquired hernias<sup>1</sup> may be :-

- (a) *Traumatic* - which may be due to weakness of chest wall developed as a result of penetrating chest wounds, surgical intervention, fractured rib, etc.
- (b) *Consecutive* - These occur sometimes after localised trauma and following healing of wound.
- (c) *Spontaneous* - These occur due to local weakness of chest wall with increased intrathoracic pressure as a result of protracted cough, weight lifting etc.
- (d) *Pathological* - These occur when thoracic wall has been weakened by a pathological process i.e. a lung abscess penetrating chest wall, abscess of chest wall or caries of rib. Of the acquired type, 52% are secondary to penetrating and non-penetrating trauma to chest<sup>5</sup>.

Only 1% of the acquired hernias are secondary to tuberculosis, inflammatory or neoplastic disease of the chest wall and pleura<sup>6,7</sup>.

For a lung hernia to develop there are two essential criteria<sup>5</sup>.

- (a) Weakness of thoracic wall which usually occurs anteriorly from the costochondrial junction to the sternum because of the absence of external intercostal muscles, posteriorly from the costal angle to the vertebra because of the absence of the internal intercostal muscle, and superiorly in the cervical pleura and neck muscle, because of a congenital weakness of Sibson's fascia.

(b) Increase in intrathoracic pressure due to continued violent cough, as in chronic infection of lung, COPD, bronchial asthma, etc., blowing of musical instruments, straining, weight-lifting etc. Thirtyfive percent of lung hernias are located in cervical region and 65 percent in thoracic region<sup>1</sup>. True diaphragmatic hernia of lung is very rare and difficult to identify. Diagnosis of lung hernia can easily be made<sup>1</sup> in the presence of soft, crepitant protrusion which is reducible on quiet respiration and again bulges forward on coughing, forced expiration or Valsalva's manoeuvre. The defect in the chest wall can often be palpated.

Chest roentgenograms<sup>1</sup> show pulmonary parenchymal tissue protrusion beyond the normal confines of thoracic cage on tangential exposure. Computed tomography confirms the protrusion beyond the thoracic cage.

Conditions that require differentiation are : tumours of the chest wall (lipoma, angioma), subcutaneous emphysema, emphysema necessitatus and cold abscess.

Treatment is usually conservative, such as control of cough and a supportive truss. Lung hernia should be repaired if it produces constant pain, recurrent infection, respiratory distress, cosmetic concern or progressive increase in size, or there are chances of increase in intrathoracic pressure and impending rupture as a result of heavy physical activity such as musicians blowing their instruments. Surgical repair of the defect in the chest wall is done by means of periosteal flaps from the adjacent rib<sup>8,9</sup>.

Donate et al advocate reinforcing teflon bands to approximate the ribs and give stability to the repair<sup>7</sup>.

In our patient, intractable cough led to increased intrathoracic pressure. This, along with the weakened chest wall muscles due to tuberculous toxemia and malnutrition and his occupation involving lifting of heavy loads, led to sudden

development of hernia. We are not aware whether the chest wall abscess communicated with the herniated cavitating lung as reported in another case<sup>10</sup>.

Bronchogenic cyst, pulmonary cyst and bronchial cyst herniating in the form of cervical masses have been reported in literature<sup>10</sup>, but could not be investigated by a sinogram, and C.T. Scan could not be done since the patient left the hospital.

#### Acknowledgement .

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#### References

1. Bidstrup P., Nordentoft M. and Petersen B. : Hernia of the lung : Brief survey and report of two cases. *Acta Radiol.*; 1966, 4, 490.
2. Morel-Lavellec A. quoted by Donato A.T., Hipona I<sup>7</sup>. A . Nawani S. : Spontaneous lung hernia : *Chest*; 1973, 64, 254.
3. Salizberg M. : Pulmonary disorders in Disorders of respiratory tract in children. Edited by Edwin L. Kendig Jr., W.B. Saunders Co. Philadelphia. 1972 I, 506.
4. Fraser R.G., Peter Pare, J.A. : *Diagnosis of Diseases of the Chest*: W.B. Saunders Company, Philadelphia, 1970, p. 1240.
5. Prasad R., Mukerji P.K., Gupta H., Herniation of the lung : *Ind. J. Chest Dis. & All. Sc.*, 1990, 32, 129.
6. Hiscoe B., Digman J.: Types and incidence of lung hernia : *J. Thorac. Surg.*; 1955; 30 : 335.
7. Donato A.T., Hipona F.A., Navani S. : Spontaneous lung hernia : *Chest* 1973 : 64 : 254.
8. Maurer E., Blades B., : Herniation of lung. *J. Thorac. Surg.* 1946, 15, 77.
9. Goodman H.L., Hernia of lung. *J. Thorac. Cardiovasc. Surg.* 1933 : 2 : 368.
10. Raj B., Bihari K., Arora K. : Ectopic herniation of pulmonary cavity. *Lung India* 1991, 9, 156.



