Editorial

**RNTP—BEYOND, ABOVE AND BELOW**

The revised NTP differs from the existing NTP in one basic aspect i.e. drugs are to be administered, at least in the initial intensive phase, under direct supervision (DOTS). The only other differences are minor such as the exact dosage and its frequency and the choice of drugs. The base for the programme is our firm belief that we will be able to drastically reduce the transmission of infection and will assist natural forces in finally controlling the disease. This presupposes that the programme, as outlined is faithfully carried out, both by the deliverers and the recipients. This has led to our using the term ‘Compliance’ rather liberally so, much so, that we have finally landed ourselves into putting the burden of compliance entirely on the recipient i.e. the patient. Facts, however, have demonstrated a different reality as has recently been stated in one of the authoritative journals by a leader in the fight against Tuberculosis

“One of the serious areas of lack of compliance is that of the WHO”

(International J. Tuberculosis and Lung Dis.; 1997, 1, 3)

The various governments and organisations responsible for delivering the tuberculosis programme all over the world are equally at fault, of course, with some honourable exceptions.

In our country, we have the phenomenon of irregular drug supply, vacant posts of specialists and paramedics, even at the peripheral level i.e. PHIs. The infrastructure is either poorly utilised or even misutilised. A PHI has a vast sanctioned strength of staff of all types whose main work appears to be to sit in the PHI and wait for the people to attend there, when the need is for them to go out and treat the patient at his doorstep. This becomes doubly important for the RNTP, if we have to really deliver the supervised treatment. We have, in a previous editorial, dealt in detail with the need for utilisation of existing health infrastructure in a proper manner. Today, we go on to examine some other factors which may tend to render RNTP as ineffective as the NTP has been.

Firstly, the targets laid down are low enough, both for coverage and cure, so that the slightest inefficiency at any level of implementation can lead to a totally unacceptable and undesirable situation as has been happening so far, where targets have hardly ever been achieved in any place. Another lacuna is that a fairly high percentage of infective individuals is expected to be left uncovered. It we take into account the fact that as many as 60% of those suffering from pulmonary tuberculosis will not be found positive by sputum microscopy, we can realise that an overwhelming majority of the active cases will be left uncovered by the programme. It has repeatedly been emphasized by various workers that active smear negative cases will, if left untreated, become smear positive and grossly infective.
Another aspect to be considered is that even with short course chemotherapy, residual lesions are left to the extent of almost 50%. Majority of these patients remain symptomatic or develop respiratory symptoms off and on, thus placing a burden on the existing tuberculosis services and creating the probability of unnecessary chemotherapy. This probability becomes emphatically greater when we consider that the phenomenon of resistant mycobacteria is with us and is well entrenched. ‘Persistence of symptoms in those who have undergone the requisite course of chemotherapy naturally leads to a sense of dissatisfaction in the population and their disillusionment with the programme.

We have to seriously consider what steps can be taken to avoid this type of pitfall.

Those of us who have been in the field sufficiently long remember that, in the pre-chemotherapy era, rest, good food and collapse therapy used to be the mainstay and cures did result, though only in a small percentage. With the advent of chemotherapy, these lost their relevance, at least for the treating physician. Even extirpative surgery was almost banished from the armamentarium.

Of late, some of the older workers have been experimenting with the revival of pneumo-pentoneum and have reported fair results in salvaging chemotherapy failures, including those with resistant bacilli. Although these studies have not been conducted with proper controls, etc., sputum conversion also has been fairly impressive, even among those with MDR Tuberculosis. Others have experimented with the indigenous drugs which appear to be directed towards modifying human immune system and good results have been claimed.

Would it not be appropriate, apart from removing the lacunae in the delivery systems, etc., to bring in the active smear negative cases within the purview of the RNTP? The argument that this may lead to gross over-treatment does not hold water as numerous studies have revealed that false positive diagnosis is very rare when some routine procedures are followed before deciding to treat such individuals. It may also be practicable to consider adjuvant treatments like pneumo-pentoneum and surgery as part of the programme. Immuno-modulators and emphasis on high protein and adequate carbohydrate diet are indicated. A proper scientific evaluation of indigenous drugs which have been claimed to be effective in the treatment of tuberculosis, whether by themselves or in conjunction with modern chemotherapy, etc.,is urgently needed too’.

S.C. Kapoor
At the outset I would like to express my deep sense of gratitude to the Executive Committee of Tuberculosis Association of India for selecting me for the award of the P.K. Sen-TAI Oration to be delivered on the occasion of 51st National Conference on Tuberculosis and Chest Diseases. Friends, it is indeed a singular honour and a matter of pride for me to be selected to deliver this oration.

The TB Association has been in the forefront of the fight against tuberculosis since 1939 and continues to be the torch bearer for anti-tuberculosis work in the country. It has had the blessing of many of the doyens of tuberculosis specialists, like Drs. Ukil, Senior and Junior Frimoldt Moller, P.V. Benjamin, B.K. Sikand, R. Viswanathan, P.K. Sen, M.D. Deshmukh and S.P. Pamra. With their guidance, the Association was able to establish model sanatorium in Kasauli and TB Clinic in New Delhi, for emulation by others.

Dr. P.K. Sen has devoted his life to tuberculosis work. He is one of the architects of the National Tuberculosis Programme with vast experience as a clinician, teacher, researcher, planner, administrator, and has not only spearheaded the forward march of anti-tuberculosis activities of the country but has made indelible impression on the country’s tuberculosis control movement. He took active part in organization of the country’s Tuberculosis Prevalence Survey 1955-1958. His competence in medical science and technology is par excellence and thus he continues to be popular with his students and patients. In him there is good blend of public service and individuals’ welfare, which is worth emulating. By instituting the P.K. Sen TAI Oration, Dr. Sen has been made immortal.

I presume that my selection for the award is a measure of high esteem that the three top level institutions, the NTI, the New Delhi TB Centre and the TRC, with which I had long association are held in, nationally and internationally.

In paying my respect to Dr. P.K. Sen and appreciation of the efforts that TAI has been making for control of tuberculosis, I have ventured to speak on the topic of an “Overview of the National Tuberculosis Programme”, in particular when we are going to face MDR-T’B and H1V infection. Secondly, I am deeply interested in NTP because I, with my WHO counterpart at NTI, Dr M. Piot, was actively involved in planning, implementation, management and supervision of country’s pilot District Tuberculosis Programme (DTP) in 1961-62 in Anantapur district of Andhra Pradesh. The objective of the pilot project was to study the practicability, suitability and applicability of the programme, to meet the country’s requirement of TB control.

Development of the National Tuberculosis Programme

In the pre-independence era the approach to the management of tuberculosis consisted of advocating rest and nutritious diet, calcium, cod liver oil, gold and collapse therapy These were non-specific measures aiming at raising body’s resistance. There were no organised plans for prevention of tuberculosis infection and control of the disease.

In 1943, the Central Government appointed a Health Survey and Development Committee under the chairmanship of Sir Joseph Bhore to review the country’s health problems and recommend measures for their management. The recommendation for tuberculosis control consisted of establishing 100,000 tuberculosis beds (1 bed for every 5 deaths), one main tuberculosis clinic at the district headquarters town, and sub clinics at taluk towns, one mobile clinic per district for the whole country all costing about Rs. 200 crores at 1946-47 prices. The recommendation, being impractical, was shelved. However, BCG vaccination was accepted by India’s Planning Commission for prevention of tuberculosis and was started in 1951 with WHO assistance. Tuberculin testing on a large scale in ui-
ban, semi urban and rural areas, as a prerequisite to BCG vaccination, revealed that tuberculosis infection rates in rural areas were no less than those in the urban areas. To obtain authentic information about the magnitude of the tuberculosis problem in the country, in rural, semi rural and urban areas, a tuberculosis sample survey was carried out under the aegis of ICMR (1955-58).

The survey revealed that 2-8 per thousand of population had active bacillary pulmonary tuberculosis and 13-25 per thousand had sputum negative disease. The prevalence rates, in rural, semi-urban and urban areas were similar and of the total tuberculosis problem, 80% was estimated to be in rural area. These findings have been confirmed subsequently, by smaller surveys conducted in different parts of the country.

The discovery of INH in 1951 and subsequent findings of efficacy of domiciliary chemotherapy in 1958 by the Tuberculosis Research Centre (TRC), Madras, led the planners to conceive the idea of making a frontal attack on tubercle bacilli, aiming at the control of the disease. And to evolve a suitable Tuberculosis Control Programme, the National Tuberculosis Institute (NTI) was established at Bangalore in 1959. The NTI, on the basis of findings of epidemiological studies, sociological and operational studies, and with full consideration of operational, economic and technical factors, formulated the DTP, which is the unit of the National Tuberculosis Programme (NTP). The DTP was accepted by the Government of India in 1962 as the only feasible Tuberculosis Control Programme for the country.

### National Tuberculosis Programme (NTP)

The NTP is designed to detect a large number of tuberculosis cases and provide them with domiciliary chemotherapy near their residence through the existing general health institutes throughout the country.

The priority for case finding and treatment is given to sputum positive cases of pulmonary tuberculosis. The sputum negative patients of pulmonary tuberculosis have low priority for detection and treatment.

### Review of NTP-1994

During the course of over 32 years that NTP has been in operation, out of 496 districts, 391 (81%) districts have been covered by the NTP (Table I). A DTP, with an average population of 1.9 million per district has a potential of finding about 2530 sputum positive pulmonary tuberculosis cases in a year, whereas the actual case finding (CF) achievement in 1994 was 770 cases (about 30.4%) (Table I). The overall sputum confirmation among the new pulmonary tuberculosis was 21.6%; at the DTC, it was 20.5% and at PHIs 22.65. The above figures suggest that both at PHIs and DTCs the emphasis had been more on X-ray diagnosis.

Similar sputum confirmation rates of pulmonary tuberculosis patients both at DTC and PHI is against the expectation of high confirmation at

<table>
<thead>
<tr>
<th>Activity</th>
<th>Expectation</th>
<th>Achievement</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Quarterly report</td>
<td>1564*</td>
<td>Received 1213</td>
<td>77.6%</td>
</tr>
<tr>
<td>B Supervisory visits</td>
<td>68816*</td>
<td>Made 28483*</td>
<td>41.4%</td>
</tr>
</tbody>
</table>

**Per DTP**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Expectation</th>
<th>Achievement</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>C Sputum examination of new patients</td>
<td>21000*</td>
<td>Examined 11094</td>
<td>55%</td>
</tr>
<tr>
<td>D Case Detection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i Sputum Pos.</td>
<td>2530*</td>
<td>Detected 770</td>
<td>30.4%</td>
</tr>
<tr>
<td>ii X-ray Pos., Sputum Neg</td>
<td>Detected 2797</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iii Non-pul TB</td>
<td>Detected 221</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E Regimen-wise treatment completion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Standard</td>
<td>SCC-A</td>
<td>32%</td>
<td>53.6%</td>
</tr>
<tr>
<td>35%</td>
<td>SCC-B</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*NTI Annual report 1995*
TUBERCULOSIS- AN OVERVIEW

Table 2. NTP-TB case finding by sputum status at DTCs and PHIs- (1994)

<table>
<thead>
<tr>
<th>Place</th>
<th>Sputum+</th>
<th>X-ray+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTCs</td>
<td>110349</td>
<td>426887</td>
<td>537236</td>
</tr>
<tr>
<td>PHIs</td>
<td>116194</td>
<td>396017</td>
<td>512211</td>
</tr>
<tr>
<td>'total'</td>
<td>226543</td>
<td>X2204</td>
<td>1049447</td>
</tr>
</tbody>
</table>

Source NTI Annual Report, 1994

DTC, for at DTCs there is a trained District Tuberculosis Officer (DTO) well versed in chest X-Ray interpretation, hence the confirmation by sputum at DTC should have been higher.

Of the total cases in the country, 80% have been estimated to be residing in rural area. However, the case detection by PHIs in rural area was 49% of the total cases detected in the year 1994 (Table 2). The rate was similar to that reported by Nagpaul for 1988. The case finding performance over a period of 7 years (1987 to 94) had not shown any change. The number of sputum positive patients found by NTP in 1987 was 227,000 and that found in 1994 was also almost same (226,543) (Table 2). The conjecture is that prevalence and incidence rates remaining same as in 1954-58, and with the increase in the country’s population, the absolute number of TB cases must have increased. This however, is not reflected in case detection—even though the number of DTPs has increased from 371 to 391 from 1988 to 1994.

On the treatment aspect, the case holding (CH) was also poor. Of the patients put on standard drug regimen 35% completed 12 collections, whereas of those on intermittent short course chemotherapy (SCC) 32% and on daily SCC 54% completed satisfactory therapy (Table 1). The above data on FC and CH of NTP show that the achievements were far below the expectations, even 32 years after the acceptance of the DTP by the Central Health Ministry.

A rough estimate of the achievement of NTP for 1994 presented in Table 3 shows that out of estimated 920 million population of the country in the age bracket of 10 years and above (that is 70% of the total population) the expected total incidence of new TB sputum + cases likely to occur at the rate of 130/100,000 per year (NTI 1974) could be estimated to be 8,37,200, whereas estimated number of cases detected in 1994 was 393,980 (226,540 by the NTP + 167,440 detected by GPs and others) - i.e. 47% of the total estimated incidence of new cases. The treatment completion could be estimated to be 50% of cases detected, that is 23.5%, and the sputum conversion is presumed to be 21%. With such a low level of overall efficiency, no programme can make any dent on the problem of TB.

Table 3. NTP Achievements- 1994 (estimated)

<table>
<thead>
<tr>
<th>NOS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Total population 1994 (estimated)</td>
</tr>
<tr>
<td>2</td>
<td>Population aged 10 years and above (70% of 1)</td>
</tr>
<tr>
<td>3</td>
<td>Total no of ‘incidence cases’ of 1994 (130/100,000) (NTI)</td>
</tr>
<tr>
<td>4</td>
<td>Case detection 1994-total</td>
</tr>
<tr>
<td></td>
<td>(a) By NTP-(NTI report)</td>
</tr>
<tr>
<td></td>
<td>(b) By GPs (assumption)</td>
</tr>
<tr>
<td></td>
<td>(c) Not detected (assumption)</td>
</tr>
<tr>
<td>5</td>
<td>Treatment completion of new cases 50% of 47%</td>
</tr>
<tr>
<td>6</td>
<td>Sputum conversion (assumption) 80% of No 5</td>
</tr>
<tr>
<td>7</td>
<td>Achievement - sputum</td>
</tr>
<tr>
<td>8</td>
<td>Conversion of ‘incidence cases’ among detected cases</td>
</tr>
</tbody>
</table>

Note • Inclusion of ‘Prevalence Cases’ in above calculation will bring down the efficiency
The reasons of shortfall of NTP performance are:

- Perfunctory implementation of DTPs;
- Poor acceptability of principles of integration of NTP into general health services;
- Scepticism of medical fraternity;
- Inadequate supervision, guidance and assistance;
- Shortages in drugs, etc.;
- Lack of information to patients about disease and therapy;
- Indifferent attitude of the personnel;
- Inconvenient timings of health delivery services;
- Poor utilization of trained DTP key personnel.

Remedial measures for better performance are:

- Provision of enough funds and items of supply and drugs;
- Proper training of grass-root level workers;
- Ensuring accountability on part of senior health administrators;
- Enlisting cooperation of GP’s and NGO’s;
- Enhancing political support;
- Extensive health education.

Salient findings and recommendation of Review Committee:

A thorough review of the NTP performance was undertaken jointly by the Government of India, S1DA and WHO in 1992. The Review Committee observed that the optimum level of CF and CH was yet to be achieved even 30 years after the formulation of NTP. The Committee more or less corroborated the known findings and over-reliance on X-Ray diagnosis and low cure rates already detailed earlier.

To improve the performance, and the logistics and achievement of the NTP, the review committee recommended:

- Augmentation of CF by examination of three samples of sputa, aiming at detection of 70% of community’s sputum positive case load;
- Augmentation of case holding at 80% treatment regularity and completion of therapy, and 85% sputum conversion of newly detected cases;
- Creation of sub district TB centres for better supervision, monitoring and guidance;
- Provision of binocular microscopes; uninterrupted and adequate drug supply;
- Financial, administrative and political support to NTP;
- Involvement of NGOs, and General Practitioners (GP) for CF and CH;
- Offering direct observation short course therapy (DOTS);
- Continuous operations research for evaluation and modification of programme.

Tuberculosis control & Non Governmental Organizations (NGOs)

An officially sponsored programme however practical, scientifically sound and community wide applicable it may be, cannot be effective without active participation of community and the NGO’s. Tuberculosis being a medical as well as a social problem, the official agencies, NGOs and voluntary bodies should work together as equal partners in tackling the problem, for full and effective utilization of any service meant for community. The participation of community and NGOs at all stages, from resource development to planning, implementation and supervision of strategies, is essential. However, such participation of NGOs can come only by their clear understanding of the problem, the modalities for its solution, ultimate likely benefits to the community and the extent to which their needs will be met with.

The medical and public health service can offer service and facilities for cure and control of the disease. The NGOs can work towards alleviation of apprehension about the disease by extensive community health education, motivating community to avail of the diagnostic and therapeutic facilities offered by official health services and augment FC and CH, ensure treatment regularity and full compliance, for ultimate success of NTP. The NGOs should actively participate within the framework of the official TB control programme and supplement the governmental effort without duplicating it.

In the urban areas, NGOs like general practitioners, TB Associations, Lions and Rotary Clubs, IMA and other Trust-run Voluntary Organizations can be approached to participate in the programme, whereas in the rural areas, Aganwadi workers (AWs), village level workers (VLWs), Health Guides (GHs), Community leaders.
Panchayat members and other social welfare organizations could be associated with NTP.

Tuberculosis situation—the future perspective: the effect of MDR-TB and HIV

The NTP even after 34 years of its existence continues to be a major health problem. The prevalence and incidence rate remaining the same, as were reported by several surveys between 1950 and 1980, the problem has in recent times acquired a new dimension i.e. the emergence of “Multi Drug Resistant Tuberculosis” (MDR-TB) and the inroads made by entry of “HIV” Infection”. If proper timely measures to tackle these are not taken, the epidemic of tuberculosis may blow up beyond control, particularly in developing countries having meagre resources. Specially, under the given situation of low programme efficiency, the twin threat is likely to further affect the course of tuberculosis and jeopardize control efforts in a major way in the coming decades.

Multi-Drug Resistant-Tuberculosis (MDR-TB)

The phenomenon of the drug-resistant strain was recognized in 1947 for the first time 3 years after the use of Streptomycin. Iseman called it an inadvertent genetic engineering which is conferred by altered structure of drug target points in the bacillary body (DNA) or an efficient drug degradation or drug permeability barrier.

Type of Drug Resistance (DR)

The DR is categorized as (1) primary (2) natural (3) initial (4) acquired or secondary including MDR-TB.

The organisms resistant to drugs, without prior exposure to them are classified as primary or natural drug resistance strains. The occurrence of natural/primary drug resistance is either due to acquired infection with resistant bacilli or is spontaneous chromosomally borne mutation in bacillary cells which occurs at a predictable rate and is usually to a single drug. Thus, therapy of naturally resistant mutants, even with two drugs is generally successful as the primary resistant mutation to two drugs is very rare.

Patients reporting for the first time with drug resistant strains are categorized as having initial drug resistance. Many of them deny or conceal history of previous treatment or are unaware of the drugs prescribed earlier and are categorised as excretors of initial drug resistant strains.

