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Editorial

PUBLIC HEALTH AND PUBLIC

Public health, almost always is, discussed-whether in regard to the status of public health in the country or state of the public health services-without talking much about the public. The result, often, is the projection of a somewhat lopsided view of the situation. Obviously, we must strive to take a balanced view. There is a popular saying that a people get the government they deserve. Could we not, in the same refrain, say that a people get the kind of public health that they deserve ?

Why do we, as a people, persist in doing things and living in ways which we often know could lead to indifferent health and even result in sickness (and suffering) which may sometimes prove fatal ? The prevailing poverty, the social focus on employment and adequate earnings, and deficient means available to most, though important, are not enough to justify the rampant uncleanness, garbage strewn everywhere except within the four walls of dwellings, and inappropriate health behaviour of the people. Cleaner living does not require much money or means but a social consciousness. In all seriousness, how can we as a people continuously ignore most of the laws of healthful living, yet vociferously blame the government, whenever and wherever there is a breakdown of the public health system ? We are only too conscious of the deficiencies present in our public system and hold no brief for it, but are viewing the scenario from the social consciousness aspect and holding the people partly responsible for public health.

The apparent apathy of the society - rich as well as poor, the sick as well as healthy and the educated as well as well-informed and the rural yokels - towards public health is truly amazing; nay, even frightening. True, some individuals, NGOs, and commercial houses have come forward, and rightly so, and are helping in supplementing health facilities and providing succour to the needy, especially during epidemics. But, when it comes to promoting public health, the society's interest is often minuscule. In fact, sometimes this "so-called" social interest may verge on the ridiculous. For example, during epidemics of cholera, gastroenteritis and plague, scores of social busybodies and political leaders parade streets and enter homes with brooms in hands to clean up and set things right. Expectedly, numerous camera bulbs flash and their pictures are splashed in media. Soon after, everything is forgotten. And sooner still, the *status quo ante* of filth and squalor is restored.

Media's main role, of course, is to purvey news and if the social craving for publicity gets satisfied in the process, no harm is done. However, media must also inform correctly

and create a public opinion. And these could become powerful tools in creating social consciousness, in favour of public health. However, when the media bold headlines ascribe the occurrence of the malaria epidemic in Rajasthan to excessive rains and in Assam to untimely rains, there comes the element of purveying half truths which results in pointing away from society's role and responsibility in avoiding the occurrence of well known epidemics. Involving God/nature in epidemics as if a part of some kind of a conspiracy to maintain the fear of God in human beings, should not be suggested in one way or other.

While we must discuss public health and public health services, and spotlight the deficiencies in them, we must not forget society's paramount role, in general, in this regard. Nothing will succeed better than a proper social health consciousness and the will to live cleaner and healthier lives. Some NGOs could make it their objective to create and sustain a social health consciousness instead of offering services and succour. Besides, in metropolitan cities the neighbourhood welfare programmes are taking roots. At present they are concentrating on security but must encompass promotion of environmental sanitation, nutrition and the like among its members.

D.R. Nagpaul

IMPACT OF HIV INFECTION ON TB PREVALENCE- EFFECTIVENESS OF PREVENTIVE CHEMOTHERAPY*

V. Sivaraman, V. Balu, R. Sambasiva Rao and S.K. Amarnath

Summary: A computerised epidemetric model, for decision making on offering preventive chemotherapy to persons inflicted with *M. Tuberculosis* and HIV is presented. It shows that coverage of the dually infected persons is the crucial input. A preventive chemotherapy coverage of less than 39% has no appreciable impact. A minimum chemopreventive efficacy of 80% and coverage of 100% is needed, if the HIV induced upsurge is to be contained by 2000 A.D. The short term predictions (i.e. less than 7 years) are not sensitive to assumptions on coverage, efficacy of chemotherapy breakdown rate of the dually infected.

number of persons infected with *M. tuberculosis* and the low rate of disease likely to arise from this pool, from the cost benefit angle. The arrival of HIV infection has altered the picture since the annual incidence of disease from the dually infected is considerably higher than that among those infected with *M. tuberculosis* only.

Since no field study has been undertaken so far, the paper aims to forecast the potential impact of HIV infection on TB epidemiology and the reduction that is likely to occur if a hypothetical chemoprevention programme is applied. The epidemetric model methodology is used.

The Serosurveillance Centre for HIV infection in Jawaharlal Institute of Medical Education and Research has been carrying out serological tests for HIV infection in various population groups since 1986. The seroprevalence data from heterosexually promiscuous persons and TB patients are taken into consideration for purposes of this paper. Using a computer software, an exponential regression curve has been fitted to the observed cumulative seroprevalence data from Pondicherry and extrapolated to the future. Besides, TB patients are being screened by ELISA and the proportions positive are available for the period 1989 to 1993.