## POTT'S PARAPLEGIA - AN ATYPICAL PRESENTATION

P.K. Gangopadhyay<sup>1</sup>, S.P. Garai<sup>2</sup>, D. Guha<sup>3</sup>, A. Senapati<sup>4</sup>, and T. Roy<sup>5</sup>.

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*Summary:* A twenty four year old drug addict male developed acute spastic paraplegia following traumatic injury to spine. X-ray of spine was not contributory to diagnosis but MRI of spine showed paravertebral abscess and bony changes. Histopathological examination confirmed tuberculous involvement. Decompressive surgery along with anti-tuberculosis drugs produced good results.

### Introduction

Tuberculosis of spine and paravertebral cold abscess causing paraplegia is common in developing countries like India. In most of these cases, X-ray of spine usually shows characteristic changes. We are reporting a case of spastic paraplegia with retention of urine, initially diagnosed as traumatic paraplegia with normal findings in X-ray. But MRI showed abnormality in spine & paravertebral region suggesting tuberculous involvement and histopathologic study was corroborative.

### Clinical Record

S.S., a 24 years old Hindu male was admitted with sudden onset of paraplegia with retention of urine following a traumatic event in the recent past. On enquiry, it was discovered that the patient, a known drug addict was admitted in a reformatory centre five months earlier, where he incurred an injury to the spinal region for the first time followed immediately by weakness and inability to move the lower limbs. The left leg was involved first followed by right leg and

within a span of 2 days he had become totally bed-ridden.

The patient gave a history of tuberculous pleural effusion eight years back with adequate treatment.

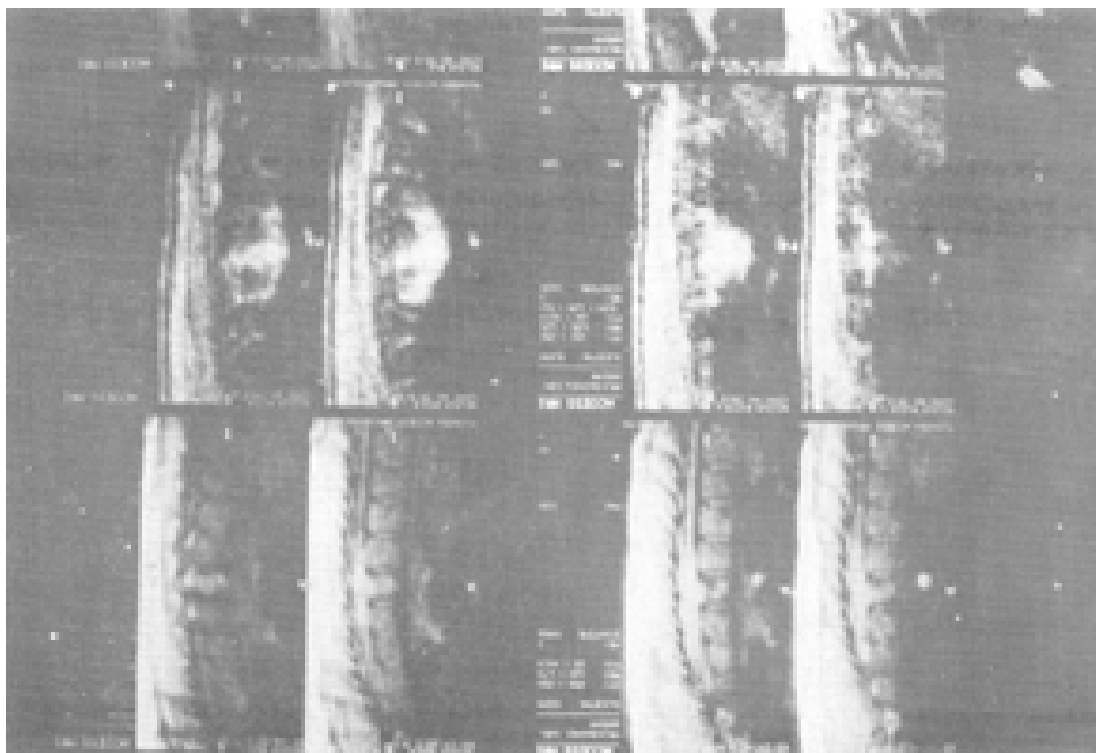
His higher functions were normal: no papilloedema and no evidence of meningeal irritation. The lower limbs were areflexic with muscle power reduced to 1/5, Planter reflex was bilaterally extensor. Urinary sphincter was involved and patient was catheterised. Impaired sensations level at D9 Spinal segment with tenderness over D7-8 spine were noticed. X-ray chest PA view was normal. X-ray dorso-lumbar spine (both A.P. & lateral views) showed no abnormality. Other findings were: Blood: Hb 10.5 gm% TLC - 8100/cu.mm. DLC - P 58, L 38, M 2, E 2. ESR 20 mm 1st hour. Blood Sugar (PP) 106 mgm/Blood Urea - 24 mgm%. Tuberculin test (1:10,000) was 9 mm x 9 mm after 48 hour.