Extent of MDR TB

The data about prevalence and incidence on primary drug resistance in the general population are not available. The proportion of sputum positive prevalence cases in community survey with INH resistant strains in BCG trial area of Madras was of the order of 12.7% in 1968 which increased to 21.4% over a period of 15 years”. The INH resistant rate, among the sputum culture positive patients of NTP longitudinal survey” population of rural area in 1961 was 11.2% and in 1968 it was 21.6%. Among patients, reportings or the first time at TRC and denying history of previous treatment, an increasing trend in drug resistance to INH from 3% in 1956 to 13% in 1986 and to Rifampicin from nil to 1% was noted (Table 4). The above could be the estimates of drug resistance among the cases in the community and self reporting patients respectively. These findings suggest a gradual increase in rate of pulmonary tuberculosis with drug resistant strains.

Acquired or secondary drug resistance results from exposure to drugs consequent to selection of mutants. It develops because of inadequate regimens and their doses, irregular and insufficient therapy. The problem of acquired resistance

<table>
<thead>
<tr>
<th>Area</th>
<th>Year of report</th>
<th>% of patients resistant</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
</tr>
<tr>
<td>Madras</td>
<td>1956-53</td>
<td>3</td>
</tr>
<tr>
<td>Madras</td>
<td>1985-86</td>
<td>13</td>
</tr>
<tr>
<td>Delhi</td>
<td>1991</td>
<td>50.7</td>
</tr>
<tr>
<td>Haryana</td>
<td>1980</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>81.4</td>
</tr>
<tr>
<td>Tamilnadu</td>
<td>1992</td>
<td>28.5</td>
</tr>
<tr>
<td>Gujarat</td>
<td>1980</td>
<td>34.5</td>
</tr>
<tr>
<td>Hospital</td>
<td>1986</td>
<td>55.6</td>
</tr>
</tbody>
</table>

*New cases - TRC Madras \(^1\)Treated patients
Table 5. Drug resistant strains: patients category

<table>
<thead>
<tr>
<th>Category of patients</th>
<th>Total + cultures</th>
<th>Drug sensitive</th>
<th>Drug resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Old treated</td>
<td>1128</td>
<td>210</td>
<td>187</td>
</tr>
<tr>
<td>New not treated</td>
<td>380</td>
<td>280</td>
<td>73 7</td>
</tr>
<tr>
<td>Treatment history not known</td>
<td>532</td>
<td>266</td>
<td>50</td>
</tr>
</tbody>
</table>

REF.: TB Conference 1995 -- NT1

The multi drug resistant strains are defined as strains (MDR-TB) resistant to more than one drug, in particular to INH and Rifampicin with or without resistance to other drugs. The rates of MDR-TB in the above three categories of old treated, not treated and history of treatment unknown were of the order of 61.6%, 8.7% and 31.7% respectively (Table 6). The overall rate of MDR-TB was 44%. The case fatality in patients with MDR is reported to be extremely high (25%). Such escalations of DR and MDR-TB are bound to have an adverse effect on NTP performance if proper steps to contain the emergence of DR are not taken.

Diagnosis of MDR-TB

Meticulous history elicitation and high clinical suspicion are indispensable when faced with the diagnosis of MDR-TB. The emergence of MDR-TB is suspected on the basis of poor clinical response to treatment, even after 3-5 months of regular treatment with an effective drug regimen. The fall and rise phenomenon on sputum microscopy and no appreciable radiological improvement and cavity closure on follow up chest skigrams are common clinical features of MDR-TB.

Laboratory investigation

The laboratory investigations for drug susceptibility tests are not freely available. However, the conventional method is inoculation of specimen on solid LJ Media for primary growth of M. tuberculosis, followed by identification of A/

Table 6. MDR strains by number of drug and patients category

<table>
<thead>
<tr>
<th>Patients' category</th>
<th>Drug sensitivity</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitive</td>
<td>Resistant</td>
</tr>
<tr>
<td>Old treated</td>
<td>210 (18.7%)</td>
<td>222 (197%)</td>
</tr>
<tr>
<td>New-not treated</td>
<td>280 (73.7%)</td>
<td>67 (17.6%)</td>
</tr>
<tr>
<td>Treatment history unknown</td>
<td>266 (50%)</td>
<td>97 (18.2%)</td>
</tr>
<tr>
<td>All</td>
<td>756 (37.1%)</td>
<td>386 (18.9%)</td>
</tr>
</tbody>
</table>

Adapted from NTI paper presented at 50th TB and Chest Diseases' Conference, 1995
Tuberculosis species and, thereafter, drug susceptibility test on drug incorporated media. The whole procedure takes about three months for the result to be available. The procedure is expensive and time consuming.

Recently new rapid culture and drug susceptibility tests, namely Bactec-460 (a radiometric method), Mycobacterial growth indicator tube (MGIT), Luciferase reporter gene assay have been developed. These are based on liquid culture media. The test takes 2-14 days for culture and drug susceptibility. In addition, advanced molecular tests, namely Polymerase chain reaction, DNA finger printing, Ligase chain reaction are in vogue in developed countries. All these tests are said to be highly sensitive, specific and rapid. However, these are extremely costly and at present not freely available for routine use.

Prevention of emergence of MDR-TB

(A) Good short course chemotherapy (SCC) daily for 6 to 8 months without interruption and full compliance are essential for prevention of emergence of MDR-TB. If possible, 2-3 times a week intermittent therapy under direct observation can also be advised.

(B) For prevention of transmission of infection and occurrence of active disease with MDR-strains, chemoprophylaxis with INH for 6 months could be advised. However, in areas of high MDR-TB prevalence or to people in contact with MDR-TB patients, Rifampicin, Pyrazinamide or quinolones have been advocated for developed countries.

Treatment of MDR-TB

Prompt and correct diagnosis and effective chemotherapy regimens are the mainstay of management and prevention of MDR-TB infection and disease. Ideally, drug susceptibility tests must be performed to identify the drug to which the organisms are susceptible. The therapy should consist of addition of two or more new drugs, not prescribed earlier, to the drug regimen which the patient is already taking; only one new drug should not be added. Intermittent therapy and Thiacetazone have no place in the management of MDR-TB. The list of additional drugs prescribed for MDR-TB includes Kanamycin, Ethionamide or Prothionamide, Amikacin, Cycloserin, Quinolones, (Ciprofloxacin, Ofloxacin, Sparfloxacin) macrolides, Clofazimine, and PAS for 3-4 months of until sputum converts, thereafter, Ethionamide, Cycloserin and Pyra/ino/mide daily with INH for 12-18 months.

In Japan, autologous immunotherapy using heat killed M. tuberculosis, and in Russia, laser therapy for multiple cavities and tracheo-bronchial disease have been tried.

Strains resistant to INH and/or Streptomycin neither pose a major problem nor effect the result of treatment in a big way, provided proper drug regimens are used. MDR-TB however poses a major problem by severely limiting the treatment results and constitutes a major threat to tuberculosis control, particularly for countries like India with poor resources, where neither the public health services nor the individual MDR-TB cases can afford expensive and toxic new drugs.

Human Immunodeficiency Virus (HIV) Infection and Tuberculosis

The acquired immuno deficiency syndrome (AIDS) was first recognized in 1978 in the city of New York. Its precursor, a slow virus of retrovirus group was isolated by Luc Montagnier in 1989, which was named Human Immunodeficiency Vims (HIV) by International Committee on Taxonomy.

The hallmark of HIV infection is derangement and progressive depletion and dysfunction of CD4 cells coupled with defects in macrophage and monocytic function. This results in immunocompetency/deficiency, whereby the opportunistic microbes continue to multiply without hindrance and produce AIDS and tuberculosis. The HIV infected people have higher risk of developing clinical forms of tuberculosis, either from activation of dormant endogenous foci or from exogenous infection. Further, the HIV infected tuberculosis patients provide an ideal condition for mutation of strain to drug resistant forms.

Narain JP et al report between 5 and 10% annual incidence of clinical tuberculosis among HIV and tuberculosis co-infected population, not compared to 0.2% among HIV seronegatives. The risk of progression of latent tuberculosis infection to clinical forms of the disease has been estimated to be 10 times in HIV seropositive population compared with that among HIV seronegatives. During first year after HIV infection risk of clinical tuberculosis
is about 5.8% whereas it is only 0.5% among HIV negatives (Table 7). The lifetime risk of tuberculosis among HIV positives is about 5 times that of HIV negatives. In relation to tuberculosis status, the risk of occurrence of tuberculosis in HIV positive tuberculosis reactors is estimated to be 30 times that of tuberculosis negative HIV positive.

Tuberculosis notification figures, in USA were gradually declining upto 1985. Thereafter, between 1985-1989, an excess of 25,000 tuberculosis patients over those of 1985, was reported. The increase was attributed to HIV infection.

The global prevalence rate of HIV infected tuberculosis is 125/100,000 of population in adults aged 15-45 years. Selwyn PA et al estimate that about 95% of HIV infected tuberculosis cases are attributable to HIV infection and remaining 5% could have developed tuberculosis regardless of HIV status. Dolin P. J. et al further estimate that in 1990, out of 7.5 million (Table 8) new tuberculosis patients, 0.3 million (4%), could be attributed to HIV infection. Of these, 0.2 million occurred in sub-Saharan region of Africa. They forecast that by 2000 A.D, the annual incidence of tuberculosis would be 10.2 million; of these 1.4 million (14%) would be attributed to HIV infection. Of the 1.4 million cases, 40% would occur in sub-Saharan Africa and another 40% in South East Asia.

### Table 7. Risk of TB morbidity by HIV infection

<table>
<thead>
<tr>
<th>HIV infection</th>
<th>Risk of morbidity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First year</td>
<td>Life time</td>
</tr>
<tr>
<td>Seropositive</td>
<td>59%</td>
<td>300%</td>
</tr>
<tr>
<td>Seronegative</td>
<td>0.5%</td>
<td>58%</td>
</tr>
</tbody>
</table>

Narain J.P et al

In Asia the HIV infection is high in Thailand. Situation in India is no better. According to Mohanty et al, the HIV seropositivity is on the rise. They reported that out of 4054 patients admitted in their hospital with various chest ailments, 205 were HIV seropositive, of these, 182 had pulmonary tuberculosis. They found 56% HIV seropositives among tuberculosis cases in 1988, which increased to 10.15% (83 out of 788 tuberculosis cases) in 1993-94. A similar rise of HIV seropositivity from 0.77% in 1990 to 3.35% in 1993 (Table 9), among tuberculosis patients had been reported in Madras by Anuradha et al.

### Table 9. HIV Seropositives among TB patients

<table>
<thead>
<tr>
<th>City</th>
<th>Year</th>
<th>% of HIV+ TB patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Madras</td>
<td>1991</td>
<td>0.77%</td>
</tr>
<tr>
<td></td>
<td>1998</td>
<td>3.35%</td>
</tr>
<tr>
<td>Bombay</td>
<td>1988</td>
<td>2.56%</td>
</tr>
<tr>
<td></td>
<td>1993-94</td>
<td>10.15%</td>
</tr>
</tbody>
</table>

TB Mortality in Relation to HIV Infection

In 1990 total deaths due to tuberculosis were 2.5 million—of these 0.11 million (4.6%) were related to HIV infection (Table 10). The above figures are estimated to increase by 38.7% and 147% respectively by 2000. The case fatality among HIV seropositive tuberculosis patients is higher than among seronegative tuberculosis cases, a small

### Table 10. Estimates of total and HIV related mortality world over at three periods (WHO)

<table>
<thead>
<tr>
<th>Year</th>
<th>Total TR</th>
<th>HIV related</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>%</td>
</tr>
<tr>
<td>1990</td>
<td>2,530,000</td>
<td>116,000</td>
</tr>
<tr>
<td>1995</td>
<td>2,977,000</td>
<td>266,000</td>
</tr>
<tr>
<td>Increase from 1995</td>
<td>177%</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>3,509,000</td>
<td>500,000</td>
</tr>
<tr>
<td>Increase from 1990</td>
<td>38.7%</td>
<td></td>
</tr>
</tbody>
</table>
proportion of which may be on account of other opportunistic infections.

The above observations indicate that tuberculosis in India, despite the National Tuberculosis Programme, is likely to become worse because of the breakdown in cell mediated immunity due to rise in HIV infections and AIDS. This will have adverse effect on tuberculosis epidemiology, if steps are not taken on war footing to contain both HIV infection and tuberculosis simultaneously.

**Treatment of HIV Positive tuberculosis**

WHO recommended that all HIV + Tuberculosis patients should be treated with standard doses of short course chemotherapy regimens, consisting of a combination of 3 or 4 drugs administered daily. Intermittent therapy and Thiacetazone have no place in the management of HIV + Tuberculosis. The reasonable duration of treatment remains to be known. However, CDC recommends that it must be at least for 6 months more after sputum culture conversion or life long INH. The result of chemotherapy among uncomplicated HIV tuberculosis patients are as satisfactory as among HIV negative tuberculosis patients (Hopewell 1989V

**Prevention**

Testing of HIV and tuberculosis infection is essential for control of the interrelated infection and diseases. HIV and tuberculin positive persons should have chest skigrams, those found to have radiological active disease should be treated with 3-4 drugs SCC regimen. Others Tuberculin and HIV + but without radiological evidence of tuberculosis should be advised INH chemoprophylaxis for 12 months.

In summary, HIV infection has affected the tuberculosis epidemiology and clinical presentation and natural history of tuberculosis. It has contributed to the epidemic of MDR-TB, affected tuberculin sensitivity, led to increase in total number of TB patients, increase in the cost of treatment and case fatality. The marriage of old scourge of tuberculosis infection with new HIV infection has presented an enormous challenge to the medical and public health technocrats.

**Advance in TB Diagnostic Techniques**

During the last 2 decades, a number of new laboratory investigations for diagnosis of tuberculosis have been developed. These are (a) Sero-immunologic investigation for identification of circulating antibodies or specific Mycobacterial tuberculosis antigen in the body secretions and tissues; (b) Rapid Mycobacterial culture techniques using liquid media (c) Molecular biological investigations to identify specific DNA, RNA or Nucleic acid of Mycobacteria (d) New imaging techniques (MRI-CTS).

1. Sero-immunological investigation A number of serological tests for detection of specific antibodies against Myco. tuberculosis or their antigen fraction have been developed and advocated. Some of these are Radio Immune Assay (RJA); Enzyme Linked Assay (ELA), antibody tests (SAPA) and Enzyme Linked Immunosorbent Assay (ELISA). All these lack both specificity and sensitivity. The techniques aim at detecting specific antibodies-the IgA or IgG. The procedures, however, cannot differentiate between old treated and new active tuberculosis patient.

2. Identification of Isolates. Rio-chemical Test Gas-chromatography and Mass spectrometry The technique is based on detection of specific fraction of Mycobacterial antigen and is useful for detection of tuberculostearic acid in sputum and other clinical specimens. It is being used as a primary means of identification of mycobacteria isolates and for diagnosis of tuberculosis meningitis. The high cost of the equipment for the technique limits the use of the procedure.

3. Rapid Mycobacteria detection by culture techniques Recently developed rapid culture techniques are : (1) Bactec 460 (Radiometric method) (2) Mycobacterial Growth Indicator Tube (MGIT), (3) Luciferase Reporter Mycobacterial phage; (4) Biphasic system, MB Septi-Check.

Bactec-460 Radiometric method is based on principle of monitoring of 14 Co, produced during growth of Mycobacteria. In other words, the procedure detects metabolic product rather than direct visible growth of Myco tuberculosis. The material is cultured on Middlebrook 7H12 broth media, incorporated with radio-active 14C labelled palmitic acid. During growth, the Mycobacteria metabolize 14C labelled palmitic acid and produce
14 Co, which is collected in the culture bottle above the liquid surface of the media. The Bactec system withdraws the 14 Co, and measures the amount of radioactivity. This is termed growth index. The method is very rapid, (takes 2-10 days time) highly sensitive and specific but requires sophisticated expensive equipment.

**Mycobacterial Growth Indicator Tube (MGIT)**: The technique detects bacterial growth with the help of oxygen sensitive fluorescent sensors. The actively growing Mycobacteria deplete the dissolved O₂ of broth and allow sensor to fluoresce in a 365 nm UV Light which can be seen with naked eye. The time of growth of organisms (including their identification) varies from 4 to 14 days. The technique has been found to be sensitive and specific for isolation and drug susceptibility tests of Mycobacteria.

**Luciferase Mycobacterial Phage Technique** utilizes Mycobacterial phage cloned with luciferase gene. When patient’s specimen is cultured in presence of the cloned bacterial phage incorporated in liquid culture media, the newly growing *Mycobacterium tuberculosis* cell take up the cloned phage and incorporate the Firefly Luciferase (FFLUC) gene in their own DNA and start producing Luciferase enzyme. This is picked up within a few hours with the help of luminometer in presence of luciferin-ATP. The photon emission indicates positive culture.

**MB Septi Check Biphasic System for culture and identification of Mycobacteria**: The technique consists of inoculation of specimen in Middlebrook broth media. The inoculated media is flooded on solid culture medium slide, which on one side has 7H10 agar and on the other side, 1/2 portion the solid culture media is incorporated with p-nitro-acetylamine 3 hydroxypropiophenone (NAP), and the other half is agar with chocolate. Mycobacterial other than tuberculosis (MOTT) grow on plain agar media and agar NAP part forming visible colonies; organisms other than Mycobacteria grow on chocolate; the growth on agar only indicates *Mycobacterium tuberculosis* species.

**Molecular Biological Technique**: These are based on identification of Mycobacteria DNA sequences in body secretion. The techniques are known as Polymerase chain reaction (PCR) (i) The PCR - detects specific Mycobacterial DNA by amplification of Mycobacterial DNA sequence. These are compared with DNA sequence of known Mycobacterial tuberculosis and with Non-Tuberculosis Mycobacterial DNA sequence, (ii) DNA finger printing is used for identification and typing of Mycobacteria. The technique is useful for epidemiological studies and for tuberculosis surveillance, (iii) The Ligase chain reaction technique is believed to be of great value for detection of drug resistance strains.

Among the molecular biological techniques, PFC has been found to be a very promising non invasive approach. Its application for diagnosis of pleural and extrapolmonary tuberculosis, particularly for tuberculosis meningitis is most helpful. However, its prohibitive cost, special equipment and high technical expertise do not permit its routine application.

In addition to the above laboratory techniques, the new radiological and magnetic imaging technique namely C.T. Scan and MR! are also helpful procedures of investigation. These primarily reveal abnormalities and not the specific aetiology. These are very expensive and are neither freely available nor applicable in routine investigation.

For developing countries, the clinical index of suspicion of tuberculosis remains the *sine qua non* of any attempt to suspect diagnosis of tuberculosis followed by sputum microscopy and radiography. Empirical therapy too has an important role for presumptive diagnosis of tuberculosis in sputum negative cases.

**Stray thoughts**

Medical teaching today is dominated by the teachers of clinical medicine whose main interest is to impart high academic standards and sophisticated knowledge to the students aimed primarily to offer curative services to individual patients. There is hardly any emphasis on preventive and social aspect of community wide disease control in the teaching curriculum. Neither the teachers of clinical medicine nor their counterparts in the department of social and preventive medicine (PSM) lay importance or create interest in their students for community wide disease control programmes. As a result, the medical professionals do not like to
participate in the activities of “National Disease Control Programmes”.