Myelography could not be done due to presence of a pressure sore.

MRI Scan of dorsal spinal region showed fusiform enlargement of spinal cord between D6-D9, isointense in T weighted image and hyperintense in T2 weighted image, producing compression of the thecal sac. There was also destruction of vertebrae (increased marrow signal intensity) D6 to D9 (more marked in D8) & bilateral paravertebral soft tissue swelling (Fig. 1). Patient was operated and histopathology showed the picture of tubercular granulation tissue. Patient was put on anti-TB drugs and he showed clinical recovery after 4 months.

1. Lecturer, Nemo Medicine, 2. Lecturer, Nemo Surgery, 3. Lecturer, Pathology, I.P.G.M.E. & R., Calcutta, 4. Medical Officer, Neuro Medicine, 5. Reader, Neuro Medicine, Bangur Institute of Neurology, Calcutta - 700 025.

Correspondence : Dr. P.K. Gangopadhyay, 6/8, Netaji Nagar, Calcutta - 700 092.



**Fig.1 - MRI Scan of dorsal spine shows fusiform enlargement of spinal cord D<sub>6</sub> -D<sub>6</sub> segment and with bony changes (increased marrow signal intensity) with bilateral paravertebral soft tissue shadow**

### Discussion

Vertebral tuberculosis is the commonest form of skeletal tuberculosis and it constitutes about 50 per cent of all cases of skeletal tuberculosis

Spinal tuberculosis is most common during first three decades of life Paraplegia is the most dreaded and crippling complication of spinal tuberculosis. The overall occurrence of paraplegia has been reported between 10 and 30 per cent and the highest incidence of paraplegia is associated with involvement of lower thoracic region<sup>1</sup>

This patient presented as one of traumatic paraplegia Trauma is a known but non-specific precipitant of paraplegia in 15%<sup>2</sup> of patients

Pott's disease can rarely be detected by conventional radiographs before 6 months Bony

changes and calcification of paravertebral abscess do not occur before the above mentioned period

The changes in conventional radiographs which occur in around 6 months are termed as pre-destructive/early-destructive These comprise straightening of curvature and spasm of paravertebral muscles with diminished disc space But these changes are difficult to demonstrate and also nonspecific, Radio Isotope Bone Scan ( $p^{32}$ ) is said to be very sensitive even in the early stages, but this is also non-specific

Paraplegia due to tuberculosis of spine has been classified into two main groups<sup>3</sup>

Group I - Early onset of paraplegia - This comes during active phase vertebral disease, in first 2 years of the disease The underlying lesions are inflammatory oedema, tuberculous granulation tissue, tuberculous abscess and caseous tissue

Group II - Late onset of paraplegia - This appears many years (more than 2 years) after the disease has persisted in the vertebral column. Neurological complications may be associated with recrudescence of the disease or due to mechanical pressure of the cord. Underlying pathology is tuberculous caseous tissue, tuberculous debris, sequestra of vertebral body, internal gibbus, and deformity.

In early onset group, the prognosis regarding recovery of neural deficit is favourable and in late onset group, even with surgical removal of mechanical causes, the prognosis is less favourable.

The prognosis for recovery of neural function depends on many factors. The prognosis is said to be better if neurodeficits are of short duration, there is early onset of paraplegia, slow in onset, younger patient with good general condition, active vertebral disease and kyphotic deformity is minimal (less than 60°)<sup>4</sup>

The involvement of cord in acute (early) stage due to tuberculous myelitis or vasculitis as seen as a cord swelling can only be visualized properly

with MRI Scan and even better with Gd - DTPA enhanced MRI Scan<sup>5</sup>.

Thus, it may be opined that the newer imaging techniques namely MRI may play a major role in early diagnosis of tuberculous involvement of spine and spinal cord with early chemotherapy and better prognosis.

#### References

1. Tuli, S.M. - Tuberculosis of the Skeletal System, Jaypee Brothers Medical Publishers (P) Ltd., New Delhi.
2. Wayne Massey, E. - Pott's Disease in Neurology *in* Clinical Practice, Ed. by W.G. Bradley, R.B. Dross, O.M. Feinchel, C.D. Marsden, Vol. III, 1989, 1653. Butterworth - Heinemann.
3. Griffiths, D.L., Seddon H.L., Roaf, R. - Pott's Paraplegia, Oxford University Press, London 1956.
4. Goel, M.K. - Treatment of Pott's Paraplegia by operation, J. Bone Joint Surg. 1967. 49B, p. 647.
5. Shoukimas, G.M. - "Thoracic Spine" *in* "MRI" Vol. 2, edited by Stark D.D., Bradley W.G. Jr. 2nd edition Massachusetts - Mosby Year Book, 1992, 1331.