The situation can be remedied if the teachers of clinical medicine and PSM co-ordinate their approach and lay equal emphasis on preventive and curative aspects of diseases and themselves actively participate in the diseases control activities thereby motivating the students/future doctors to participate in the disease prevention programmes, which will certainly go a long way in achieving the national goal of control of various diseases. To achieve satisfactory performance in NTP, medical teachers must be motivated for active participation in the activities of NTP.

The health programme directors at all levels should be made accountable for tardy performance of NTP. It is only with their guidance, supervision, monitoring and improved logistics of programme that the DTOs and their staff can achieve the expected efficiency in NTP.

Steps should be taken to enhance public awareness about tuberculosis problem, its clinical manifestations, mode of transmission, steps for prevention (health education), centres for diagnosis and treatment and to offer socio-economic assistance to the needy patients. These will improve patient co-operation for case-finding and treatment compliance as well the overall performance of NTP.

Finally, development of a single shot depot therapy for tuberculosis will make matters much easier. The efforts required for motivation for regular therapy and full compliance will be obviated, tubercle bacilli could be overpowered and the disease be controlled within our life time.

Friends, with the introduction of specific anti-tuberculosis drugs and subsequent formulation of DTP, we thought that we were fast moving on the road towards control of the disease. We became over-optimistic, assuming that modality to tackle the problem and ultimate goal of TB control was within sight. No doubt, with the passage of time, we have become conscious of many hurdles. However, we must pursue our activities and research to achieve the ultimate goal of relieving human suffering and control the disease. I would, however, like to emphasize that sophisticated technology alone will not solve the gigantic problem of tuberculosis. We have the necessary expertise, but resources are inadequate and essential tools (drugs) are meagre and still bigger shortages are of interest, mutual co-operation, devotion, understanding and education in its real sense.

In the end, I would like to express my gratitude to you all for your kind indulgence in bearing with me patiently.

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ANTI-TUBERCULOSIS TREATMENT FAILURE IN CLINICAL PRACTICE*

S.K. Jindal**

Inspite of over thirty years of National Tuberculosis Programme (NTP) and the availability of near 100 percent effective treatment regimens, control of tuberculosis (TB) is nowhere in sight. In fact, the challenge of TB has increased. Besides the increase in the number of patients, we have an increased incidence of drug resistance. In this context, the multi drug resistant (MDR) organisms are of particular concern. The ominous threat of dual infections by the Human Immunodeficiency Virus (HIV) and Tubercle bacilli (TB) seems to threaten the very fabric of our national health care structure and programmes. We now see more patients with extensive and resistant pulmonary disease. Extra pulmonary involvement of gastrointestinal, genitourinary, neurological and skeletal systems also appear to be on the increase. It may not be entirely imaginary to say that we are doomed to enter the 21st century with the major health problems of TB and HIV infections in full blown forms.

There have been several analyses dealing with the NTP and the factors responsible for its limited success (or failure)1-4. A high prevalence is easily attributed to a large number of treatment failures, chronic and relapse cases produced by ineffective treatment programmes5. A large number of TB patients are treated outside the purview of NTP. In neighbouring Pakistan, for example, 80 percent of patients sought treatment from general practitioners6. Over 50 percent of patients are likely to be treated in private and semi-private clinics or hospitals spread allover the country. In an earlier study, it was estimated that of the total of 2506 persons visiting general dispensaries who were questioned about the presence of chest symptoms, 1170 (46.7%) admitted having symptoms suggestive of pulmonary TB7. It was concluded that TB patients do not bypass the city health institutions. Even the governmental hospitals and institutions are not necessarily covered by NTP. There is a major problem of treatment of this group of patients. Unfortunately, the treatment component itself is far from satisfactory. Discussion in this paper is focused on this very group.

Factors responsible for treatment outcome

The factors which influence the outcome of anti-TB treatment can be classified as “intrinsic” i.e. those related to the patient and “extraneous” (Table 1). The intrinsic factors, although not under the direct control of the physician, are important in tailoring the anti-tubercular treatment for a particular patient. Although the scope for individualized treatment is limited under programme conditions, it is not so in clinical practice. It is precisely for this purpose that the physician is required to be more vigilant and informed. The extraneous factors are those which are not directly related to the disease or the mycobacteria, but influence the treatment outcome. The factors related to the patient such as an enormous load, wide spread illiteracy and ignorance, general poverty and limited availability of resources are beyond the scope of this article. I shall limit my discussion to the factors related to the treatment-the physicians and the drugs.

1. Prescription Errors

Unfortunately, the story of errors committed in anti-TB prescriptions is almost global. In USA, for example, a review of the treatment prescription of 35 patients with multi drug resistant pulmonary tuberculosis revealed errors in 28 patients at an average of 3.93 errors per patient8.

Nearer home, in urban Sind in Pakistan, the front line management of pulmonary TB in the private sector, especially the general practitioner, was found inadequate and inappropriate9. In Bombay, in a study on private doctors, 100 of them prescribed 80 different regimens, most of which were inappropriate and expensive9. Further, 49.6 percent

* Guest Lecture Delivered at 51st National Conference on Tuberculosis and Chest Diseases, Bangalore, 3-6 November, 1996;
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Table 1. Factors influencing treatment outcome

A. “Intrinsic” Factors

1. Disease related
2. Drug related
3. Coexisting diseases

B. “Extraneous” Factors

1. Physician related
2. The drug confusion
3. Patient related

Table 2. Treatment review of 241 patients before PGI visit

<table>
<thead>
<tr>
<th>Index per patient</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (months)</td>
<td>22.4 ±8.7</td>
</tr>
<tr>
<td>No. of drugs</td>
<td>4.5 ±2.3</td>
</tr>
<tr>
<td>No. of changes</td>
<td>4.3 ±3.6</td>
</tr>
<tr>
<td>Sputum testing</td>
<td>38 ±3.5</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>42 ±3.8</td>
</tr>
</tbody>
</table>

Table 3. Errors made in initial prescription of 78 patients

<table>
<thead>
<tr>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappropriate drug combination</td>
<td>36</td>
</tr>
<tr>
<td>Inadequate dosages</td>
<td>53</td>
</tr>
<tr>
<td>Improper schedules</td>
<td>52</td>
</tr>
<tr>
<td>Unnecessary drugs (non anti TB)</td>
<td>61</td>
</tr>
<tr>
<td>Insufficient information provided to patient</td>
<td>58</td>
</tr>
</tbody>
</table>

Table 4. Errors in prescribing retreatment (163)

<table>
<thead>
<tr>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doubtful indication</td>
<td>134</td>
</tr>
<tr>
<td>Inappropriate choice</td>
<td>138</td>
</tr>
<tr>
<td>Inadequate number</td>
<td>121</td>
</tr>
<tr>
<td>Inadequate dosages</td>
<td>134</td>
</tr>
<tr>
<td>Insufficient duration</td>
<td>130</td>
</tr>
<tr>
<td>Insufficient monitoring</td>
<td>130</td>
</tr>
</tbody>
</table>

detected in over 80 percent of 163 prescriptions (Table 4).

Prescription errors can be attributed to multiple reasons some of which are listed below:

(i) Prescriptions by unqualified and/or non-allopath “doctors” who may not be too familiar with the drug regimens,
(ii) Lack of knowledge and awareness amongst even the qualified practitioners who do not update themselves with the standard recommendations or are too whimsical to change their set-prescrip-
tions.
(iii) Pressures and incentives offered for particular brands of drugs.
(iv) Limitations due to patient factors such as inability to afford the costs, intolerance, hypersensitivity or toxicity of drugs, non-availability of drugs in remote villages etc.

2. The Drug Confusion

There is a plethora of drug preparations available in the open market. Besides single, individual drugs there are multiple combinations or kits of 2 to 5 drugs in different dosages and differently priced. It is very difficult for a busy practitioner to rationalize the prescription for any individual patient.

We used a simple questionnaire to assess the practitioners’ awareness of anti-TB drug combinations available in the market. We chose 12 combinations of 2, 3 and 4 drugs (4 of each group) which are used most frequently in the region. Of 134 practitioners, who responded about the contents dosages, toxicity and recognition, the accuracy went down as the number of drugs in combined preparation increased (Table 5).

The drug confusion is further complicated by several other interrelated variables such as the methods employed for drug-promotion and distribution. The prescriptions may also be substituted at the retail-shops where the drug is finally available to the patient.

Table 5. Awareness (% of total) of 134 medical practitioners of combined anti TB drug-preparations

<table>
<thead>
<tr>
<th>Drug number</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Content</td>
<td>64</td>
<td>52</td>
<td>41</td>
</tr>
<tr>
<td>2. Dosages</td>
<td>61</td>
<td>48</td>
<td>38</td>
</tr>
<tr>
<td>3. Toxicity</td>
<td>51</td>
<td>42</td>
<td>30</td>
</tr>
<tr>
<td>4. Recognition</td>
<td>47</td>
<td>41</td>
<td>31</td>
</tr>
</tbody>
</table>

Suggested approach

Of the three main extraneous issues (Table 1), the factors related to the drugs and the physician need to be addressed immediately. Their control is also relatively easily achievable than that of the patient related factors.

1. Physicians’ education

An extensive and comprehensive plan which provides education repeatedly at regular intervals is required. There is already an existing infrastructure of national centres, medical colleges and other institutions. But there is a need to thoroughly relook into the existing programme and improve the educational and training design. Both “in-house” and “at-site” programmes are required. The “in-house” training is to be imparted to the trainers at the main centre. More importantly, the education design should be more dynamic. Stress may be shifted from didactic lectures and pamphlets to informal and interactive sessions. Examples and sham prescriptions could be introduced. An element of “compulsion” for reorientation of prescribing practices may be considered.

2. Drug Rationalization

Inspite of the provision of free supply of anti-TB drugs through NTP, a large number of patients including the poorest of the poor are unable to avail of the treatment. There is a need to enlarge the scope of the NTP for drug supply. The distribution centres for drugs may be increased to include private and semi-governmental health institutions, clinics and chemists. The governmental supply can be distinguished from commercially available preparations.

There is a need to limit the choice of first line anti-TB drugs in the free market to a few standardized preparations. The recommendation may appear to be contrary to the free market policy which we pursue, but a national programme such as TB control is a matter of concern to all rather than an issue for commercialization.

Prescription of second line drugs should be severely restricted and availability made at specialized centres only. These drugs are misused more often than used. Moreover, in practice they serve little purpose in the overall treatment programme.

In conclusion, prescription errors and drugs confusion are two important factors responsible for failure of treatment of TB. Both these factors are potentially preventable if greater inputs are made in programmes related to physician’s education and
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A 5 YEAR FOLLOW-UP STUDY OF CHILDREN TREATED FOR TUBERCULOUS MENINGITIS WITH SHORT COURSE CHEMOTHERAPY*

Padma Ramachandran, M. Duraipandian and A.M. Reetha**

Summary: A total of 215 patients with tuberculous meningitis were treated for a period of 9 months. Of these, 30 patients were excluded from analysis for various reasons. Of the remaining 185, 57 died during treatment leaving 128 patients (5 with severe sequelae, 43 with moderate, 18 with mild and 62 with complete recovery) for long term follow-up. The noteworthy features of the study are 100% coverage, low relapse rate and development of late sequelae in 10 patients during follow-up period.

INTRODUCTION

Of all forms of tuberculosis, tuberculous meningitis (TBM) still carries a high mortality and morbidity. Infections of the central nervous system, unlike other infections cause irreparable damage unless diagnosed early and promptly treated. The resulting neurological sequelae can manifest either during treatment or subsequently. Long term follow up of treated TBM patients is therefore essential to find out the course of the residual lesions and also the relapse rates. This report gives the 5 year follow up status of 128 survivors out of 185 patients treated with short course chemotherapy. The study was undertaken by the Tuberculosis Research Centre in collaboration with the Institute of Child Health and Hospital for Children, Chennai from where the patients were drawn.

MATERIAL AND METHODS

A total of 215 patients aged between 1 and 12 years, who had not received more than 2 weeks of previous anti-tuberculosis chemotherapy and had no evidence of renal or hepatic disease and no optic atrophy were admitted to the study. They were treated for 9 months with one of the following regimens.

Regimen-1: 2 SHER/Z/7R,H, Patients received streptomycin, isoniazid and ethambutol daily supplemented with rifampicin and pyrazinamide thrice a week for the first 2 months followed by rifampicin and isoniazid twice a week for the next 7 months.

Regimen-11: 2SHER/Z/7R/H2 Patients were treated with streptomycin, isoniazid and ethambutol daily supplemented with rifampicin and pyrazinamide twice a week for the first 2 months followed by rifampicin and isoniazid twice a week for the next 7 months.

In addition to anti-tuberculosis drugs, non-specific therapy was also given in the form of intravenous fluids, anti-oedema measures, anti-convulsants and vitamins. Steroids were administered to all the patients for a period of 6 to 12 weeks.

The results (awaiting publication in The Indian Journal of Tuberculosis) were similar in both the regimens with a mortality rate of 31%. There was a clear association between the stage on admission and the mortality rate, the latter being highest in stage III patients and lowest in stage I. At the end of treatment, there were 128 survivors, 66 (36%) with neurological sequelae and 62 (34%) with complete recovery.

Neurological sequelae were classified as follows. Patients classified as with severe residual damage either remained unconscious or even if they had regained consciousness, were incapable of independent existence. Moderate residual damage included defects like involuntary movements, hemiparesis and substantial mental impairment. Mild sequelae included hyperactivity, irritability, mild perceptual defects and limited motor impairment like facial weakness or monoparesis.

All the patients who completed 9 months of

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treatment were seen once a month till 24 months, once in 3 months till 36 months and thereafter once in 6 months till 60 months. The period of follow up was 51 months after completion of therapy. At all these visits, a complete neurological examination was done on all the patients. Lumbar puncture and CSF examination for cell count biochemical and bacteriological examination was repeatedly undertaken for those who had abnormal CSF findings at the end of treatment, till the results became normal.

RESULTS

Table 1 shows the status at the end of 5 years for the 128 patients who completed the treatment. Eleven patients died during the follow up period - 7 due to TBM sequelae and 4 due to non tuberculous causes. The remaining 117 patients were seen upto 60th month from the start of treatment.

Of the 5 patients with severe sequelae at the end of treatment, 4 patients died-all due to sequelae, in the 14th, 15th, 19th and the 44th months respectively, while the fifth patient showed improvement.

Of the 43 patients with moderate sequelae, 2 patients died of TBM sequelae in the 11th and 30th months while 2 others died of non-tuberculous causes. In 36 patients the status remained the same while 2 patients improved to mild sequelae and one had complete recovery.

Of the 18 patients with mild sequelae, 2 patients died, the first patient due to non-tuberculous cause while, the second relapsed at the 12th month and died in the 31st month despite intensive therapy for 9 months. Ten patients maintained their status while 3 other developed moderate sequelae, namely, secondary epilepsy. Three had a complete recovery.

Of the 62 patients who had complete recovery status quo was maintained in 54 patients, while 7 developed sequelae-1 patient developed diabetes insipidus, 3 had secondary epilepsy, while the remaining 3 had behaviour problems. One patient died of a non-tuberculous cause.

Seven patients had CSF abnormality (increased protein level) at the end of treatment. All the 7 had hydrocephalus and 6 of them underwent ventriculo-peritoneal shunt surgery. In the surgery group, the CSF protein level became normal in all the patients. In the 7th patient whose parents refused surgery, the last CSF examination at the 47th month was still abnormal. Repeat lumbar puncture was not possible because of non-cooperation. The patient was alive at 60th month with moderate sequelae.

Relapses during follow-up

In all, 3 patients relapsed, 1 in regimen I and 2 in regimen II. All of them had clinical signs and symptoms of meningitis with abnormal CSF biochemical findings and bacteriological positivity. In the first patient who had mild sequelae at the end of treatment and relapsed in the 12th month, the CSF cultures (both initial and at the time of relapse) were sensitive to all the drugs. Despite retreatment with intensive therapy for 9 months, the patient died in the 31st month. The last CSF was normal biochemically and bacteriologically. The remaining 2 patients (1 with mild sequelae and the other with moderate) relapsed in the 11th and 22nd month of follow-up (from the commencement of treatment) respectively. The first patient relapsed with organisms sensitive to all the drugs while the 2nd relapsed with organisms resistant to streptomycin and isoniazid (both initially and at the time of relapse). Both the patients were treated with

<table>
<thead>
<tr>
<th>Status at 9 months</th>
<th>No. of pts.</th>
<th>Deaths after 9 months</th>
<th>Status at the end of 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Seq.</td>
<td>5</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Moderate Seq.</td>
<td>43</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mild Seq.</td>
<td>18</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Comp. recovery</td>
<td>62</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>All</td>
<td>128</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>
intensive chemotherapy and both recovered with moderate sequelae. The CSF at the end of retreatment was normal biochemically and bacteriologically.

**DISCUSSION**

There are very few reports available on long term follow-up of patients treated for tuberculous meningitis. In our earlier report on long term status (4’iii - 8 years) of 119 survivors treated for TBM the salient features were: out of 10 deaths due to TBM sequelae, 9 occurred in those who had severe sequelae at the end of treatment and of the 52 patients who were classified as fully recovered, 10 developed mild to moderate sequelae during follow-up period. Fitzsimons treated 289 patients between the years 1946 and 1959. There were 198 survivors who were followed for a period of 2 to 15 years after discharge and the results showed that 122 patients (62%) had a complete recovery, 42 (21%) had minimal restriction, 19 (10%) had moderate disability and 15 (8%) severe disability. A follow up study on 100 survivors out of a total of 170 children treated for TBM between 1947 and 1955 is reported by Lorber. He followed them for a period of 5 to 13 years and found neurological sequelae in 23 patients. In another study by Miller et al 116 patients were treated between 1947 and 1957 and the results showed that 36 (31%) patients died and 80 (69%) survived. The survivors were followed for a period of at least 2 years and residual neurological sequelae were found in 38 (48%) patients.

The salient feature of the present study is that the coverage was 100% despite 50% of the patients hailing from semi-urban and rural areas. This was possible because of initial and periodic subsequent motivation. The relapse rate was low and 10 patients (in the complete recovery and mild sequelae group) developed late sequelae during the follow up period stressing the necessity for long term follow up of treated TBM patients.

**ACKNOWLEDGEMENTS**

The authors thank the social workers of the Centre specially Miss. T.V. Mathibushanam, Mr. A.S. Kripasankar, Statistician and Mrs. S. Padma, Clinic Nurse for the assistance rendered.

We are grateful to Dr. N. Deivanayagam and Dr. Merlyn Joseph, former Directors of the Institute of Child Health and Hospital for Children, Chennai for their kind cooperation.

We also acknowledge with thanks the secretarial assistance provided by Mr. P. Karthigayan.

**REFERENCES**

VALUE OF HIGH RESOLUTION COMPUTED TOMOGRAPHY IN DIAGNOSIS AND ASSESSMENT OF BRONCHIECTASIS*

S. Rajasekharan1, R. Bhanusree2, V. Vallinayagi3, V. Gopal4 and S. Nirmaladevi

Summary: Contrary to common belief, bronchiectasis is a major respiratory problem among children and young adults in India. Bronchography is no longer used routinely in establishing the diagnosis and for assessing the extent of the affection as the contrast medium used in the procedure has become a scarce commodity. Alternatively, High Resolution Computed Tomography (HRCT), a non-invasive procedure, offers maximum advantage in the evaluation of bronchiectasis.