**TUBERCULOSIS OF THE MIDDLE EAR - A CASE REPORT**Manju Mahajan<sup>1</sup>, D.S. Agarwal<sup>2</sup>, N.P. Singh<sup>3</sup> and DJ. Gadre<sup>3</sup>

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**Summary: A case of protein malnutrition with pulmonary tuberculosis and tuberculosis of the middle ear is reported. Direct examination of the ear discharge revealed acid fast bacilli. *Mycobacterium tuberculosis* was isolated in culture which was sensitive to Rifampicin, Streptomycin, Ethambutol, Isoniazid and Pyrazinamide. The patient was treated with anti-tuberculosis drugs.**

**Introduction**

Tuberculosis is one of the major infectious diseases with predominant involvement of lung and lymph nodes but tuberculosis of the middle ear is uncommon. Primary tuberculosis of the ear has rarely been reported, and the disease is usually secondary to infection in lungs, larynx, pharynx and nose<sup>1,2,3</sup>. *M. tuberculosis* from sputum or unpasteurised milk reaches the middle ear through the eustachian tubes. Infection can also reach the middle ear via external auditory canal or by hematogenous spread. The latter results in the direct involvement of the mastoid bone producing necrosis and it progresses to involve the middle ear<sup>4,5</sup>.

We describe here a case of protein malnutrition with pulmonary tuberculosis and tuberculosis of the middle ear in a child.

**Case Report**

A 2 year old male child was admitted to the pediatrics department of UCMS and G.T.B. Hospital, Delhi with the complaints of fever, cough, discharge from left ear of 2 months'

duration and oedema feet of 3 days' duration. On physical examination he was malnourished. Weight was 6.1 kg. He had bilateral, enlarged, matted, nontender, cervical lymph nodes. Examination of the left ear showed external auditory canal to be full of thick pus. Clearing of pus revealed 2 small attic perforations.

There was no history of BCG vaccination. History of contact was positive. Child's elder sister was on ATT. Investigations showed: Hb 7.6 g%, TLC 9000/cumm; DLC N-35, L-65; ESR 64 mm for first hour; Serum sodium 140 m mol/l, potassium 3.3 m mol/l; Total proteins 6.9 g/dl, albumin 3 g/dl, globulin 3.9 g/dl, A/G 0.7:1. Montoux test was negative. X-ray chest showed right sided infiltration. Fine needle aspiration cytology (FNAC) of the enlarged cervical lymph nodes was that of tuberculosis.

Gastric aspirate yielded *M. tuberculosis* on culture. Specimens from ear discharge were negative for pyogenic organisms on Gram's staining, but were positive for AFB. Culture of discharge grew *Mycobacterium tuberculosis* which was sensitive to Rifampicin, Streptomycin, Ethambutol, Isoniazid and Pyrazinamide. Enzyme linked immunosorbent assay was positive for IgM antibodies. Antituberculosis chemotherapy was started with Rifampicin, Isoniazid and Pyrazinamide and the otitis media slowly resolved with healing of perforation.

**Discussion**

Tuberculosis of the middle ear is characterised by painless otorrhoea, multiple tympanic perforations, abundant granulation tissue, bone necrosis and severe hearing loss<sup>1,2</sup>. Involvement

<sup>1</sup>Pool Officer, <sup>2</sup>Professor, <sup>3</sup>Lecturer  
Department of Microbiology, UCMS and GTB Hospital, Delhi.

of the middle ear by tuberculosis has been described in all age groups, though more commonly in children. In the pre-antibiotic era, 2.8% of all the cases of chronic suppurative otitis media were tuberculous in nature and infants below one year of age comprised 50% of these<sup>6</sup>.

Demonstration of AFB in the ear discharge is difficult. The positivity for AFB in ear discharge varies from 5 to 35% and on repeated examinations it improves to 50%<sup>8</sup>. In the present report AFB could be demonstrated in all 3-specimens.

In the past, surgery was the primary treatment to prevent facial nerve paralysis and spread of infection to the central nervous system. At the present time, tuberculosis of the middle ear is best treated with conservative antituberculosis therapy<sup>3,9</sup>.

Tubercular otitis media should always be considered in differential diagnosis of chronic middle ear discharge that does not respond to usual treatment. Immediate antituberculosis treatment may prevent chronic ear damage and central nervous system complications.

## References

1. MacAdam A.M., Rubio T. Tuberculous otomastoiditis in children. *A.J.D.C.*; 1977, 131, 152.
2. Sharan R., Issar D.K. Primary tuberculosis of the middle ear cleft. *Practitioner*; 1979, 222, 93.
3. Windel-Taylor P.C., Bailey C.M. Tuberculous otitis media: A series of 22 patients. *Laryngoscope*; 1980, 90, 1039.
4. Miller F.J.W., Seal R.M.E. Taylor Mary D. Tuberculosis in children. *J and A Churchill Ltd.*, London, 1963.
5. Sinha A. Tuberculosis of Ear, Nose and Throat. In: Text book of Tuberculosis, Rao K.N., Deshmukh M.D., Panira S.P., Sen P.K., Bordia N.L., Dingley H.B. (eds) New Delhi, Vikas Publishing House, 1981, 493.
6. Turner A.L., Eraser J.S. Tuberculosis of the middle ear cleft in children. *T. Laryng. Otol.*; 1915, 30, 209.
7. Wallner IJ. Tuberculous otitis media. *Laryngoscope*; 1965, 63, 1058.
8. Jeanes A.L., Friedman I. Tuberculosis of the middle ear. *Tubercle*; 1960, 41, 109.
9. Skolnik P.R., Nadol J.B., Baker A.S. Tuberculosis of the middle ear. Review of literature with an instructive case report. *Rev. Infect. Dis.*; 1966, 8, 403.

**ROLE OF NGOS IN TUBERCULOSIS CONTROL\*****D.R. Nagpaul**

To bring tuberculosis under control in this country, we have the National Tuberculosis Control Programme (NTP). Planned and organised by the Government, at the Centre as well as in the States, the NTP has a nationwide sweep. It has been in operation since 1962 and already 393 districts in the country have fully operative District Tuberculosis Programmes (DTP).

The size of the tuberculosis problem in the country and its ubiquitous distribution in urban and rural areas, however, make it pretty obvious that Government's NTP, carried out alone, may not be able to succeed in controlling tuberculosis. It is no wonder, then, that the efficiency of case-finding under NTP has not gone beyond 30 per cent and that of treatment has hovered around 40 to 50 percent. Information on results of treatment is not even available. Such levels of achievement can hardly be expected to take us near to our goal. At least, not in the near future. Experts believe that with the said levels of achievement, the fall in the incidence of infection and prevalence of the disease would be only slightly better than the natural decline in tuberculosis. The prospect of tuberculosis remaining as a health problem, for decades, if not a century or so, is therefore inescapable.

Meanwhile, an epidemic of HIV infection (and AIDS) is knocking at our doors. There is still insufficient information on how severe and rapid the Indian HIV epidemic will be, because most of the quoted estimates are based on experiences from countries which are ethnically, sociologically and economically quite different. And, these factors are known to vitally influence the character of HIV epidemic. Nonetheless, the very close unfavourable relationship between the HIV infection and prevalence of tuberculosis is by now well established, which suggests that whatever be the character of the HIV epidemic in India, the tuberculosis situation is bound to get worse, perhaps in the near future. Therefore, we have

nothing but a grim scenario before us, unless urgent steps could somehow be taken to get quicker and better results under the NTP.

Irrespective of whatever we are actually able to do in the future, one aspect is so clear that it looks like the proverbial writing on the wall. The present paternalistic pattern of tuberculosis services is bound to have insufficient efficiency until people's cooperation and participation in NTP is obtained. The people must be made more aware of the importance of their health and the value of actively utilising the provided facilities for their own health's sake, notwithstanding some problems they may have to face under the existing configuration. Several studies have shown that the people are sufficiently aware of tuberculosis and what needs to be done to alleviate their suffering. But they get easily put off by the problems of delays, attitudes and shortages in the "system", which translates into an inefficient NTP. Instead of continuing with the now unnecessary KAP studies or blaming the patients or the system, we must change the strategy: organise the people through action-oriented health education to avail of NTP services through a social approach of self-help.

It may be unrealistic to expect the Government to undertake the newly suggested "social strategy", busy as they are in tackling the many organisational insufficiencies in the NTP system. NGOs are not only the most suitable for such a purpose, being closer to the people from the top levels to the grassroots, but also on account of the kind of work they have been doing for decades. And the Government having recognised their past contributions to NTP have been helping them out with financial grants and supply of anti-tuberculosis drugs. Therefore, instead of resting on their past laurels, NGOs should bestir themselves and assume leadership in the "social strategy", as the Government are doing by revising the "technical strategy" of NTP. In other words, NGOs should

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\* This article was written for the Tuberculosis Issue of the Voluntary Health Association Journal

play their role more aggressively, in line with the demands of the situation, instead of being content with the importance of their role.

There is no doubt that NGOs have certain strengths which make them more suitable for playing the social leadership role. For example, they have the lodestar of idealism to guide them and a band of "do-gooder" volunteers who are willing to give their time and talent for free; greater financial and administrative freedom to act compared with that in Government and a degree of cohesion which makes them strong, though small in size. Their weaknesses are equally far-reaching. They are often content with small achievements, which in a larger perspective may not amount to much, remain self-centred instead of reaching out to other organisations/people and cooperate with them for higher stakes and not employing the available modern technologies, especially management by objectives (MBO). The chief concern of many NGOs is survival.