Fifty patients with clinical features of bronchiectasis were assessed using HRCT at Thanjavur Medical College Hospitals. In all of them, HRCT not only confirmed bronchiectasis but also accurately demonstrated the extent of involvement.

Haemophilus influenzae, the most common offending bacterium, was isolated from sputum of 23 patients (46%). Of the 14 tuberculous bronchiectasis patients, 12 were expectorating tubercle bacilli. The HRCT features were similar in tuberculous as well as non-tuberculous bronchiectasis.

INTRODUCTION

Bronchiectasis, which simply means bronchial dilatation, has many causes. There are many conditions in which bronchi get dilated and, hence, bronchiectasis cannot be considered as a primary disease1. Bronchiectasis, as a clinical syndrome, does exist and has the classical “symptoms triad” of cough, excess sputum production and repeated infection. It is a fairly common condition in India, and nearly 0.3% of patients seen in Delhi hospitals had this disorder1. The five years data of a major chest hospital showed that bronchiectasis constituted just over 3% of all patients suffering from respiratory diseases, other than tuberculosis7.

Resectional surgery for bronchiectasis provides a radical cure in suitable cases. For the determination of actual pulmonary segments involved, bronchography has been the gold standard for many years4. However, the standard bronchographic contrast medium, Prophylodone (Dianosil), is no longer available in India. The consequent widespread use of computed tomography (CT) for evaluation of pulmonary diseases has revealed mild and moderate forms of bronchiectasis to be fairly common, even in patients without clinical or plain radiographic suspicion of bronchiectasis2. Several published reports5,6,7 confirm that CT is the most suitable replacement for bronchography for diagnosis and assessment of bronchiectasis.

The present study was undertaken to evaluate the value of High Resolution Computed Tomography (HRCT) for confirming the diagnosis and in assessing the severity of the disorder, obtaining the bacteriological profile of sputum specimens obtained from such patients and to assess the pattern suggestive of tuberculous bronchiectasis.

MATERIAL AND METHODS

Fifty patients admitted in Thanjavur Medical College Hospital and Govt Raja Mirasudar Hospital, Thanjavur with clinical features suggestive of bronchiectasis were selected for this study. All these patients had productive cough for more than 6 months and audible persistent coarse crepitations on pulmonary auscultation.

Apart from the routine urine and blood examination, all the selected patients were subjected to the following investigations

1. Sputum smear microscopy for AFB by

* Paper presented at 51st National Conference on Tuberculosis and Chest Diseases, Bangalore, 6-9 November, 1996

1 Professor of Thoracic Medicine, 2 Post-graduate student, 3 Professor of Radiology, 4 Additional Professor of Medicine, Thanjavur Medical College

Correspondence: Dr S. Rajasekharan, Professor of Thoracic Medicine, Thanjavur Medical College Hospital, Thanjavur.
Ziehl-Neelsen technique
2. Sputum smear examination by Gram-staining
3. Sputum culture for non-tuberculous organisms
4. Mantoux Test: 1 TU of PPD RT 23
5. X-ray chest (Postero-anterior view)
6. High Resolution Computed Tomography
7. X-ray of sinuses and barium meal follow through in patients with Kartagener’s syndrome

HRCT Protocol

HRCT was tailored to each patient’s clinical features and plain chest radiograph findings. In patients with chest radiography showing several areas of abnormality, standard 8 or 10 mm slices plus 1 mm high resolution slices at 10 to 15 mm intervals were made, from top of the aorta to the diaphragm.

In patients who had focal abnormality, standard 8 or 10 mm slices were obtained initially and 1 mm high resolution slices were made subsequently in the afflicted region.

**Items assessed in CT scan**

- Number of segments affected by bronchiectasis
- Types of bronchial dilatation
- Associated parenchymal lesions, like consolidation, fibres and emphysema
- Position of trachea and mediastinum
- Intra-bronchial growth or extra-luminal compressive lesion

**RESULTS**

Thirty seven of the 60 bronchiectasis patients were 11 to 40 years old; 32(64%) were males.

**Predisposing factors**

Possible predisposing factors leading to the development of bronchiectasis are given in Table 1. An important cause in this group was tuberculosis (14 of 50 patients (28%) had confirmed pulmonary tuberculosis). Besides, 5 of the patients had Kartagener’s syndrome (a triad of bronchiectasis, situs inversus and frontal sinus agenesis or sinusitis) in whom ciliary dyskinesia could be the possible factor.

**Clinical features**

All the 50 patients had cough and copious expectoration, 21 (42%) had haemoptysis and 17 (34%) had exertional dyspnoea. Finger clubbing was present in 23 patients (46%); persistent coarse crepitations were found in all the patients and bronchial breath sounds were elicited in 28% of them.

**Bacteriological profile**

Table 2 shows that the commonest organism producing secondary infection was *H. influenza* (46%) followed by *S. Pneumoniae* (16%) and Beta-haemolytic streptococci (14%).

Besides these isolates, 12 patients were found to be expectorating *M. tuberculosis* in their sputa (smear microscopy) and the remaining two

**Table 1. Predisposing factors causing bronchiectasis**

<table>
<thead>
<tr>
<th>Cause</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>14</td>
</tr>
<tr>
<td>Dyskinetic cilia syndrome (Kartagener syndrome)</td>
<td>5</td>
</tr>
<tr>
<td>Exanthematos fever</td>
<td>4</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Lung abscess</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
</tr>
</tbody>
</table>

**Table 2. Sputum : Non-Tuberculous Bacteriological Isolates**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Pts.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemophilas Influenzae</td>
<td>23</td>
<td>46</td>
</tr>
<tr>
<td>Streptococcus Pneumoniae</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Beta-Haemolytic Streptococci</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Coliform group</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Klebsiella Pneumoniae</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Pseudomonas aeroginosa</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
provided details of previous anti-tuberculosis treatment received. This clearly pointed out the necessity of sputum smear examination for AFB in all the bronchiectasis patients.

**Plain chest X-ray findings**

Tram lines, increased and crowded bronchial markings, cystic spaces, honeycombing pattern, areas of consolidation and atelectasis were noticed alone or in combination in all the 50 patients.

**CT/HRCT findings**

The abnormalities observed were bronchial dilatation, lack of bronchial tapering, bronchial wall thickening, mycoid impaction and visualization of bronchi in the areas where they are usually not seen. Of the 50 patients, 12 (24%) had bilateral bronchiectasis and the rest had unilateral disease. Left lower lobe was predominantly affected in 30 patients (60%).

HRCT delineated accurately the sequential involvement and the frequency of each segmental affliction could be studied (not on Table). Left lateral basal and left posterior basal segments were found to be ectatic in 23 (46%) and 20 (40%) patients respectively. CT was able to reveal an intra bronchial growth causing obstruction in a patient having left lower lobe bronchiectasis. HRCT also showed 30 patients (60%) to have cystic bronchiectasis and cylindrical (tubular) bronchiectasis accounted for 18 patients (36%). Two patients had bronchiectasis of mixed pattern - both cystic and cylindrical.

**DISCUSSION**

Bronchiectasis was a significant cause of respiratory distress, failure and death in the pre-antibiotic era. Though the frequency of advanced bronchiectasis is now on the decline, most of the affected patients are being managed with episodic drug treatment and physiotherapy. Radical surgical management, even in suitable cases, becomes impracticable for want of the confirmatory diagnosis procedures in the absence of the time-tested Dionasol bronchography in India.

Various other radio-opaque contrast media were tried for performing bronchography but with varied results. Choudary had found barium sulphate contrast medium to be effective, cheap and safe but subsequent barium sulphate elimination was unduly delayed, for more than 6 months, in at least 10% patients leading to foreign body granuloma formation. Tantalum was another contrast agent tried with encouraging results. However, tantalum powder is currently available only as an experimental drug.

With the advent of computed tomography, diagnosis and assessment of bronchiectasis has become non-invasive and easier, making bronchography unnecessary. CT also provides an excellent cross section view of dilated airways making it of immense value (1) for identifying the abnormality as bronchiectasis, (2) determining its severity and extent, (3) evaluating the status of the surrounding lung tissue and (4) excluding other abnormalities, especially neoplasm.

Earlier CT studies had shown high specificity (92-100%) but less sensitivity (51-79%) in detecting bronchiectasis. Those results were obtained with 10 mm computed tomographic sections during the early days of CT. However, high quality thin sections with HRCT have demonstrated the abnormalities of bronchiectasis exquisitely and improved the diagnostic confidence level. By incorporating the use of medium thick (4-5 mm) and thin sections (1-2 mm), the sensitivity of HRCT has equaled that of bronchography. Therefore, HRCT has become a proper replacement for bronchography and the investigation of choice. However, thin HRCT sections are not absolutely necessary for all patients; 5 or even 10 mm sections can be diagnostic, particularly if a high resolution algorithm is used. In this study HRCT confirmed presence of bronchiectasis, accurately assessed the extent of the disorder and enabled precise localisation in all the 50 patients studied.

Active tuberculosis was present in 12 out of the 14 tuberculous bronchiectasis cases in this study. Occasionally, associated granulomatous tissue might accumulate in sufficient quantity to cause a polypoidal endobronchial mass that can result in atelectasis and cause obstructive pneumonitis. It is a common belief that bronchiectasis, secondary to tuberculosis and other granulomatous diseases is usually located in the upper lobes. However, in the present study, tuberculous bronchiectasis was found to be in the upper lobes in only 5 out of 14 patients and in the remaining 9 patients, lower lobar involvement was observed. HRCT features of tuberculous bronchiectasis were similar to HRCT.
findings in non-tuberculous bronchiectasis.

REFERENCES

FEASIBILITY OF UTILISING TRADITIONAL BIRTH ATTENDANTS EV DTP*

Rani Balasubramanian

Summary: The study shows that it is feasible to train Dais residing in villages effectively in selection of the chest symptomatics of their villages, for door-delivery of antituberculosis drugs to the cases placed on treatment and for sputum collection at the end of treatment as well as their future follow-up. Under Dais 85% treatment completion and over 63% cure rate were achieved. Dais are available in every village in India and could be trained and utilised for NTP in rural areas. They could also be entrusted with delivering antituberculosis drugs under direct observation (DOTS) under RNTCP.

INTRODUCTION

DTP has been in operation for the past 3 decades. The case-finding and case-holding efficiencies of DTP need still to be improved. Hence, a study was undertaken by TRC to investigate the feasibility of involving a NGO by training their traditional birth attendants (Dais) in case-finding and door-delivery of drugs to tuberculosis patients. The study was undertaken in 44 villages in Sriperumbudur Taluk situated about 40 km from Chennai. The results of the study during a period of 5 years are presented.

MATERIAL AND METHODS

The non-governmental organisation that co-operated in the study is “PREPARE”. They function in 68 villages in Sriperumbudur Taluk of which the study involved 44 villages. The Dais of these villages were trained by PREPARE in conducting home deliveries in an aseptic manner, undertaking ante-natal and post-natal care of pregnant women, in organizing immunization camps and in the supply of simple drugs for minor ailments and documenting it by putting “tallymarks” on the records. Dais are traditional birth attendants. They reside in the same villages where they conduct deliveries. Hence, they are well-known in the community and have good rapport with the villagers. They are quite often illiterate, and are not on the payroll of the government. They are provided with proper delivery kits, after their training, for conducting deliveries at patients’ homes in a hygienic way.

The design of the study comprised several steps. As a preliminary step, practical training of Dais was arranged in the field, in tuberculosis case-finding as well as home-delivery of anti-tuberculosis drugs to confirmed cases put on treatment.

The field training was repeated at monthly intervals, for a period of 5 years, initially by a TRC team for 2 years and later by the nurses of PREPARE. During this period, health education of the community, regarding TB, was organized in the 44 villages. The health education methods used were: exhibitions, role-plays, participation in village meetings and film shows on tuberculosis. After their training, the Dais could identify the chest symptomatics, collect 2 sputum specimens from each chest symptomatic and transport the specimens carefully to PREPARE office in Sriperumbudur. All the collected specimens were subsequently transported to TRC laboratory for sputum microscopy, by a messenger, every day.

For the sputum positive patients, found by smear or culture, the TRC team initiated treatment at patients’ homes. The drugs needed for each patient were issued to PREPARE office wherefrom the drugs were delivered to Dais, in the field. Then, Dais delivered the drugs at patients’ door-steps, fortnightly.

To check on regularity of drug intake by patients, a weekly check was done by Dais by putting a tally mark against each name. In addition, TRC team exercised spot drug-check during field visits by doing a pill count and collection of urine for testing drug excretion.

After completion of treatment, a list of patients due for follow up was sent to PREPARE office.

* Paper presented at the 51st National (Conference on Tuberculosis arid Chest Diseases, Bangalore, 6-9 November, 1996

Correspondence: Dr Rani Balasubramanian, *Assistant Director, Tuberculosis Research Centre (ICMR), Chennai-600 031
which intimated the Dais concerned to collect sputum from those patients. The collected specimens were then transported to TRC laboratory for sputum microscopy.

Monitoring of the study was done by TRC team consisting of a medical officer, a clinic nurse and a medical social worker. Fortnightly visits were made without intimating the field staff, to validate the work of Dais.

RESULTS

Case-finding

Case-finding done through Dais during a period of five years is presented in Table 1.

In the total population of 26,413 persons, the eligibles for symptom questioning, i.e. those aged 15 years or more were 16,740. Total number of Dais in the 44 villages was 55, i.e. one or more in each village. Total number of chest symptomatics identified by them was 600, that is 3.6% of the eligible population. Total number of sputum positive patients detected among 600 symptomatics was 77, that is 2.8% of the chest symptomatics.

In order to ascertain whether Dais had made proper selection of chest symptomatics, the TRC nurse assessed all the chest symptomatic identified by them. In addition, to check whether the Dais had correctly identified all the chest symptomatics present in the community, an independent estimate was prepared by visiting two households (for every chest symptomatic identified) one on either side of the household of the identified chest symptomatic, and symptom-questioned them. The result of the validation of the work of Dais is shown in Table 2.

A total of 2,330 persons was screened for presence of chest symptoms. There were 654 chest symptomatics in the community sample, of whom 61 had been missed by Dais, and 7 were wrongly labelled as chest symptomatics (sensitivity 91.9%, specificity 99.6%). In all, 68 persons out of 2330 were mis-labelled by Dais. It is evident that Dais proved to be efficient in identification of chest symptomatics in the community.

Treatment

In the 44 villages, 78 sputum positive cases put on standard chemotherapy were placed in the care of Dais. This number included one detected by TRC clinic nurse. Their status at the end of 12 months is shown in Table 3.

Anti-tuberculosis treatment (ATT) could be initiated only in 62 cases (79%). The reasons for not starting treatment in 16 are also given in Table 3. During the prescribed treatment period, 6 cases died and 3 migrated while 53 (85%) completed treatment. These findings suggest that by door-

<table>
<thead>
<tr>
<th>Table 1. Case-finding by ‘Dais’ during 5 years in 44 villages</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
</tr>
<tr>
<td>Population ≥15 years</td>
</tr>
<tr>
<td>Total no. of ‘Dais’</td>
</tr>
<tr>
<td>Chest symptomatics identified</td>
</tr>
<tr>
<td>Sputum positives</td>
</tr>
<tr>
<td>(S+C-18; S + C + 49; S – C + 10)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Validation of work of Dais’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest symptomatics*</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Assessed by ‘Dais’</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Sensitivity 91.96; Specificity 99.69%

*As per DTP definition

<table>
<thead>
<tr>
<th>Table 3. Status of sputum positive cases after 12 months of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
</tr>
<tr>
<td>ATT initiated by TRC</td>
</tr>
<tr>
<td>Died</td>
</tr>
<tr>
<td>Lost</td>
</tr>
<tr>
<td>Completed treatment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ATT Initiated by TRC 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalised</td>
</tr>
<tr>
<td>Died</td>
</tr>
<tr>
<td>Outside area</td>
</tr>
<tr>
<td>Migrated</td>
</tr>
<tr>
<td>Refused ATT</td>
</tr>
<tr>
<td>Not identified</td>
</tr>
</tbody>
</table>
FEASIBILITY OF UTILISING Dais IN DTP

Follow-up

The results of follow-up sputum examination at 12 months and after 18 or 24 months of treatment are given in Table 4. The proportions of sputum specimens collected by Dais were 80% of 53 at 12 months and 79% of 42 at 18 or 24 months. Smears and cultures were negative in 63% at 12 months and 82% at 18/24 months. The number of patients retreated was 6 at 12 months and 4 were being retreated at 18/24 months. The Dais were asked to give each dose of retreatment under direct supervision for a period of 3 months or till their smears became negative. The point of interest is that Dais were able to administer drugs under supervision, without much efforts, because the patients were residing in the same villages. These findings suggest that Dais are efficient in the different activities engaged under DTP in a rural setting.

Results of surprise checks done during the 12 months of treatment by TRC team are shown in Table 5. Of the 53 cases who continued their treatment and were eligible for a drug intake check, TRC team did such a check in 81% of cases. In all, 70% of the 53 patients had intake 80% or more of their scheduled chemotherapy.

---

### Table 4. Results of sputum examination at 12 and 18/24 months of treatment

<table>
<thead>
<tr>
<th></th>
<th>12 months</th>
<th>18/24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number eligible</td>
<td>53</td>
<td>42</td>
</tr>
<tr>
<td>Number sputum collected</td>
<td>42</td>
<td>80</td>
</tr>
<tr>
<td>By Dais</td>
<td>33</td>
<td>79</td>
</tr>
<tr>
<td>Number cured (S-, C-)</td>
<td>63</td>
<td>82</td>
</tr>
<tr>
<td>Number of failures (S+ or C+)</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Retreated NTM/Cont.</td>
<td>23</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug intake check done</td>
<td>43</td>
<td>81</td>
</tr>
<tr>
<td>Number eligible for check</td>
<td>53</td>
<td>100</td>
</tr>
<tr>
<td>number who missed ≤20% of doses</td>
<td>37</td>
<td>70</td>
</tr>
</tbody>
</table>

---

*delivery of anti-tuberculosis drugs, 85% could complete chemotherapy even in rural areas.*
TRANSCATHETER BRONCHIAL ARTERY EMBOLIZATION FOR MANAGEMENT OF MASSIVE HAEMOPTYSIS*

Liesel D'Silva, P.M. Basheer Muhammed and K.C. Mohanty

Summary: Massive haemoptysis can be a life threatening emergency. Transcatheter embolization of bronchial artery has been advocated to deal with such an emergency. In a series of 40 cases where this procedure was applied, 90% success with stoppage of bleeding within 24 hours was achieved. In 2 cases, mild haemoptysis continued up to 1 week after embolisation and the remaining 2 continued to have recurrent haemoptysis even after repeated embolisation for which one had to undergo emergency lobectomy and the other expired.

INTRODUCTION

Massive haemoptysis is a life threatening emergency with a mortality rate of 30-80% if treated conservatively. Transcatheter embolization of bronchial artery, which was first described in 1973 has now become an accepted method of therapy for massive haemoptysis. When the systemic blood supply to the lungs is the source of bleeding, then therapeutic embolization of the affected bronchial artery achieves rapid and safe control of haemoptysis and can be used to stabilize the patient prior to surgery or for other definitive therapy.

Bronchial arteries were first described by Leonardo da Vinci. In the early 1950s and late 1960s, attempts were made using non-selective as well as selective thoracic aortography to visualize the bronchial arteries in pulmonary diseases. In 1973, the first bronchial artery embolization was done for control of haemoptysis.