It must be acknowledged that Government has taken several positive steps to encourage NGOs to play a far more active and positive role in NTP. In September 1991, on the recommendation of a high powered group of experts which met at Surajkund, Government agreed to make NGOs partners in NTP. That step was seen as a highly cost effective step to improve NTP relatively quickly. However, the organisational steps that were needed to make the partnership real could

not be taken, perhaps because it is a completely uncharted field. Again, in January 1994, a workshop was organised, in which representatives of several NGOs participated, to discuss ways and means by which the NGOs could play their rightful role in NTP. The outcome of this effort is not yet visible. While the initiatives taken by the Government are laudable, the relative passivity of NGOs appears strange, if not completely out of character. It is possible that NGOs, long used to the cliches about the importance of their role in NTP, failed to realise that that phase was over and they have now to get involved in the nitty gritty of playing that role.

The need of the hour is serious thinking, wide ranging discussion, active planning and close collaboration with the Government in NTP. For this, NGOs must first put their houses in order, then come forward and reach out to the people as well as the Government. Their success will be judged by the extent of community participation in NTP. For collaboration with Government, the attitudes of officials, which are peculiar to the exercise of power through a bureaucratic set up, must be studied and understood well and their offer of partnership welcomed enthusiastically. For working with people, instead of doubting their awareness and action-taking, the natural social leaders could be made privy to the problems of NTP which are making the tuberculosis services inefficient and planning with them to increase the utilisation of the services through a participatory approach.

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**HUMAN GENOME  
PROJECT****ETOPOSIDE- FRESH  
HOPE  
FOR CANCER?**

A Human Genome Project has been set up to collect and catalogue all available information about human genes. Also, to identify the factors that enable normal cells to turn into cancer cells. It has increasingly become crucial to determine where the cancer genes are located through a close study of the normal and cancer causing genes.

Genome is the total genetic information available in the millions of cells in the human body. All the dispersed information is ultimately derived from, the single fertilized zygote. The information is found coded in the language of DNA molecule and its four chemical constituents A, T, G and C. By deciphering the information and studying the distribution of the respective genes, a genome map of the human body can be prepared.

Recent researches have already identified the genetic "abnormalities" which are believed to cause cancer of breast as well as of colon. Thus, in 80% of bowel cancer cases, abnormal changes have been found in APC gene, but what triggers all abnormal growth in such cells remains obscure.

It is hoped that the Human Genome Project Will offer some therapeutic options, because many cancers are mostly due to genetic causation while some are environmental in their causation, such as lung cancer due to smoking. A cure for colon, skin, brain and kidney cancers may, therefore, lie in gene therapy, by triggering cell changes that can help fight a cancerous growth. AIDS offers another attractive option for gene therapy. In animal models, the rapidly proliferating tumour cells are removed and "treatment genes" are introduced into those. These cells are then put back into the animal. The immune system of the animal gets activated in a way that regards tumour cells as "foreign body" leading to their rejection. Another way of introducing the "treatment genes" into the body is through "stem cells" obtained from bone marrow.

Etoposide, a new anti-cancer drug, has been undergoing extensive clinical trials, principally in the United States and Japan. Quite a few of the studies have been conducted on patients of lung cancer, mostly refractory cases. Of particular interest is the finding that this drug appears to produce at least a standstill, not only in small cell carcinoma, but in other varieties as well.

Given alone, the usual dose has been 50 mgm/M<sup>2</sup>/day for 21-28 days. The only limiting factor leading to stoppage of the drug seen so far is myelo-suppression, mainly neutrophils and, to a larger extent, platelets. Chronic usage ranging over multiple courses, has not resulted in any serious adverse reactions and myelosuppression reverses on stopping the drug.

The drug can be given intravenously or orally, and seems to have good tissue penetration when given by the oral route. It has also been reported that minimal serum levels of 1 mg/ml are present for a longer time after oral administration compared to IV dosage.

The degree of response to oral therapy is 23% in small cell carcinoma and almost similar in non-small cell carcinomata.

Alopecia, like in other cytotoxic agents, is an annoying, but reversible side effect.

The drug has been continued with other anticancer drugs with moderately good results and no increase in toxic reactions.

Further studies will doubtless add to our understanding of this drug. However, there is a ray of hope that chemotherapy may be able to induce remission of a few months in resistant lung cancer.

## NEWS & NOTES

### 45TH TB SEAL CAMPAIGN

The 45th TB Seal Campaign organised by the Tuberculosis Association of India and its affiliates in the States was inaugurated on 2nd of October, 1994, by Hon'ble Dr. S.D. Sharma, President of India and Patron, Tuberculosis Association of India, at Rashtrapati Bhawan. The 45th TB Seal depicting the 'Endangered Species of India' was presented to Rashtrapatiji for release by Dr. P.K. Sen, President, Tuberculosis Association of India. Dr. A.K. Mukherjee, Director General of Health Services and Chairman, Tuberculosis Association of India, presented the Special Souvenir brought out on the occasion of the 45th TB Seal Campaign - 1994, to the President of India, in the presence of representatives of the Tuberculosis Association of India, Delhi TB Association and some special invitees. The function was widely covered by the media.

### 49TH NATIONAL CONFERENCE ON TUBERCULOSIS AND CHEST DISEASES

The 49th National Conference on Tuberculosis and Chest Diseases organised by the Tuberculosis Association of India, the Pondicherry TB Association, in association with Department of Tuberculosis and Chest Diseases, JIPMER, Pondicherry was held in JIPMER, Pondicherry from 6th to 9th October, 1994. The Conference was attended by about 500 delegates from all parts of the country. The Conference was inaugurated by Shri Paban Singh Ghatowar, Hon'ble Union Deputy Minister for Health & Family Welfare. Dr. R.C. Jain, Director, L.R.S. Institute for TB and Allied Diseases, New Delhi, was the President of the Conference.

The Hon'ble Union Deputy Minister for Health presented the various awards and distinctions of the Tuberculosis Association of India to the recipients. The Tuberculosis Association of India conferred honour and distinction on Dr. P.K. Sen, President of the Association and Editor Emeritus, Indian Journal of Tuberculosis and Dr. M. Zakir

Husain, Director, Programme Management, WHO, for their outstanding contributions to the TB Control Programme.

An important feature of this National Conference was the Continuing Medical Education Programme held on 6.10.1994 which was attended by about 200 delegates. "Meet the Expert" sessions on important topics like bronchial asthma, drug resistant tuberculosis and respiratory oncology were also held on 8th and 9th October, 1994.

Important meetings of the Secretaries of State TB Associations and Standing Technical Committee were held on 7th and 8th October, 1994, respectively which were also attended by some senior TB workers as special invitees.

### 13TH U.P. STATE CONFERENCE

The XIIIth U.P. State Conference on TB & Chest Diseases sponsored by U.P. TB Association was held at Ghaziabad from 7th to 9th of January, 1995.

### CHANCHAL SINGH MEMORIAL AWARD - 1995

The Tuberculosis Association of India awards a cash prize of Rs. 1,000/- to a medical graduate (non-medical scientists working as bacteriologists, biochemists, etc. in the field of tuberculosis are also eligible) below 45 years of age and working in tuberculosis for an original article not exceeding 30 double spaced foolscap size pages (approximately 6,000 words excluding charts and diagrams) on a subject relating to tuberculosis. Articles or papers already published or based on work of more than one author will not be considered for this award. Papers may be sent, in quadruplicate, to reach the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001, before the 31st of July, 1995.

### ESSAY COMPETITION - 1995

The Tuberculosis Association of India awards

every year a cash prize of Rs. 500/- to a final year medical student in India for an original essay on tuberculosis. The subject selected for the year 1995 competition is "Smoking and Tuberculosis". The essay should be written in English, typed double spaced, on foolscap size paper and should not exceed 15 pages (approximately 3,000 words including tables, diagrams, etc.) Four copies of the typescript should be forwarded through the Dean or Principal of College/University to reach the Secretary General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001, before the 31st of July, 1995, with a certificate that the author is a final year medical student.

### **HEALTH VISITORS COURSE**

The 1995-96 TB Health Visitor Course will commence in July, 1995. The course will be of nine months' duration and will be held at the New Delhi TB Centre. The minimum qualification for admission to this course is 10+2 with Science and/or Hygiene. Relaxation of experience in TB work may however be considered by the Selection Committee. However, Science subject should normally be there upto 10th class. Application forms for admission to the course can be had from the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001. The last date for receipt of applications is 2nd May, 1995.

### **INTERNATIONAL DECLARATION OF HEALTH RIGHTS**

In our issue of January 1994, we had carried news about the formulation of an International Declaration of Health Rights. The Declaration was prepared by the Johns Hopkins School of Hygiene and Public Health, Baltimore (U.S.A.), considered as the number one school of public health in the world.

The Declaration continues to travel around the world. Of late, public health leaders in Australia, England, South Korea, Japan and several cities in USA have signed the Declaration. It is said to serve as "public health professionals' equivalent of the Hippocratic oath".

### **ANNUAL MEETINGS**

The Annual General Meeting of the Tuberculosis Association of India will be held at 11 A.M. on Thursday, the 30th March, 1995 in the Conference Hall of the Association followed by the Central Committee Meeting. The Conference of Secretaries of State TB Associations will be held at 2 P.M. on the same day. The Standing Technical Committee meeting will be held at 10 A.M. on Wednesday, the 29th March, 1995.

### **CHAIRMAN, TECHNICAL COMMITTEE**

Dr. C. Srinivasa Rao, Hony. Genl. Secretary, TB Association of Andhra Pradesh, Hyderabad, has been nominated as Chairman of the Standing Technical Committee of the Tuberculosis Association of India for the year 1995-96. Dr. Srinivasa Rao will also be the President of the Golden Jubilee National Conference on TB & Chest Diseases to be held at Thiruvananthapuram in October-December 1995.