The lung parenchyma, bronchioles and outer surface of pulmonary vessels receive their nutrient supply from pulmonary arteries, combined with oxygen from the air. But the thick walled bronchi, their glands and cartilages derive their mitrical supply from the bronchial arteries. Bronchial arteries arise from the anterior branches of the aorta; 70% from the descending thoracic aorta, between the cranial margin of D5 and caudal margin of D6 and partly from the upper intercostal arteries. These arteries course alongside the oesophagus and penetrate, on both the sides, into the hilum. Bronchial arteries extend to the most peripheral bronchi but not into the bronchioles. They course along the septa to reach the pleura, some anastomose with the peripheral branches of the pulmonary arteries. They also supply the vasavasorum of the pulmonary vasculature, diaphragmatic and mediastinal pleura and middle 1/3 of oesophagus and the subcarinal lymphnodes. Bronchial veins begin as peribronchial venous plexus and drain into pulmonary veins.

Therefore, whenever in a bronchial artery angiogram the lesion cannot be detected the intercosto-bronchial trunk, axillary, subclavian and internal mammary arteries should be catheterised to locate the aberrant origin of the bronchial arteries. In the mid-thoracic area, the major radiculo-medullary feeder artery of the spinal cord arises from intercostal artery between D3-D5, due to rotation of the upper thoracic aorta. The intercostal and bronchial arteries on the right side arise from a common stem, thus accounting for a high chance of cord damage during right bronchial angiography. At the thoraco-lumbar level, the radiculo-medullary...
feeder artery of Adamkiwicz arises between D8 and D4 but may originate at D5.

AIMS and Objectives

The objectives of this study were to:

1. Study the vascularity of lung lesions causing haemoptysis.
2. Locate the site of haemoptysis.
3. Evaluate the role of bronchial artery embolization as an emergency life saving measure.

Etiopathogenesis of Haemoptysis

The most common causes are tuberculosis, chronic bronchitis, bronchiectasis, bronchogenic carcinoma, pneumonia, lung abscess and fungal infection.

Less common causes are mitral stenosis, Goodpastures’ syndrome, endobronchial foreign bodies, bronchial asthma, pulmonary arterio-venous fistulae, pulmonary infarction and coagulopathies.

Material and Methods

Forty patients (28 males and 12 female) aged between 22-27 years, admitted to Respiratory Diseases ward of the Sir J.J. Hospital underwent transcatheter embolization for the treatment of haemoptysis. The severity of their haemoptysis was classified into three categories:

(a) Daily haemoptysis of 200 ml to 500 ml (n=11)
(b) Massive haemoptysis of 500 ml (n = 17)
(c) Profuse haemoptysis of 200 ml per hour (n=12)

Chest roentgenogram (PA view) was taken of all the cases prior to the procedures. Bronchoscopy was not performed in any of these patients. Transcatheter embolization was undertaken during peak haemoptysis in 28 patients (70%) and during a relatively quiescent period in 12 patients (30%).

Procedure

The procedure was carried out in the supine position using trans-femoral Seldinger technique under local anesthesia. Either 4F or 5F curved Shepherd or Cobra catheters were utilized for catheterization of the bronchial arteries. Search for the bronchial artery opening was made at D4 to D6 levels and if necessary it was extended to the intercostal, diaphragmatic and internal thoracic arteries. Diatrizoate Meglumine (Urografin), 8-12 ml was injected into the bronchial artery at 2 to 3 ml/second/rate. Anterior, lateral and different oblique views were obtained following the injection.

Angiographic signs for locating haemorrhage were: extravasation of the contrast agent, thrombosis of branches of bronchial artery, pathologic hypervascularisation, broncho-pulmonary anastomoses, periarterial diffusion and bronchial artery aneurysms. The dye was then injected under continuous fluoroscopic guidance, taking care to see that there was no reflux of gelfoam particles into the aorta. Embolisation was termed as complete when 95% of the peripheral branches of the bronchial artery were occluded and the antegrade flow stopped.

Results

The causes of haemoptysis considered at the time of diagnosis in all the 40 cases are shown in Table 1. History of haemoptysis intensity prior to arterial embolisation is given in Table 2.

After X-ray examination, the disease processes which probably caused bleeding were established.
Table 3. Chest roentgenology findings among cases treated by embolisation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Right lung</th>
<th>Left lung</th>
<th>Both lungs</th>
<th>Clear chest X-ray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>11</td>
<td>4</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Chronic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Fibro-cavitary lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>due to ankylosing spondylitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>5</td>
<td>22</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 4. Details of haemoptysis intensity at the time of embolisation

<table>
<thead>
<tr>
<th>Description</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massive</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>Moderate</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Streaky</td>
<td>9</td>
<td>22.5</td>
</tr>
<tr>
<td>No haemoptysis</td>
<td>3</td>
<td>7.5</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 5. Angiographic signs of haemoptysis

<table>
<thead>
<tr>
<th>Signs</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Extravasation of contrast agent</td>
<td>11</td>
<td>27.5</td>
</tr>
<tr>
<td>- Thrombosis of bronchial artery branches</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Indirect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hypervascularization</td>
<td>14</td>
<td>35</td>
</tr>
<tr>
<td>- Bronchial Pulmonary Anastomoses</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>- Penarternal diffusion</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>- Bronchial artery aneurysms</td>
<td>3</td>
<td>7.5</td>
</tr>
</tbody>
</table>

and the findings are shown in Table 3. The intensity of haemoptysis at the time of embolisation is shown in Table 4.

Radiographic signs considered pathognomonic of the site of haemoptysis prior to embolisation are shown in Table 5.

The sites of embolisation procedure appropriate to each case are shown in Table 6 and post-

Table 6. Details of embolisation procedure according to arterial site

<table>
<thead>
<tr>
<th>Artery</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right intercosto-bronchial trunk</td>
<td>7</td>
<td>17.5</td>
</tr>
<tr>
<td>Right bronchial artery</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Left bronchial artery</td>
<td>5</td>
<td>12.5</td>
</tr>
<tr>
<td>Right and left bronchial artery</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>Common trunk</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Right intercosto-bronchial and left bronchial artery</td>
<td>12</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 7. Post complications of embolisation

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>5</td>
<td>12.5</td>
</tr>
<tr>
<td>Chest pain</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>Chest pain and Fever</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td>Difficulty in passing urine</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Transient neuromuscular palsy</td>
<td>1</td>
<td>25</td>
</tr>
</tbody>
</table>

embolisation complications met with in Table 7.

We could achieve complete control of haemoptysis in 90% of the patients within 24 hours. Two patients had mild haemoptysis up to 1 week after embolisation. The other 2 patients had massive haemoptysis even after repeated embolisation; one underwent emergency lobectomy and the other expired. Recurrence of haemoptysis was met with in 4 cases (10%) within 72 hours and in 6 cases (15%) between 1 week to 6 months. Of the first 4 cases, 2 needed repeat embolisation. Overall success rate at end of six months was 75%.

DISCUSSION

Massive haemoptysis is defined as expectoration of blood of 200 ml to 1000 ml in 24 hours. Since most of our patients were anaemic, we considered a blood loss of 200 ml or more in 24 hours as life threatening. The main causes of haemoptysis were tuberculosis, bronchiectasis, chronic lung abscess and fungal infections. The primary source of haemoptysis was found to be from the systemic vasculature of the lung. In our series, the major site of bleeding was the right intercosto-bronchial trunk alone or together with left bronchial artery (47.5%), followed by the right bronchial artery alone or to-
gether with the left bronchial artery (35%). Among 40 patients, 4 patients had HIV infection, 3 had diabetes mellitus and 1 had hypertension. None of those illnesses were considered as contraindications, after the necessary precautions had been taken.

Gelfoam was used as the embolic agent in all the cases. Other materials that can be used are polyvinyl alcohol particles, isobutyl cyanoacrylate and absolute alcohol. Permanent occlusion of the bronchial arteries can be achieved by Gianturco steel coins and steel spirals.

Our results show that mortality from haemoptysis can be decreased 3 to 5 times as compared with what can be achieved by surgical methods. Besides, surgery is associated with 17.6% to 35% mortality while we had 2.5% mortality in our series.

Bronchial artery embolisation is a simple and life saving procedure and should be considered as the primary method of treatment in haemoptysis or as a preoperative method to stabilize the patient before surgery.
AN UNCOMMON CASE OF MULTIPLE PULMONARY ASPERGILLOMAS

Manoj K. Goel¹, Abdikarim Y. Mussa², J.N. Banavaliker³, D.C. Sharma¹, and Sanjeev Dikshit⁴

(Received on 8.1.97; Accepted on 8.3.97)

Summary: Concomitant occurrence of intrabronchial and intracavitary aspergillomas in a case of healed pulmonary tuberculosis is reported for the first time in the literature. Serum precipitin antibodies suggesting Aspergillus fumigatus involvement were demonstrated and its importance in the diagnosis of aspergillomas is stressed.

INTRODUCTION

The most recognised and common form of non-invasive aspergillus pulmonary involvement is the presence of aspergilloma. An aspergilloma consists of masses of mycelial hyphae which grow within a cavity to form a dense ball of fungal filaments in a matrix of fibrin, mucin and inflammatory cells. Aspergillomas have been met with in cavities associated with wide array of lung diseases including tuberculosis, histoplasmosis, sarcoidosis, asbestosis, ankylosing spondylitis and malignant diseases. The occurrence of multiple bilateral aspergillomas is an uncommon phenomenon. We present concomitant occurrence of intrabronchial and intracavitary aspergillomas in a case of healed pulmonary tuberculosis which, to the best of our knowledge, has not been reported in the literature.

CASE REPORT

S.D., a 30 year old female was admitted to Rajan Babu Tuberculosis Hospital with complaints of cough with excessive mucoid expectoration for 1 month and about of haemoptysis, of about 50 ml, a week ago. There was no history of fever, breathlessness, anorexia or weight loss. There was a history of pulmonary tuberculosis 2 years back for which the patient had taken regular antituberculosis short course chemotherapy (2RHEZ/4RH) with favourable clinical, radiological and bacteriological outcome.

On clinical examination, the general physical status of the patient was satisfactory. Examination of chest revealed trachea shifted to right side, right shoulder drooping and flattening in right infraclavicular area. On percussion, there was impaired resonance in right suprascapular and infraclavicular areas. On auscultation, coarse crepitations and increased vocal resonance were heard in right suprascapular and infraclavicular areas. The clinical examination of other systems showed no abnormality.

Investigations such as haemogram, urine analysis and blood chemistry comprising sugar, urea and creatinine estimation was within normal ranges.

Fig. 1. Chest roentgenogram (PA) showing shift of trachea to right, a cavity with fibrosis in right upper zone and calcified lesions with scattered fibrotic bands on left side.

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Sputum smear examinations by Gram and Ziehl-Neelsen staining were negative. Sputum culture for pyogenic bacteria showed no growth. However, on KOH mount, the sputum examination repeatedly revealed hyaline septate dichotomously branching hyphae suggestive of aspergillosis. Sputum culture grew *Aspergillus fumigatus* on Sabouraud’s glucose agar medium. The chest roentgenogram (Fig. 1) revealed a cavity with fibrosis in right upper zone and calcified lesions with scattered fibrotic bands on left side but showed no radiological deterioration when compared with the skiagram taken at the completion of the antituberculosis treatment 2 years back. The CT scan of thorax (Fig. 2) showed a cavity containing a hypodense ball with surrounding halo in left upper zone and a fibrocavitary lesion in right upper zone. Fiberoptic bronchoscopy showed a glistening ball like matter in the bronchus leading to the anterior segment of right upper lobe. Forceps biopsy of the ball followed by histopathologic examination of the biopsy material as well as examination of bronchial aspirate (Fig. 3) revealed hyaline septate branching hyphae and conidial structures i.e. vesicles with phialides of aspergillus species. *Aspergillus fumigatus* was isolated in culture. In addition, multiple bands of precipitin antibodies in the serum against *Aspergillus fumigatus* were demonstrated by Ouchterlony’s double immuno-diffusion test (fig 4). Thus, diagnosis of healed pulmonary tuberculosi with intrabronchial and intracavitary aspergillomas was made.

**DISCUSSION**

Aspergillomas usually come to notice in one of two ways: incidentally, on a routine chest roentgenogram or during evaluation for haemoptysis as in our patient. The investigations revealed that the patient had both intrabronchial and intracavitary aspergillomas concomitantly with healed pulmonary tuberculosis.

Aspergilloma formation occurs rarely within the bronchial lumen in cases of bronchiectasis associated with chronic sarcoidosis, ankylosing spondylitis and rheumatoid disease. In a study, spanning 25 years, only 6 cases of intrabronchial aspergillomas were detected out of a total of 77 patients having pleuropulmonary aspergillomas.
AN UNCOMMON CASE OF MULTIPLE PULMONARY ASPERGILLOMAS

Another report\(^8\) described a persistent aspergilloma within an area of bronchiectasis in a 52 year old man who later developed squamous cell carcinoma in the bronchial wall.

Computerised tomography is a more accurate technique than conventional chest radiography in defining the fungal ball, particularly within fibrotic and distorted lung fields.\(^9,10\) However, the radiological ball and the halo appearance around is nonspecific and can be found in a variety of other conditions. However, a positive precipitin test is characteristic of aspergillomas.\(^9\)

The exact incidence of pulmonary aspergillomas is not known. The estimated figures range between 0.016% and 17% in various studies\(^11,12\) but no estimate is available for India. The natural history of aspergillomas is variable: the fungal ball and the cavity in which it lies may enlarge, invasive aspergillosis may develop and in 7 to 10% cases aspergillomas may undergo spontaneous lysis.\(^12\) Our patient responded clinically to symptomatic treatment but aspergillomas persisted without any complication during 3 months of follow-up. Resection of aspergillomas was not done as surgery is recommended only if patients have massive or recurrent haemoptysis.\(^8,12\)

ACKNOWLEDGEMENT

We are extremely thankful to Prof H.S. Randhawa, Head, Department of Medical Mycology and Director, Vallabhbhai Patel Chest Institute, University of Delhi, for his valuable guidance and assistance.

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DEVELOPMENT OF PLEURAL EFFUSION DURING CHEMOTHERAPY FOR PULMONARY TUBERCULOSIS

U.K. Dasgupta

(Original received on 6.8.96 : Revised version received on 11.2.97 : Accepted on 22.2.97)

Summary : Three patients who developed pleural effusion after 55, 40 and 31 days respectively of starting antituberculosis chemotherapy for pulmonary tuberculosis are presented.

INTRODUCTION

Pleural effusion in tuberculosis is due to actual infection of the pleura by tubercle bacilli, although tuberculin hypersensitivity has a part to play in potentiating the reaction. Although tuberculous pleural effusions are quite common in our country, almost all such cases present initially with features of effusion. Rarely do we come across effusions developing after one or more months of chemotherapy. Three cases, one ipsilateral and two of bilateral pulmonary tuberculosis, who developed pleural effusion after 55, 40 and 31 days of starting chemotherapy with Rifampicin, INH, Ethambutol and Pyrazinamide are reported.

CASE REPORT

Case No. 1 : HR, a 32 year old male came to our clinic with complaints of fever and cough for 3 weeks. On examination, he was found to have a normal general condition, with average body weight. Body temperature was 101.2°F. Anaemia, cyanosis, clubbing of fingers and lymphadenopathy were absent. On auscultation, breath sounds were vesicular with prolonged expiration in the right mammary and right infrascapular regions. Coarse crepitations were audible in the right infra-axillary, interscapular infrascapular areas. No pleural rub was audible nor could pleural effusion be suspected on percussion. Examination of the other systems was within normal limits. Routine blood counts showed Hb-12.2g% RBCs 4.1 million/cmm; WBCs 6,900/cmm, N-60%, E-2%, L-37%, M-1%, ESR 84 mm/1 hour and sputum was positive by smear examination. X-ray chest revealed disease with multiple cavities in right middle and lower zones suggestive of tuberculosis. He was put on 2RHEZ/4RH schedule on 17.03.06. After one month of therapy, he was symptomatically better but still having a mild persistent fever. He was found to be regular with his drugs; blood smear was negative for malaria parasite and there was raised ESR (52 mm). Routine urine examination showed 6-8 pus cells/HPF with a trace of albumin. A repeat sputum examination (by smear microscopy) done on 3 consecutive days was negative for AFB. Culture for AFB was not possible, although the possibility of emergence of drug resistance was kept in mind. It was concluded that fever could be due to associated urinary tract infection. Cefadroxil 500 mg twice daily was given for 7 days and fever subsided after 4 days. However, on 12.05.96 he came back with complaints of heaviness and moderately severe right side chest pain with fever. Body temperature was 101.1°F. Physical examination and radiological investigation revealed right side pleural effusion. Thoracentesis revealed clear deep straw-coloured pleural fluid, deeper than usually seen in tuberculous effusions (possibly indicating penetration of Rifampicin into the pleural fluid). Laboratory examination of aspirated fluid showed no blood tinge, proteins 32.8%, sugar 98 mg%, RBCs (700/cmm, WBCs 3100/cmm with 92% lymphocytes and AFB negative by smear. Pleural biopsy could not be done due to lack of facilities. The same regimen was continued together with Prednisolone 30 mg daily tapered off over 4 weeks. He was re-examined after one month. Air entry was found to be equal on both the sides on auscultation. Chest X-ray PA view showed complete clearing of the effusion. His chest X-ray at the end of 6 months of treatment much

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improved and then the drugs were stopped.

Case No. 2 • UN, a 26 year old female came to our clinic with complaint of persistent fever. Her general condition was poor. On auscultation, a few crepitations were heard in the right infraclavicular region. Investigations revealed Hb 10.9 g%, RBCs 3.9 million/cumm, WBCs 7,800/cumm with N-68%, L-29%, E-3%; ESR 78 mm/1hr and sputum positive for AFB on smear examination. Chest X-ray revealed bilateral pulmonary tuberculosis. She was found to be a treated case of pulmonary tuberculosis having completed antituberculosis treatment 1 year ago with a 2RHZ/4RH schedule for 6 months. No sputum examination was done then. Since culture and sensitivity facilities were lacking, it was presumed that she had relapsed with drug sensitive strains. She was put on 2RHZ/SRH on 14.02.96. She was found to be sputum negative on 24.03.96 on follow-up but on the same day she complained of a recent pain on the right side of the chest. Clinically and radiologically she had developed a right sided pleural effusion. On thoracentesis, 100 cc of straw coloured clear pleural fluid was aspirated. It had 66.95 proteins, 82 mg% sugar, RBCs 300/cumm WBCs 3,700/cumm with 84% lymphocytes. She was kept on the same regimen but prednisolone was added as described in Case No. 1. She was re-examined after one month. Her pain was, by then, limited to a catching sensation on deep inspiration. There was no fever. Chest X-ray revealed a residual pleural thickening. On 18.08.96, she was again examined. By this time, only a mild discomfort on deep inspiration was felt. Before her treatment was terminated on 14.09.96. She had gained considerable weight, was afebrile but a mild pain remained on deep inspiration. Her chest X-ray showed fibrotic old lesions bilaterally and minimal pleural thickening.

Case No. 3 : ED, a 29 years old male who had his first chest X-ray done 1 'A' years ago which was suggestive of pulmonary tuberculosis. No antituberculosis treatment was given then because sputum was negative for AFB but 8 months later, he had another chest X-ray done and reported to another physician who gave him HEZ daily (no known reason for excluding Rifampicin in the schedule) which he took regularly for 3 months. Four months later, he reported to our clinic with haemoptysis and a mild left side chest pain and fever. On auscultation, a few crepitations were heard in right infraclavicular region. His sputum was still negative for AFB. Investigations revealed that Hb was 12.7 g%, RBCs 4.2 million/cumm, WBCs 7,300/cumm with N-73%, L-25% and E-2%. ESR was 97 mm/1 hr and Chest X-ray showed patchy infiltrations in right upper zone and old scars in left lower zone. Sputum was negative for AFB by smear. Based on the increased shadowing in right upper zone compared with the old X-ray and more opacities in left lower zone, he was given a 2RHEZ/4RH schedule. After one month, he was symptomatically better but a fresh chest X-ray revealed a small left side basal pleural effusion. No aspiration was done. He was advised to continue the same drugs and was re-examined after 1 'A' months when it was found that there was complete clearing of the basal pleural collection. There was also fibrosis in the right upper and left lower zones with significant clearing of the lesions. He was continued on the drugs for 6 months. A fresh chest X-ray then showed further clearing and his sputum status was negative.

DISCUSSION

Short course chemotherapy is very effective in the management of active pulmonary tuberculosis. Development of pleural effusion after more than 30 days of specific chemotherapy is, therefore, an uncommon event. In all such cases, as also in our cases, there was nothing to suggest treatment failure. All cases attained complete recovery without change of therapeutic regimens. Usually tuberculous pleural effusions develop:-

(a) By rupture of a peripheral focus or caseous lymph node into the pleura or the bacilli may reach the pleura via the lymphohaematogenous route.
(b) By rupture of a tuberculous cavity into the pleura.
(c) By rupture of caseous mediastinal node into pleural space or from a caries rib which can rarely cause pleural effusion.

In our cases, the likely mechanism was rupture of a subpleural caseous focus (in case 1) and spread via lymphatics or blood (case 2 and 3).

The absorption of the pleural fluid with the same drugs continued after aspiration, together with sputum conversion, implies that there was no failure of the therapeutic regimen. A predominant
lymphocyto’sis in pleural fluid and absence of acid fast bacilli in pleural fluid suggested that no change of therapy was indicated. Matthay et al state that a change in therapy can be considered if the following are noted - (i) progressive parenchymal infiltrates, (ii) increasing number of AFB on smear and culture, (iii) demonstrated microbial resistance, and (iv) progressive constitutional symptoms. Since none of the above were observed in our cases the same chemotherapy was continued with the addition of prednisolone in the first two cases to facilitate reabsorption and clearing of the pleural fluid.

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S. Rajasekharan, R. Bhanusree, V. Vallinayagi, V. Gopi

(Paper is being published in full)

Feasibility of Utilizing Traditional Birth Attendants in DTP

Rani Balasubramanian

(Paper is being published in full)
### Management of Multi-drug Resistant Tuberculosis-A 10 Year Experience

*Tuberculosis Research Centre, Chennai*

Of 3025 culture positive patients treated over a period of 10 years at Chennai and Madurai, 158 were found to be multi-drug resistant (HR) including 93 who were HR resistant initially. During initial short course chemotherapy (HRZE) only 12 (8%) responded favourably and 2% died. Of those 137 where chemotherapy was changed 45 (33%) responded to further treatment which included various combinations including such reserve drugs as Ethionamide, Kanamycin, Cycloserine besides SHZ and 34% died while 26% defaulted in treatment. The management of MDR cases with available drugs was not found to be satisfactory and hence it is important to prescribe judicious combination of drugs at start and improve patient adherence.

### Effectiveness of Default Retrieval Action in Tuberculosis Control Programme of India

*P B Prajapati and P. V. Kotecha*

Various reasons have been reported for shortfalls of NTP and one of them is lack of follow-up and deficient default retrieval actions leading to inadequate treatment.

The present study was designed to evaluate the effectiveness of default retrieval actions under DTP. The treatment cards of defaulting tuberculosis patients were studied at 20 randomly selected peripheral health institutions (PHIs) from two District Tuberculosis Centres (DTC) of Gujarat State.

The default retrieval success rates (DRSR) with different types of defaulter actions were analysed. The D.R.S.R. was maximum (60%) when the action was taken by direct contact with patient at home through health workers. The standardised default retrieval rates with and without effect of a defaulter action were 22.69% and 18.68% respectively giving 17-67% fraction of default retrieval to the defaulter action.

### Neopterin As Marker for Cell-mediated Immunity in Patients with Pulmonary Tuberculosis

*C. Immannel, Raji Swamy, M Kannapiran, S Vijayalakshmi, V. Sundaram, K. Jagannath and C.N. Paramasivan*

Cell mediated immunity (CMI) involves macrophage activation and T cell proliferation. These two parameters are compared in this study.

To ascertain the role of neopterin as a biochemical marker for CMI in patients with pulmonary tuberculosis, we measured neopterin levels in serum and the culture supernatants of peripheral blood mononuclear cells (MNC) after stimulation with PPD in 11 patients with pulmonary tuberculosis and 10 healthy individuals. Lymphocyte proliferative response to PPD was carried out in these two groups.

The mean concentration of serum neopterin was significantly higher in patients than in controls (P < 0.01). The spontaneous release of neopterin was significantly higher in culture supernatants of MNC from patients when compared with those of healthy controls (P < 0.05). Release of neopterin from MNC stimulated with PPD, however, was similar in both the groups. The neopterin release and the stimulation index (SI) in lymphocyte proliferation assay were not comparable suggesting that these two parameters do not run in parallel for measuring the status of CMI. However, serum concentration of neopterin was inversely related to the SI in a large proportion of subjects (66%).

Measurement of neopterin, a soluble product of immune cells (macrophage), may provide information on the state of CMI.

### Diagnostic Utility of Serum Effusion Albumin Gradient in Pleural Effusions

*K. Subhakar and G. Thippanna*

Serum effusion albumin gradient was measured in 60 individuals with effusion of varied aetiologies and compared with traditional Lights criteria for distinguishing between exudate and transudate. Us-
ing a gradient of 1.2 gm/dl or less to indicate exu-
date, and greater than 1.2 gm for transudate resulted
in correct classification of 59 out of 60 cases, while
3 cases of CHF were misclassified using Light’s cri-
teria. It is concluded that a gradient of 1.2 gm/dl is
both sensitive and specific.

**Estimation of specific Tubercular Immunoglob-
ulin “G” (TB IgG) in cases of Tuberculosis**

_S.K. Katiyar, R.P. Singh, S. Chaudhri, B.N. Tripathi
O.K. Sharma and Manoj Kumar Agarwal_

Estimation of specific tubercular immunoglobulin, “G”, TB IgG, was performed on the sera of 84
patients and controls in which 21 sputum smear
positive pulmonary tuberculosis patients and 42
healthy controls by using andraelsia mycobacteria
IgG kit (having antigen A-60 derived from _M. Bovis_
BCG). The sensitivity, specificity, accuracy and
positive predictive values were 71.43, 73.81, 72.63
and 73.17% respectively.

Among healthy controls, 26.19% were false
positives and among patients 28.57% were false
negatives.

**Trend of Sputum Positivity and Effect of Short
Course Chemotherapy**

_Anil Kumar Jain_

In 13 years (1983 to 1995), 7170 sputum posi-
tive cases were detected, with the help of 55 PHI’s
by this DTC catering to district of about 1.4 million
population. 3676 of these patients were treated with
short course chemotherapy. The number of cases
has shown a downward trend during 1992 to 1995,
the fall being uniform in men and women.

**Antimycobacterial Activity of Cephalosporins**

_N. Selvakumar and Vanajakumar_

The paper is not a research study but an expose
dealing with the scope of use of cephalosporins in
tuberculosis patients. Multi-drug resistant tubercu-
losis (MDR - TB) is being increasingly reported es-
pecially in HIV infected individuals. Therefore, re-
search has been intensified to identify new and po-
tent drugs to effectively treat such cases. Over six
hundred cephalosporins screened for their activity
against _M. tuberculosis_ H37 Rv generally displayed
poor activity as a result of their inactivation by
betalactamase enzymes produced by mycobacterial
species. Betalactamase resistant cephalosporins,
such as ceforanide, cefozoxime, cepahirin
cephalothin, cefazolin and cefataxime were found
more promising. Cefadroxil inhibited 60% of the
drug sensitive and 50% of the drug resistant clinical
isolates of _M tuberculosis_ at concentration which is
less than the peak plasma concentration attained in
human beings. These antibiotics, in combination
with betalactamase inhibitors, such as clavulanic
acid, sulbactam, tazobactam and BRL 42715 might
provide some insights into the suitability and ac-
ceptability of these drugs in the treatment of tuber-
culosis.

**Intra-thoracic Manifestations of HIV Infection**

_S.C. Tewari, B.N. Panda, R.S. Chatterji,
Sangameswaran and K.S. Rao_

The study is an attempt to analyse the pattern of
intrathoracic manifestations in HIV infected army
personnel from August 90 to January 96. Out of
573 registered cases of HIV positive patients (all
males), 103 were found to have one or more
intrathoracic manifestations (17.8%). Of them, 97
cases were of tuberculosis aetiology (95%) and 6
(5.8%) had _pneumocystis carinii_ pneumonia,
Bronchoscopy was not done in any case. Dissemi-
nated cryptococcal infection was found in five cases
on investigation. Pericardial effusion was diagnosed
clinically, radiologically and echo studies in 7 of
these 103 cases (6.8%). It was minimal in 2, moder-
ate in 4 and required repeated aspiration for im-
pending tamponade in one.

**HIV Sero-Prevalence in Patients of Pulmonary
Tuberculosis**

_K. C. Mohanty, Vijn Salve and Ajit Lale_

300 patients of pulmonary tuberculosis were
screened for HIV infection by ELISA and results
compared with a similar screening of 300 pregnant
women from the antenatal clinics. Whereas 9 (3%) pregnant women tested positive, the incidence of HIV infected among tuberculosis patients was 34/300, 30 of them being male (of 242 i.e. 12.39%) while only 6.8% i.e. 4 of 58 were females.

Among male tuberculosis + HIV patients, the majority were professionals and white collar workers, while labourers constituted the largest segment of HIV infected pregnant ladies.

**HIV Infection in Patients of Pulmonary Tuberculosis Including those with Atypical Presentation**


1670 patients, diagnosed as suffering from pulmonary tuberculosis, were screened for HIV infection using ELISA (Innotest HIVI/HIV2 Antibody sp. or UBI HIVI/2 EIA). In case of positive result a repeat test was undertaken for confirmation. Seven of 1034 males and 2 of 636 females were found to be seropositive to HIV. Disease pattern was typical in 2 and atypical in 7. None of the 47 patients with MDR tuberculosis tested positive for HIV. Six of the seven with atypical disease showed noncavitary focal infiltrates while one had hilar mediastinal lymphadenopathy.

**Mycobacteriology of HIV related Tuberculosis**


Between January 1990 and March 1996, 114 (20%) out of 573 HIV seropositive patients in the tertiary referral hospital of the Armed Forces in Pune were diagnosed to have tuberculosis on the basis of clinical, radiological and/or laboratory parameters. In 18 cases, AFB were demonstrated by direct microscopy whereas culture was positive in 245 patients. In 7 of the smear positives, culture was found to be negative while 13 of the culture positives were smear negative. Some of the cases had extrapolmonary tuberculosis.

Smear positivity was 39.4% in tuberculosis cases with negative HIV status in comparison with 15.8% in HIV positive TB cases (P < 0.05). Similarly, culture positivity was 43.6% and 21% respectively (P < 0.05). Overall bacteriological positivity in the seropositive patients of tuberculosis was 27.2% in comparison with 45% in our HIV negative tuberculosis patients during the corresponding period.

Isolates from the 24 culture positive patients were subjected to identification and sensitivity testing. Drug resistance was detected in 6 (25%) patients using indirect susceptibility testing against HRSZE compared to 12% resistance among HIV negative tuberculosis cases during the corresponding period. No atypical mycobacteria were isolated in any of the HIV seropositive patients. All patients showed good therapeutic response to anti-tuberculosis treatment in a sanatorium setting.

This study suggests that even with meticulous effort, in the HIV associated TB cases, there is a chance of missing up to 42% bacteriologically positive cases if total reliance is placed on 3 consecutive specimens for AFB examination by smear microscopy only.

**Place of Artificial Pneumoperitoneum in the Management of MDR Pulmonary Tuberculosis**

A.K. Janmeja and Baldev Raj

Thirtyeight patients having persistently positive sputum after long term chemotherapy whose mycobacteria were resistant to at least two but up to 5 of the antitubercular drugs in common use, were selected for pneumoperitoneum (PP), continuing the same at weekly intervals for 1½ to 2 years, along with HT or HE, irrespective of the resistance pattern. Only 14 completed the planned duration of PP while 17 defaulted and PP had to be discontinued due to side effects. Quiescence was achieved in 13 of those who completed the course, but two of them relapsed during a one year follow-up. Amelioration of toxaemia, weight gain and sputum conversion were achieved in 30, 21 and 18 cases respectively taking the population as a whole. Minor complications like pain abdomen and shoulder were encountered in 8 cases, while 4 had major complications e.g. hernia and mediastinal emphysema. It is concluded that some cases of MDR tuberculosis can
be salvaged and rendered non infective by adding PP to the regimen.

**Pneumo-peritonum in Modern Management of MDR Pulmonary Tuberculosis**

*R P. Bhagi, S.C. Kapoor and S.R Mathur*

The recent resurgence of tuberculosis worldwide and rapidly increasing multidrug resistance necessitate a look for other methods of treatment, so that twin objective of patient cure and elimination of infectivity are met. Pneumoperitonum, a common method of treatment in the pre-chemotherapeutic era, has almost totally been abandoned, due to euphoria created by modern chemotherapy. However, it may be recalled that a fair percentage of patients did have their disease arrested in that age, when treatment consisted of rest, diet and collapse therapy of which pneumoperitonum was a prominent constituent.

Mathur SR and Kapoor SC (1975) reported good measure of success in chemotherapy failures responding to pneumoperitonum with chemotherapy.

In present study, in 137 cases with extensive bilateral disease and relapses, treated with pneumoperitonum and SHREZ for 9 months to a year, 91 (66.42%) showed improvement, 28 (20.44%) cases showed no change and 18 (13.14%) died.

Sputum smear conversion was attained in 115 out of 137 patients, of which 104 (76.9%) converted in 6 months or less.

From this study it can be concluded that pneumoperitonum can be a useful additive to SCC in the management of MDR/Drug failure cases.

**Lung Abscess : an Analysis Based on 200 Cases**

*A L. Anand*

Acute lung abscess is a serious, sometimes even fatal, thoracic disease. 200 cases of this condition were treated at K.J. Mehta TB Hospital, Amargadh during 1966 to 1990. Radiographic diagnosis rested on cavity with fluid level, usually with surrounding consolidation. Secondary abscess and fungal parasitic diseases were excluded from the analysis. Prompt, appropriate and adequate antibiotic therapy resulted in cure and surgery was necessary in only 10 of the cases.

**Profile of Lung Cancer Patients in Government General and Chest Hospital, Hyderabad**

*G. Thippamma, K. Venn, K. Subhakar and B. G Saicharan*

A retrospective analysis of 160 cases of bronchogenic carcinoma diagnosed between January 1994 and May 1996 showed that they constituted 1.2% of admissions to this general hospital. These patients ranged between 38 and 72 years in age, and 17 of the 160 patients were females. Lymphomas, primary cases of the lungs and metastatic tumours were excluded. Cough and chest pain were the commonest symptoms (47%) and clubbing (29%), scalene node enlargement (25%) and pleural effusion (30%) were the more frequent findings. FOB (biopsy) was used for confirmation in 46% transmoralc needle biopsy in 40% and FNAC of scalene or cervical nodes in 14% cell carcinoma was found in 108/160 i.e. 66%.

**Role of NGOs in the Control of Tuberculosis in Pakistan**

*Dr. Saeed-ul-Majid*

The Pakistan Anti-tuberculosis Association (PATA) came into existence in February 1949. It was affiliated to IUATLD in 1953. As the main NGO in Pakistan, it plans, co-ordinates, guides and supervises the activities of its branches. And, it complements and supports Government’s efforts to control TB in the country.

The branches, established country wide, provide diagnostic, curative and preventive services. PATA also has diagnostic TB clinics, hospital beds, drug distribution centres, rehabilitation centres, health education programme and BCG Vaccination programme. Besides, it has a panel of chest specialists, school health programme, population control programme, publications, participation in national and
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international conferences and fund raising.

Besides PATA, there are a few other NGOs as well. These are: Anti-tuberculosis Association (Geneva, Switzerland) in NWFPA, since 1984, with branches at Asadabad, Bannu and Attock; Red Crescent Society running 5 TB clinics and 55 TB beds, Italian Cooperation for Development (ICD) working for Afghan refugees and Pakistan Chest Foundation with chest societies at Central and provincial levels for arranging workshops and conferences.

Government’s Tuberculosis Control Programme was started in 1962 and revised in 1989 and 1994. It is integrated with general health services. It aims at reducing mortality, morbidity and transmission of the disease by the year 2000. Since 1994, DOTS pilot projects have been introduced in Peshawar and Karachi.

Ashwagandha as Immunoadjuvant with Chemotherapy in Management of Pulmonary Tuberculosis

O.K. Pandey, A.K. Kapoor and M.S. Agnihotri

An immunomodulatory drug Ashwagandha was used in the treatment of 20 patients with newly diagnosed sputum positive pulmonary tuberculosis as an advent to chemotherapy. A control group received only chemotherapy for tuberculosis. The patients were followed up for two months. The parameters compared included speed of clinical recovery, rate of sputum conversion, rate of weight gain, clearance of radiological lesions and increase in TB lymphocyte percentage.

The results showed significantly better response in fever, weight gain, sputum clearance and increase in T Lymphocyte percentage in study group as compared to control group. However, although early response in other symptoms and early radiological clearing was found in study group but statistically it was not significant.

Smoking as Risk Factor in Tuberculosis

T.M. Dhamgaye

The study was undertaken to assess if smoking is associated with development of active pulmonary tuberculosis. A case-control study in which 135 cases with active pulmonary tuberculosis and 106 controls were included. The overall prevalence of smoking in pulmonary tuberculosis cases was 25%, whereas in control patients it was 23%. The prevalence of heavy smokers in pulmonary tuberculosis was high (14.8%) while in control group it was 5.6%. Smokers of 20 years and more duration had a threefold greater risk than that of ‘never smoked’; their risk was significantly higher (OR = 2.7; 95% CI = 1.1-7.0; P< 0.05).

Treatment of Chemotherapy Failures: An interim report

U.K. Dasgupta, S. Mukhodadhay, B. Banerjee and S. Dutta Choudhury

29 cases of sputum positive pulmonary tuberculosis admitted to K.S. Ray TB Hospital, Jadavpur, Calcutta who had failed to respond to various chemotherapeutic regimes containing S, R, H, E, Z and T after at least 6 months’ hospital treatment were isolated and treated in a separate ward with individualised drug schedules, under direct supervision, depending chiefly on their previous treatment history (in absence of culture and sensitivity facilities). The drugs were the ones already in use, with the addition of Ethionamide, Amikacin, Ciprofloxacin, Cycloserine, Kanamycin and Morphazinamide, at least two drugs being added to existing regimen.