### **NEW TB SEALS**

Six colourful designs on 'MONUMENTS OF INDIA' - Gwalior Fort, Mysore Palace, Parliament House, Taj Mahal, Golden Temple and Golconda Fort - have been selected for the TB Seals for the 46th TB Seal Campaign for presentation to the respected President of India on 2nd October 1995 at Rashtrapati Bhawan.

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**IMPORTANT ANNOUNCEMENT****GOLDEN JUBILEE NATIONAL CONFERENCE ON TUBERCULOSIS AND CHEST DISEASES - THIRUVANANTHAPURAM (KERALA) -1995****CALL FOR ABSTRACTS**

The 50th National Conference on Tuberculosis and Chest Diseases is scheduled to be held at Thiruvananthapuram (Kerala) sometime in October-December, 1995. The exact venue, dates and other relevant details of the Conference will be announced shortly. The subjects selected for this Conference are: (1) Management of Bronchial Asthma/Fiberoptic Bronchoscopy, (2) National TB Control Programme including its assessment (3) Follow-up studies on patients completing short course chemotherapy (4) Management of Treatment failure cases under field conditions (5) Newer diagnostic methods in tuberculosis/Controversies in Respiratory Diseases (6) Smoking and Tuberculosis (7) Role of Indian Systems of Medicine (8) Multi-drug resistance and its management (9) Improvement of host factors in Tuberculosis (10) Drug interaction with ATT and (11) Serum concentration ATT and MDR.

There will be a Continuing Medical Education Programme also during the Conference days. Free communications and poster presentations would, as usual, be eligible for presentation.

Those who wish to present papers on the above subjects may kindly send three copies of an abstract of their papers latest by 30th April, 1995 to the Secretary General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi - 110 001 for consideration by our Programme Committee.

It would be appreciated if the abstracts are sent by registered post/UPC so as to ensure their safe receipt. The guidelines for the authors are: (A) For preparing abstracts: 1. The length of an abstract should not normally exceed 250 words, including the heading, 2. The abstract should be as informative as possible, comprising the (a) objectives of the study, (b) methodology of investigation and (c) main findings. In respect of some papers (b) and (c) will comprise the idea/hypothesis discussed and the conclusion, 3. If analysis is incomplete at the time, a revised abstract should be sent, at least six weeks prior to the Conference for printing in the Programme and Summaries for distribution among delegates. 4. An abstract which is considered inadequate may not be selected by the Programme Committee for presentation of the paper at the Conference. (B) For preparing project slides/overhead transparencies: 1. Material on the slide should be relevant, minimum, in bold letters/figures and either printed or typed out. 2. Material should normally cover 3/5 of the available space on the slide, with margins on all slides, 3. Blue on white background is better than black and white slides. For multi-colour slides, the preferable colours are red, black and green, 4. Overhead transparencies should preferably not be handwritten. Typed or computer composed print-outs could easily be photocopied, to the desired size, on to a transparent plastic sheet for use on an overhead projector.

# THE INDIAN JOURNAL OF TUBERCULOSIS

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- \* Tuberculosis Mortality and Cure Among Treatment Defaulters: Epidemiological Implications by V. Sivaraman *et al.*
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**The Indian Journal of Tuberculosis**

**ABSTRACTS**

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**OCULAR INVOLVEMENT IN SARCOIDOSIS**

R.S, Mathur, R.H. Muljiani and J.R. Shah;  
*J.A.P.I., 1994, 42, 646.*

Forty consecutive patients of sarcoidosis with respiratory manifestations, were submitted to detailed ophthalmic examination, including slit lamp examination and fundoscopy. Seven of them showed ocular manifestations, such as acute and chronic iridocyclitis, hard exudates, and even optic atrophy in one case.

The ocular lesions were generally more resistant to therapy than the pulmonary and hilar lesions. The authors advocate routine ophthalmic investigation in all cases of respiratory sarcoidosis, so that ocular involvement may be detected early enough for treatment to be effective.

**DIAGNOSIS OF TUBERCULOUS MENINGITIS BY ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA) USING AN AFFINITY CHROMATOGRAPHY PURIFIED MYCOBACTERIAL ANTIGEN**

V.V. Radhakrishnan, Annamma Matliai and P.K. Mohan, *J.A.P.L., 1994, 42, 684.*

An antigenic isolate from culture filtrates of *Mycobacterium tuberculosis* (H<sub>37</sub>Ra) was obtained. ELISA with this antigen detected IgG antibodies in CSF of all culture positive cases and in 70% of culture negatives. No false positives were detected among controls with pyogenic meningitis. Taking an endpoint titre of 1/80, the sensitivity was 100% in culture positives and 70% in culture negatives. However, lower titres showed overlap between negative cases and controls.

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**THE TUBERCULOSIS ASSOCIATION OF INDIA**

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**45TH TB SEAL CAMPAIGN**

2ND OCTOBER 1994 TO  
23RDFEBRUARY1995

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