An interim analysis after 3 months of supervised chemotherapy revealed death of 1 patient (following severe haemoptysis and asphyxia) and 1 opted for discharge. Of the remaining 18 patients, 12 were rendered sputum negative (60%). It is concluded that in the absence of information about sensitivity in cases of presumed MDR, judicious individualised treatment with second line drugs, under strict supervision, can be very effective in the management of such cases.

Role of Intracath in Acute Primary Spontaneous Pneumothorax


During January, 1993-October 1995, 25 cases of
acute primary spontaneous pneumothorax were treated with 14G Venflon intracath underwater seal drainage at bedside. All patients received simultaneous oxygen and broad spectrum antibiotics. The lung expanded completely in all the cases within 24 to 48 hours. Only in 2 cases localized emphysema occurred. No recurrence occurred during the study period. The procedure can be done as first line life saving procedure even in remote places.

Rapid Diagnosis of Extra Pulmonary Tuberculosis: Fine Needle Aspiration Cytology Versus Histopathology

R. Sreelatha, C. Jyothi Prakash, Y.A. Manjunath, N. Gandhi and B.K. Arun Kumar

Out of 612 FNACs carried out, peripheral lymph nodes constituted 149 (24.3%), majority from cervical group. Tuberculosis was diagnosed in 54 (36.2%) of the cases using the strict criteria of presence of caseation and epithelioid cells with or without Langhans giant cells. 75 (50.3%) of the lymphadenopathies were non-specific, 14 (9.4%) acute lymphadenitis, 4 (2.7%) metastatic deposit and 2 (1.4%) malignant lymphoma.

During the same period 1427 biopsies were carried out of which 85 (6%) were peripheral lymph nodes. Of the lymph node lesions, tuberculosis was diagnosed in 42 (49.4%) followed by non specific reactive lymphadenitis 33 (42.3%) acute lymphadenitis 3 (3.5%) metastatic deposit 3 (42.3%) acute lymphadenitis 3 (3.5%) metastatic deposit 3 (3.5%) Hodgkin nodular sclerosis 1 (1.2%) and Castleman's preponderance. Majority of the patients were in second and third decade. The youngest patient was a male child aged two and a half years and the oldest, a 60 years old male.

Bronchoscopy in the Diagnosis and Management of Respiratory Diseases - Our Experience

Shashidhar Buggi, M.D. Patil, T.K. Ravindranath and Sathyaprakash

A prospective study of 1619 bronchoscopies over 5 years and excluding diagnosed cases of pulmonary tuberculosis is the basis of this report. Bronchoscopies in 175 of these cases yielded definite malignancy, in 8 suspicion of malignancy, in 10 inflammatory in 103, squamous metaplasia in 23 and allergic appearance in one. Normal cytology was seen in 30 cases.

In pediatric age group, bronchoscopy was usually performed for therapeutic indicators, such as a removal of foreign body.

Treatment of Multi Drug Resistant Tuberculosis: Strategies and Outcome


During the period April 1992-December 1995, 4011 patients of Pulmonary tuberculosis (PTB) were treated at our centre. Sputum culture demonstrated Mycobacterium Tuberculosis (MTB) in 1629 (40.6%), out of which 203 (12.5%) showed drug resistant strains. More than one drug resistance was noticed in 76 cases. Fifty eight patients showed resistance to two drug (SH-26, SR-18, HR-07, SZ-04, HE, ER and RZ, 1 each), 3 or more drug resistance was found in 18 (SHR-10, SHE-3, SHE and SHZ-1 each, SHRE, HRZE and SHRZE 1 each). All these cases were analysed for their treatment outcome and followed up for 8-52 months (Mean 25.2 months).

There were 6 deaths in this group and 4 cases were lost to follow up. Patients with two drug resistance, except those with RH resistance, responded well to additional 2-3 new reserve drugs. Patients with RH resistance and with resistance to 3 or more drugs responded well to a combination of 5-7 drugs which included 3 or more reserve drugs. In 5 patients drug regimes had to be changed as response to initial reserve drug combination was not satisfactory. With good culture and ABST support there was good response in 61 cases (80%). Multi-drug resistance is a dangerous situation in tuberculosis chemotherapy and it is being increasingly encountered not only in Indian population in general but also in Armed Forces. With initial hospitalisation and regular monitoring including culture and ABST support excellent response can be expected.
Hyperuricaemia in Tuberculosis patients on Pyrazinamide

B.B. Samanta and A. Madan

In a case control study, serum uric acid was estimated in 50 (34 males, 16 females) confirmed cases of tuberculosis on PZA divided into 3 age groups (Group A < 20 years, Group B 21-39 years, Group C > 40 years) after one month of Pyrazinamide (PZA) therapy and after one month of omission of PZA. Serum uric acid was also estimated in 50 age and sex matched controls. Serum uric acid concentration of cases on PZA was significantly higher than in controls (8.88 ± 2.21 mg/dl Vs. 4.42 ± 0.99 mg/dl, P < 0.01) and the level came down to nearly the same as that of controls (4.64 ± 1.27 mg/dl P > 0.05) after month of omission of PZA. All cases on Pyrazinamide had biochemically detectable hyperuricaemia of varying extent. Hyperuricaemia was asymptomatic in 46 (92%) cases, 4 (8%) cases developed polyarthralgia, 3 cases responded symptomatically to NSAID, in one case Pyrazinamide had to be discontinued due to intractable arthralgia not responding to NSAID.

Atypical Mycobacteria in Patients of Pulmonary Tuberculosis in Lucknow

K Saresh Babu, P.K. Mukherji, Rajendra Prasad and S.K. Agarwal

Two hundred and thirty six sputum specimens from patients diagnosed as active cases of pulmonary tuberculosis aged 12 years and above were subjected to culture on Lowenstein - Jensen slopes. Of these 46.2% (109/236) showed growth of acid fast bacilli. 10 (9.2%) of these cultures were identified as atypical mycobacteria. Runyon’s group III was the most frequently isolated organism (50%) followed by group II and IV (30 and 20%) respectively. The most frequently isolated species was M. malmoense and M. gordonae (2 each) followed by M. avium intracellulare, M. cxnopi, M. fortuitum, M. gastri, M. terrae and M. flavescens (1 each).

Controlled clinical trial on treatment of lymphnode tuberculosis

Tuberculosis Research Centre, Chennai

(a) Twenty one percent of the patients were below 10 years and 64% were in the 10-29% group.
(b) Sixty nine percent of the patients were females
(c) Sixty percent of the patients had large reactions to 1 TU PPD (20 mms or more) and 33% had very strong reactions (40 mrtis or more).
(d) Sixty eight percent of the patients had positive lymph node culture for M. tuberculosis.
(e) Interim results at the end of 9 months of follow-up after treatment shows that both the supervised and the unsupervised regimens are effective in the treatment of biopsy proved lymph node tuberculosis in children and adult.

Unsupervised Intermittent Short Course Chemotherapy with Intensive health Education as an alternative to Dot

L.R.S. Instt. Of TB and Allied Diseases

This paper presents an alternative to DOTS where the pattern of treatment remains similar to DOTS but with the difference that the patients were given intensive health education and the therapy was not directly observed.

A total of 300 patients categorised into category-I (127), Category-II (79) and Category-III (94) were studied. On the whole 277 patients were studied as 23 patients had to be excluded for various reasons e.g. death, hospitalization, transferred to other centres. The main focus was intensive health education at the start of therapy and on every visit. For sputum positive case (n = 202), sputum conversion at the end of 2nd month and 3rd month was 56.3% and 85% respectively. Initial sputum conversion for Cat-I by two months and three months was 69% and 86% respectively . Similarly for Cat-II, at three months, conversion rate was 86%. Total defaults were 53 (19%); Cat-I 12 (17.3%), Cat-II 19 (21%) and Cat-III 18 (19.2%). Defaults were largely because of wrong address, economic causes and early relief of symptoms. The cure rate in Category-I was 71%, Category-II 65% and Category-III 73% with an overall cure rate of 70%. The compliance rate in Cat-I was 80%, Cat-II 80%, Cat-III 78%, an overall rate of 79%.
Socio-behavioral pattern of 1000 chest symptomatics attending a city TB clinic was studied using a specially designed questionnaire. The behaviour pattern was studied in respect of nature of health providers contacted, reasons for attending particular health provider, lapse of time in contacting a health provider (initial delay), delay in starting of specific treatment.

It was observed that out of 1000 chest symptomatics 308 had pulmonary tuberculosis. Symptomatics, by and large, do not delay in remedial action as 72% of the chest symptomatics contacted medical facility within 30 days of development of symptoms and nearly 18% delayed this action for more than 60 days. Majority i.e. 74% of the chest symptomatics contacted general practitioners and 18% contacted general hospitals. It is seen that 23.4% of the symptomatics attended TB clinic directly and 64% had attended after visiting one health facility.

Both tuberculous and non-tuberculous chest symptomatics behaved similarly in their relief seeking action with a preference to attend a general practitioner rather than a TB clinic even if facilities are free and conveniently located. First preference for general practitioner existed even in the study conducted by this Centre in 1971 but now, in 1996, it has increased from 31% to 71% probably due to better rapport, convenience and their large numbers.

Role of N.G.O.s and Voluntary Organisations in Case Holding and Treatment Activities in District TB Control Programme

P. Rama Rao

Conclusions:
1. For better cure rate and completion of treatment, Voluntary Organisation should be made part and parcel of National TB Control Programme.
2. Mobile Camps only for case finding but not for case holding.
3. Motivation by District TB Control Officer/ Medical Officer/Treatment Organisers is must. For subsequent motivation and retrieval of the patient, an extra worker is must.
4. Drug delivery to the nearest point of the patient’s residence is best for case holding,
5. Home visit is the best for case holding rather than letter posted.
6. After observation, one field worker for 20,000 to 30,000 population to attend the National TB Control Programme.
7. Proper and sufficient drug supply in time is must for better case holding activities.
8. Extra funds needed from other sources on par with Eye Camps, Family Welfare, and Leprosy Programmes.

Clinical Progression of Tuberculosis in HIV Patients with CD4 Levels Correlation

K. Subhakar, G. Thippanna, and B. G. Saicharan

Sixteen cases of Tuberculosis admitted in A.P. Chest Hospital tested positive for HIV and were taken into this study. The progression of the disease (including the clinical presentation and radiographic features) were correlated with the CD4 counts.

Tuberculin Reactivity in Families of Tuberculin Non-Reactor B.C.G. Vaccinated Children

S.K. Katiyar, R.P. Singh, Sudhir Chaudhri, D K. Sharma and Ashish Agarwal

Attempts to define a molecular basis m humans for susceptibility to mycobacterial infection and/or immune response to mycobacteria have been inconclusive to date. The present study was undertaken to compare the tuberculin reactivity of B.C.G. immunized parents and siblings of children who failed to respond to B.C.G. and of children who developed persistent tuberculin reactivity after immunization.

In this study a sample population from rural areas of Kanpur was selected. The study children and their families were identified and registered on individual cards by visiting them at their home. Tuberculin test was done with 5 T.U. on all B.C.G. vaccinated study children below 5 years of age and the in
duration was read after 72 hours. Parents and siblings of tuberculin reactor children were the control group.

Tuberculin test was done on the B.C.G. vaccinated parents and siblings of tuberculin non-reactor children and of tuberculin reactor children. On the basis of tuberculin test, necessary information was derived.

In our study, the comparison of tuberculin reactivity of parents and siblings of children who failed to respond to B.C.G. and of children who developed tuberculin reactivity after B.C.G. immunization did not reveal any significant difference.

The Role of Non-Governmental Organisations in Tuberculosis Control

Tuberculosis Research Centre, Chennai

The National Tuberculosis Control Programme, which has been in operation for more than 30 years has not had much of an impact on the control of the disease, mainly due to poor patient compliance with treatment. One of the reasons for this is poor awareness in the community about the seriousness of the disease and the danger it poses to the family and society. Unless this lacuna is rectified, all efforts from the Government will not achieve results.

The concept of development needs to be visualised in the context of local situations and prevailing ideologies. Development implies change, through the process of conscientisation, followed by collective action. This initiative has to necessarily start at the grass root level.

The Tuberculosis Research Centre has entered into a network of working with various Non-Governmental Organisations (NGOs) in Chennai, to explore the feasibility of utilising their services in tuberculosis control activities. The major thrust areas of this strategy are to train grass root level workers of the NGOs in order to:

(a) equip them with basic skills necessary to identify cases of tuberculosis in the community and refer them for treatment.
(b) create awareness about tuberculosis in the community,
(c) organise health camps to screen for cases of tuberculosis.

The training of the grass root level workers is carried out by a team consisting of Doctors and Social Workers according to a Training Manual Developed by the TRC. Groups of 30-50 grassroot level workers of different NGOs are trained in each session. Brief lectures on the medical and sociological aspects of tuberculosis, a role play to highlight the sociological aspects, quiz programmes and open house discussion are used as appropriate. The response of the NGOs has been very encouraging and we are optimistic that they can be trained to be an effective task force for tuberculosis control.

In the future we plan to utilise the services of the NGOs in other aspects of tuberculosis control, such as case holding and drug delivery.

Iii-Depth Study of Reporting System - Experience of Clinical Section of Lady Willingdon State TB Centre, Bangalore

H. Junjanna and B. Y. Nagaraj

State and National reports are prepared for the Tuberculosis programme based on the reports received from grass root level functionaries like Dispensaries, Primary Health Centres etc. Many a time these reports become discussion documents for remedial measures for the programme and for revising the national policies and are stressed at every level. Lady Willingdon State TB Centre, Bangalore, prepared the periodic reports for the State based on the reports received from Peripheral Health Institutions and its Clinical section. To study the validity of reports for better understanding the Lady Willingdon State TB Centre analysed the Annual Reports of its clinical section for five years - 1991 to 1995. This analysis revealed some striking factors. This paper discusses in detail these factors which need close look into the functioning and reporting of peripheral health institutions which are the components of District Tuberculosis programme.
Broncho Pleuro Subcutaneous Pneumocyst: a Case Report

E. Ravindra Reddy, K. Venn, B, T. Prasad and N.S. Reddy

A 30 year old female patient presented with cystic swelling in the right axillary region. There was a past history of right sided pneumothorax managed with rube thoracostomy. Detailed work up and the line of management is presented.

Increased Yield of Excretory-Secretory Antigen with Thyroxine Supplementation in in vitro culture of Tubercle Bacilli


Excretory-secretory antigen (ES antigen) obtained from short term • in vitro culture of Mycobacterium tuberculosis H37Rv strain, has been shown to be of immunodiagnostic interest. Attempts were made to increase the yield of ES antigen in culture medium. In this study, the effect of thyroid hormone supplementation in culture medium on the bacillary growth and on the yield of ES antigen has been evaluated.

Synthetic thyroxine (Eltroxin, Glaxo Labs, India) was added at an optimal concentration of 4 Hg/ml to Lowenstein - Jensen medium for seed culture and at varying concentrations ranging from 2 µg to 16 µg/ml in synthetic Sauton medium for subculture. Bacillary growth in Sauton medium was measured by colorimetry and ES antigen protein obtained from culture filtrate was estimated by Lowry’s method. Thyroxine supplementation in subculture medium resulted in increased bacillary growth and higher yield of ES antigen protein in dose dependant manner. Addition of 8 (µg/ml of thyroxine in Sauton medium gave four fold increase in the yield of ES antigen as measured on seventh day of subculture.

A partially purified fraction (Mtβ EST antigen) of this ES antigen was analysed for antigenic activity by Sandwich ELISA using affinity purified anti Mtβ EST antigen antibody and its seroreactivity was studied by Indirect ELISA using tubercular patients’ sera. Mtβ EST antigen obtained after thyroxine supplementation showed similar reactivity in antigenic litre and in detection of tubercular IgG antibody in patients sera as compared to that of the control Mtβ EST antigen obtained from culture medium without thyroxine.

Thus, it is concluded that thyroid hormone supplementation in culture medium of tubercular bacilli in vitro helps in getting better yield of excretory secretory antigen of immunodiagnostic importance in shorter duration.

A Case Control Study on Tobacco Smoking and Lung Cancer

R. Prasad, S. Tandon, S. Kumar, M.C. Pant, K.N. Sinha and P.K. Mukherji

A case control study was done to study the risk posed by various smoking habits in the development of bronchogenic carcinoma. All the consecutive 52 newly diagnosed and histopathologically proven bronchogenic carcinoma patients who had come to the hospital for treatment were included in the study and 156 healthy attendants of patients matched for age, sex and socio-economic status were included as controls. A pretested questionnaire was used to seek information on socio-demographic and smoking habits of cases and controls.

A fairly strong association was found between smoking and lung cancer. Out of 52 lung cancer patients, 39 (75%) had consistently smoked and only 55 (35.3%) of 156 controls had smoked. Of 39 smokers in cases, 26 (66.7%) smoked bidi and of 55 smokers in controls, 40 (72.7%) smoked bidis. Tobacco smokers on the whole had 5.5 times greater risk of lung cancer than nonsmokers (OR : 5.51 95% CI 2.56 - 12.02; ¥2 = 23.29; P < 0.001). Bidi smokers had 5 times greater risk of lung cancer than nonsmokers (OR : 5.05 95% CI 2.21 - 11.7; ¥2 = 17.68; P < 0.001). The risk increased with the number of bidis smoked per day and the duration of smoking. A comparative risk factor for lung cancer in cigarette and bidi smokers could not be assessed because of the small number of cigarette smokers in the study population.
With MDR tuberculosis being perceived as a real threat, the scientific community is increasingly turning to the quest for newer antimicrobial agents. Of particular interest to our readers would be the information that this search is also being conducted in Asia, with Indian scientists also contributing their efforts. Some institutes of national importance have been exampling Ayurvedic and Unani drugs. A senior TB specialist has been trying out henna, the common ‘mehndi’, for antimycobacterial properties and has reported good activity in animal experiments. A clinical trial has recently been initiated and preliminary results are claimed to be encouraging. It is hoped that, if this inexpensive herb proves effective, proper scientifically planned and controlled clinical trials will be conducted to determine its relevance, or other wide, as an antimycobacterial agent.

NEWSLETTER FROM KIYOSE

Alumni of the International Training Courses organised by the Research Institute of Tuberculosis (RIT), JATA, Kiyose-shi, Japan, would be glad to know that Dr. Toru Mori has been promoted as Director of RIT from July, 1996. He has succeeded Dr. Masakazu Aoki, who has been made Chairman of the Board of Directors of the RIT.

Dr. Mori, who has made notable contributions in the field of tuberculosis research and training of international programme managers as well as tuberculosis workers from all over the world, has a special message to the countries where its alumni are occupying important positions in the National Tuberculosis Programmes or Directorates of Health Services.

“With the advent of technological innovations in medical sciences..... old ideas such as community participation should be revised.” Recalling the earlier experience in Japan of working with women’s groups in order to enlist community participation, Dr. Mori has found a wonderful change in the scenario. Twenty years back, the women’s groups and similar other social organisations were considered as early channels for publishing the public services and creating public awareness. Now, in Japan, these lay persons’ groups have become an important part of the health infrastructure, becoming an integral part of the development of public health services in Japan. In doing so, these organisations have fully adopted the new technologies, yet retained the community movement and not become a financial burden on the Government. A welcome step has been the consequent close interaction with the health insurance system of the country which probably had much to do with their financial stability and successful activities in the preventive as well as curative fields. In other words, community participation in Japan has developed into good harmony with modern technology and integration with the country’s health system.

The above success story should be a beacon to our own efforts at voluntary organisations becoming equal partners with the Government in the control of Tuberculosis.
FORUM

Sir,

In the Forum column of the latest issue of the IJT (1997, 44, 53) you have invited comments on my suggestion regarding numbering of pages in the references cited at the end of articles. May I say that:

(1) It is a standard way of giving bibliographic details in literature.
(2) It gives an idea to the reader about the total number of pages in an article.
(3) It helps in cost calculation to those providing photo copying service.

Sudha S. Murthy
NTI, Bangalore

RNTCP-Need for review?

Sir,

Even though we possess highly effective anti tuberculosis drugs and regimens, control of tuberculosis is nowhere in sight. Less than 30% TB patients complete their prescribed treatment in our country. A number of solutions have been put forward to make patients take treatment regularly. Directly Observed Therapy-Short Course (DOTS) has been adopted as the best strategy for curing tuberculosis under RNTCP. However, its applicability is tied up with economic considerations. Under the Revised Strategy for National Tuberculosis Control Programme (RNTCP) supervised intermittent SCC is given to all tuberculosis patients. The intensive phase is directly observed and drugs are given three days a week, by responsible peripheral functionaries and the continuation phase is also appropriately supervised. Will this revised strategy really solve the problem of non-compliance?

The Tuberculosis Chemotherapy Centre (TCC), Madras evolved supervised intermittent chemotherapy (SIC) in early 1960s as an alternative method of treatment to overcome irregularity in self administration of drugs. The supervision of all doses in the clinic ensured that there was no hidden irregularity in treatment. The concept of intermittent chemotherapy was hailed then as one of the landmarks in the treatment of tuberculosis. However, because of the tremendous organisational problems involved, the applicability of SIC was not feasible at the national level, though a fully supervised twice weekly regimen was included in NTP. WHO has now recommended various daily, partially intermittent and fully intermittent short course regimens for various categories of TB patients. The intermittent SCC regimens prescribed under RNTCP are shown in Table 1.

The advantages of intermittent chemotherapy regimens are well known. They are equally effective as daily regimens; may cause less toxicity and may eventually be cheaper also. They contain fewer doses of medication and are, therefore, likely to be better accepted or preferred by the patients. But, to be really successful these have to be given under direct observation (DOTS).

We need to consider the following factors (many peculiar to our set-up) seriously before we can predict the outcome of DOTS.

1. DOTS has to be given under direct observation during the intensive phase and appropriately supervised during the continuation phase. After 35 years of experience with the resources made available to NTP, will it really be possible to organise RNTCP effectively in our vast country?

2. “Good quality” of supervision of drug administration will be maintained during the continuation phase through MPWs, Anganwadi workers, dais, etc. Without estimating the working potential of these workers, is it justifiable to expect “extra-ordinary” performance from these workers, who are supposed to perform numerous other health-related duties also? Or to give them incentives under DOTS and take their attention away from other duties?

3. Depending upon the needs, Private Practitioners (PPs) are planned to be fully involved in RNTCP. The idea seems laudable on paper but unlikely to succeed, keeping in view the past 35 year experience of NTP. How are we planning to involve PPs when nearly 50% of our TB patients are presently managed by PPs who can not provide supervised services? Besides, when SIC was introduced in the 1960s, the concept of intermittent chemotherapy was misunderstood by many.
Quite often, instead of giving both the drugs together twice a week, Isoniazid was given daily and Streptomycin twice weekly. This resulted in emergence of resistance to Isoniazid first and to Streptomycin subsequently. How can we ensure that a similar “mishap” will not occur now under PPS.

4. Though the RNTCP may lay maximum stress on “supervision”, in reality a majority of our patients will be “self-administering” their dosages, irrespective of what the records tell. In this regard, following factors need consideration:-

(a) In intermittent regimens, every dose of medication is very important and ideally not a single dose should be missed. Have we adequately stressed this aspect to our health workers and patients?
(b) Human nature being what it is, one is more liable to forget something which is to be done periodically than what is to be done daily.
(c) Our relatively less educated patients may interpret a regimen which is not to be taken daily as relatively less important and so can be missed.
(d) The large bulk of medicines to be taken as a single dose may not be tolerated by some patients.
(e) Under RNTCP, a patient is required to make more frequent visits to the treatment centre than under NTP presently. Frequent visits, either by patients or by treatment providers, are likely to adversely affect the compliance.

With so many queries, will it be justifiable to launch RNTCP nationwide at this stage? This revised strategy certainly deserves further discussions and deliberations before its wider implementation.

Rajinder Singh Bedi

Table 1. Intermittent short course chemotherapy regimens prescribed under RNTCP.

<table>
<thead>
<tr>
<th>Category</th>
<th>Type of patient</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>New sputum positive cases and seriously ill sputum negative pulmonary and extra-pulmonary patients</td>
<td>2 R₁ Z₁ H₁ E₁/4R₃ H₃</td>
</tr>
<tr>
<td>II</td>
<td>Relapses and treatment failures</td>
<td>2 S₁ R₁ Z₁ H₁ E₁/1R₃</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Z₁ H₁ E₁/5R₃ H₁ E₁</td>
</tr>
<tr>
<td>III</td>
<td>New smear negative (not seriously ill) pulmonary and extra-pulmonary cases</td>
<td>2R₃ Z₃ H₃/4R₃ H₃</td>
</tr>
</tbody>
</table>

The number given in front of the drug regimen indicate months of treatment and subscript number refers to number of times per week.

Need for “Genuine” CMEs for Tuberculosis

Sir,

We are nowhere near controlling tuberculosis (TB). Of the various reasons advanced as responsible for this undesirable situation, poor drug-regimens and poor patient compliance deserve maximum attention. Finding solutions to these two will help not only in managing the present pool of cases but will also help in the long run by acting as very effective measures for prevention of TB, as well as MDR-TB. If we carefully analyse the situation, the person responsible for both these factors is the treating physician, by and large, and not the patient. After all, who is expected to educate him and make him compliant? Unfortunately, we are not ready to accept this hard fact. James Jackson once quoted, “I have often remarked that, though a physician is sometimes blamed very unjustly, it is quite as common for him to get more credit than he is fairly entitled to; so that he has not, on the whole, any right to complain.” Besides books, journals, annual conferences etc, another important mean of updating our knowledge is through continuing
Medical Education programmes (CMEs).
By and large, the present day CMEs are not fully achieving this aim, at least in the field of tuberculosis. By and large, these CMEs are sponsored by pharmaceutical companies whose main aim is promotion of their products. To achieve this, companies pay more attention towards providing “comforts” to the invites than imparting knowledge. The CMEs are often held in posh hotels and a lot of time and money is spent on eating, entertainment, mementos and gifts etc. Majority of the doctors attending these large CMEs come as “guests” and not as “students”. Most of them utilize the occasion as a mean of “relaxation” from their busy schedule as well as an opportunity to meet their colleagues. A good amount of time is wasted on waiting for the chief guests, inauguration, inaugural tea, introduction of hosts and their products, etc. In this festive scenario, the real purpose of the CME i.e. education, is put in some obscure comer.

We need to give a “new look” to these CMEs, if we really want to achieve the purpose for which they are meant. Here are a few suggestions:-

(a) such meetings should be held in small towns and cities in small groups of 10-12 doctors only, more like a small round table gathering.

(b) The meetings should be arranged by respective IMA branches which should co-ordinate the venue, time and other modalities.

(c) TAI should act as “light house” for these activities. It can select speakers from different districts by inviting applications and can also nominate speakers. Only persons fully conversant with NTCP and basics of chemotherapy should be selected/nominated as speakers. TAI can also give printed guidelines for the delegates so as to maintain a uniform pattern.

(d) The meetings can be held in doctors’ clinics, Red Cross Bhawans, guest houses etc. No unnecessary formalities should be allowed. After speaker’s lecture for an hour or so, maximum stress should be laid on the question-answer session.

(e) Local IMA branches and/or TAI should bear the expenses and as far as possible, minimal or no financial assistance should be accepted from pharmaceutical companies with vested interests. Expenses should be kept to the minimum possible level.

We, the physicians, have often been given a status next to God by majority of our patients. Is it not our duty to serve them as best as we can? A lot more, and in a much better way, can be done in the management of TB patients, if we really resolve to update our knowledge through such “genuine” CMEs. The task is not formidable if a sense of sincerity and dedication can be instilled in teachers as well as “students”.

Rajinder Singh Bedi
Patiala

Ensuring Rifampicin Unavailability

Despite 40 years of availability of effective chemotherapy, control of tuberculosis (TB) is nowhere in sight. Non-compliance is one of the major hindrances and only 30% of TB patients complete their treatment in our country. Hospitalization, prolonged injectable therapy, short course chemotherapy, directly observed therapy (DOTS) have all been suggested to improve treatment compliance. Most are not implementable in our country nationwide (i.e. under NTCP), at least for the time being, because of our limited resources, poor organisational set up and other limitations. WHO has also recommended the use of blister packs (anti-TB “Kits”) whenever self-administration of drugs is permitted but such combipacks have their own problems. Moreover, the usefulness of such “Tacks” in improving treatment adherence and preventing treatment failure and relapse has not been evaluated. Another good alternative, suggested by WHO, is the use of fixed-dose combinations (FDCs) adjusted for body weight. FDCs avoid monotherapy, prevent acquired drug resistance, and are, by and large, more acceptable because of reduction in number, volume and type of pills. FDCs can thus become a pracitcable solution for reducing problem of poor compliance in our set up.

One major pre-requisite for FDCs is that the bioavailability of its ingredients, especially Rifampicin, should be ensured. It has been shown that bioavailability of Rifampicin in FDCs depends upon a number of factors like particle size, excipient used and the manufacturing process employed. Recently, WHO has observed that certain number of these FDCs being marketed in
some countries, when subjected to human bioavailability studies, have been found to be associated with low blood levels of Rifampicin.\(^4\) This deficiency will eventually result in treatment failure and acquired drug resistance.

Today, the Indian market is flooded with a large number of two to four drug FDCs, creating a totally chaotic situation. The bioavailability aspect is often being ignored and not given due importance. WHO and IUATLD have recommended the use of only those combinations for which human studies have demonstrated a satisfactory bioavailability of Rifampicin.\(^4\) Is Drug Controller of India (DCI) strictly following these recommendations? We hope and wish so. The claims and proofs provided by different pharmaceutical companies are often unreliable and may well be wrong. We should not allow the FDCs to slip out of our hands. The need of the hour is that Drug Controller of India should not act as a silent, toothless spectator. He should give approval to only those FDCs for which authenticated human bioavailability studies have been carried out. DCI should also publish a list of those FDCs which fail to fulfill these criteria. We, the physicians, should also get fully convinced about the bioavailability aspect, before prescribing any FDC. Each one of us has to share the burden of responsibility, if we are really interested in ensuring a TB free future.

Rajinder Singh Bedi
Patiala

REFERENCES

NEWS AND NOTES

52nd NATIONAL CONFERENCE ON TUBERCULOSIS AND CHEST DISEASES

The 52nd National Conference on Tuberculosis and Chest Diseases will be held under the auspices of the Tuberculosis Association of India and the Gujarat State TB Association at Dinesh Hall, Behind Income Tax Office, Navrangpura, Ahmedabad-9 from 19th to 22nd December, 1997. Those who wish to attend the Conference can obtain the Registration form from the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001.

EASTERN REGION CONFERENCES

The 19th Eastern Region Conference of the IUATLD, to be hosted by the Singapore Anti-Tuberculosis Association (SATA) would be held at Mandarin Singapore, from 5th to 8th September, 1997. The theme of the Conference is Update on TB and Lung Disease’. The Conference Secretariat address is given below:

Kind Attn : Mr. Keith Watson,
Academy of Medicine, Singapore 19th ER-IUATLD, College of Medicine Building, 16,
College Road 01-01 Singapore 169864
Tel (65) 2238968 Fax : (65) 22 55 155
E mail: monican @ pacific, net, sg.

IUAT AND LD CONFERENCE

The 12th Conference of the African Region of the International Union Against Tuberculosis and Lung Disease (IUATLD) will be held in Nairobi, Kenya from 15-17 March 1998 at Hotel Intercontinental. For further details kindly contact the following address : IUATLD Secretariat, 68 Boulevard Saint-Michel 75006 Paris, (France).

WORLD TB DAY

Delhi TB Association in collaboration with IMA New Delhi Branch arranged a video show on Tuberculosis update as a part of World TB day on 16th March, 1997 at Delhi TB Association Hall, 9, Institutional Area, Lodi Road, New Delhi. About 150 participants attended.

SAARC WORKSHOP

The SAARC workshop on “Formulation of Guidelines of Co-ordination in Government and Private Sector/NGOs initiatives on Tuberculosis Control and Meeting of the Tuberculosis Experts for compilation of Tuberculosis Control Training Manuals of SAARC Member Countries” was held in Kathmandu (Nepal) from 18-23rd June,’ 1997. Delegates from India, Maldives, Nepal, Pakistan and SAARC Secretariat attended the workshop. Among the 3 Indian delegates Dr. S.P. Khanna, Director, New Delhi Tuberculosis Centre gave a presentation on NGO’s and Govt. collaboration emphasizing the importance of NGO’s, their involvement in TB control and means for improvement in collaboration. The SAARC group recommended the guidelines for co-ordination between Government/NGOs and private sector.

INTERNATIONAL CONFERENCE ON AIDS

“International Conference on AIDS India 2000” will be held in Chennai from 27th November to 1st December, 1997. For further details kindly contact the Conference Secretariat, Department of Experimental Medicine and AIDS Education, Training and Research Centre, TN Dr. MGR Medical University, 40, Anna Salai, Chennai, Tamil Nadu.

ERRATA


1. In the Summary, line 24 : instead of 12% read 11% and in line 27, instead of 10% read 9%
2. In Table 3, the mean reaction size for undermournished children by Method A should read as 7.04 instead of 7.94.

In the April 1997 issue of the Indian Journal of Tuberculosis, the last three abstracts (pages 103-104) were prepared by Dr. Ashok Shah and not Dr. S.C. Kapoor as printed.
GUIDELINES FOR CONTRIBUTORS

General

1. All correspondence relating to the Indian Journal of Tuberculosis (IJT) may please be addressed to:
   The Editor, Indian Journal of Tuberculosis, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001.

2. The four issues of IJT, appearing every year in January, April, July and October, contain original articles on all aspects of tuberculosis and non-tuberculous respiratory diseases, case reports, reviews and leading articles (see item 6) as well as abstracts of articles/matter published in other scientific journals and books dealing with same subjects. Besides, each issue has an Editorial, sections on Contemporary Issues and Continuing Medical Education, News and Notes as well as Forum where readers can express opinion on the published articles or ask questions on the subjects covered by the Journal.

3. Three copies of the article (including diagrams and photographs) typed on one side of the paper with double spacing and wide margins should be submitted.

4. It is understood and accepted that the submitted matter would be editorially revised to make it suitable for publication. The decision of the Editor regarding acceptance or revision can not be contested. However, every effort is made to communicate the reason or deficiencies to the author in order to associate him with the steps to improve the article.

5. All the received articles are serially registered and usually published in the order of registration. However, the date of registration will be after the completion of the basic formalities, if the authors have overlooked these guidelines. The articles registered are reviewed by the IJT Editorial Board to judge suitability of publication and to give suggestions for improvement.

6. Original articles deal with planned studies that have been duly completed and convey definite conclusions from the data presented in the text. However, preliminary communication from research still in progress could be submitted, exceptionally, if the topic is important and the interim results could be of interest. Case reports present problems of unusual clinical interest which have been systematically and fully investigated and where a firm diagnosis has been established with reasonable certainty or the result of therapeutic management is of great significance. Review Articles are those specially requested from persons who have acknowledged competence in given subjects. These are useful for updating knowledge. Leading articles are contributed by those who have expertise in selected aspects of a subject.

   Forum provides a platform to readers for expressing opinion and a channel of communication with the Journal and its other readers. It could be used for making suggestions, scientific critique on published articles or for reaching independent conclusions, asking questions on the subjects covered by the Journal and for providing supplementary information either confirming or contradicting the conclusions reached in the articles.

7. Twenty five reprints of each published article are supplied free of cost to the author whose address is indicated for correspondence. More reprints are, exceptionally, supplied if the order is placed at the time of acceptance of the article. The cost of the order will be intimated and must be paid for in advance of the publication of the article.

Format and Procedure

8. All submitted articles shall have a definite format. Each article should comprise sections, ad seriatim, on Summary, Introduction, Material and Methods, Results, Discussion. Acknowledgements (if necessary) and References. Additional sections could be interposed. In Case Reports the sections on Material and Methods and Results are replaced by the section “Clinical Record” and all other sections are appropriately shortened.

   Care should be exercised in making the language grammatically correct and free flowing, ensuring that all pertinent information has been included, irrelevant details omitted and repetitions, especially from section to section, avoided. Tables and figures must be self explanatory and their number kept to the minimum. It is not usually necessary to present the same information both in a ta-
ble as well as a diagram: the more effective of the two presentations has, therefore, to be chosen. Tables must be numbered, have a descriptive legend on the top, minimum essential data in the body and necessary explanatory notes at the bottom. Tables (and diagrams) should be made on separate sheets or paper, with their place in the text indicated clearly and attached at the end of the article. Drawings are best made with black India Ink and of size larger than required in the text. Legends for the photographs should be typed separately with appropriate indication regarding the photograph to which a legend pertains. Photographs (black and white prints) should be clear, glossy and unmounted. Facilities for printing photographs in 4 colours as illustrations in case reports are available. Contributors are requested to kindly send colour photographs of their clinical material. The attached sheets should carry the title of the paper and name of the author in pencil on the backside. Photographs, inscribed in pencil at the back, should be put in an envelope and properly labelled on the outside and attached to the article last.

It is understood that the planning of the study submitted for publication as well as the analysis of the data, presentation in the text and the reaching of conclusions have been done in consultation with a statistician.

9. After the title of the article, the name of the principal author should be followed by names of other authors.

10. The position held by each author in any institution is indicated only in the footnote against Arabic numerals indicated on the top of each name. The name and address of the author to whom correspondence regarding the article has to be sent should be indicated.

11. In respect of preliminary communications, the nature of the paper must be clearly indicated so that editorial processing could be specially expedited.

12. References cited in the text and at the end should conform to the procedure recommended by the International Steering Committee of Medical Editors. Therefore, special care must be taken to ensure that:

- Only the most important published papers related directly to the study in hand are cited in the text.
- Text reference should be numbered in Arabic numerals as a suffix in the order of their mention, avoiding the names(s) of authors(s) and year of publication.
- While citing an abstract (when it is the sole source of information) or personal communication of unpublished work in the text, authors must provide the necessary particulars of the source, but this is not a preferred mode of citation. Permission from the source(s) of information of citing their work must be obtained beforehand.
- All the numbered references in the text should be typed out in detail, in the same, consecutive order, on a separate page and attached at the end. Abbreviation of the titles of the cited journals should be according to the Index Medicus. Example;

13. The abbreviations or acronyms used in the text must be defined at the first mention. Their number should be kept to a minimum.

14. Contributions to Forum should be in the form of letters to the Editor. Such letters must be brief and to the point: only the most important agreements/disagreements/suggestions on published papers may be chosen for commenting. It is usual to send a copy of such letters to the author concerned for obtaining a response, if any, after editorial reformulation. The response, similarly, has to be selective, brief and relevant.