Introduction

Human Immunodeficiency Virus, by its ability to destroy the immune system has emerged as the most significant risk factor for the progression of dormant tuberculosis infection to clinical disease. As a result, the epidemiological trend of tuberculosis might show a change for the worse.

In view of the high risk of tuberculosis in dually infected persons, prevention of tuberculosis in such persons assumes a high priority¹. Administration of preventive chemotherapy to HIV/tuberculosis co-infected persons has, therefore, been considered as one of the most critical interventions to limit the increase in tuberculous disease that is expected from the pool of HIV/tuberculosis co-infected individuals.

Preventive chemotherapy has so far not been an integral part of the National Tuberculosis Programme, primarily because of the large

Model Methodology

The population is divided into the following epidemiological classes:

- (a) Infected with neither HIV nor TB infection
- (b) Infected with HIV only
- (c) Infected with TB only
- (d) Infected with both HIV and TB

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- (e) Having TB disease only
- (f) Having TB disease with HIV infection

It is assumed that the incidence of tuberculosis infection is not affected by HIV infection; that population movements are as described by Sivaraman and Umasankar² dividing the population into 2 groups depending on risk behaviour (High and Low) and different rates are applied, wherever necessary. The population flow is shown schematically as in Fig. 1.

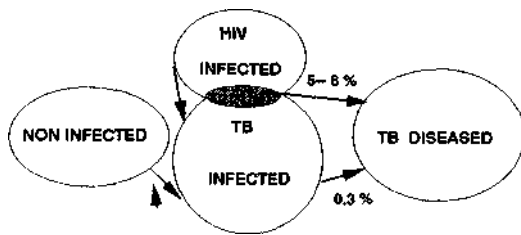


FIG. 1. HIV and TB: Epidemiological Interactions

Steps in Model Development

- (1) Fitting an exponential regression curve to the HIV seroprevalence. (Fig. 2) and Appendix III

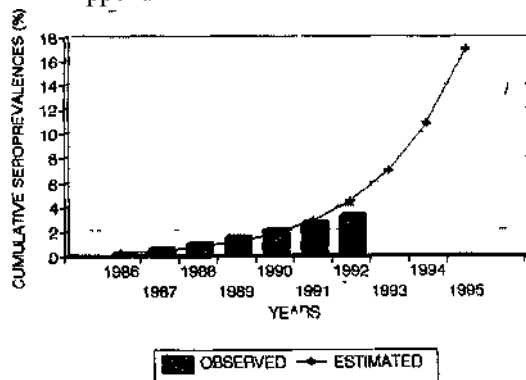


FIG. 2. HIV Infection in Pondicherry: observed and estimated trends

- (2) Population projection through similar exponential regression curves applied to the all India demographic data. (Health Information of India).
- (3) Extrapolation of regression curve (1) above upto the year 2000 to obtain future HIV seroprevalences.
- (4) The incidence and prevalence of tuberculosis

infection is obtained by the methods already described by Sivaraman and Umasankar (loc. cit).

- (5) Assuming that the prevalence of HIV infection among TB infected population is the same as in general population, the number of persons dually infected is found out.
- (6) Assuming that 5-8% of the dually infected persons breakdown to disease the incidence of tuberculosis among dually infected person is estimated.
- (7) The incidence of tuberculosis among those infected with TB only is arrived at as described by Sivaraman and Umasankar²

A hypothetical average district population is considered. The initial demographic, epidemiological and operational characteristics are as shown in Table 1A.

Table IB shows the variations in the parameters considered.

Trend Without Chemoprevention

The prevalence of tuberculosis shows a steady increase between the years 1986 and 2000 from 2.53 per thousand to 5.12 per thousand if the breakdown rate is 8% (Fig. 3).

Impact of Chemoprevention Coverage on Trend

With the addition of a Chemoprevention programme, for 31% of the dually infected the

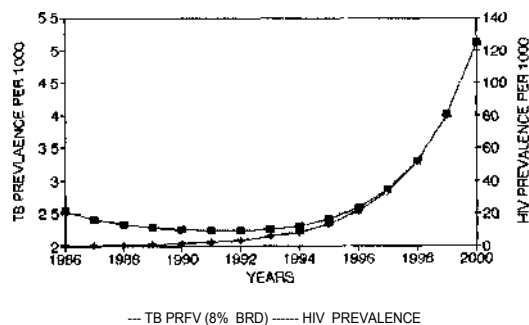


FIG. 3. Forecast of HIV & TB prevalence without Chemoprevention

TABLE 1A. Parameters Common to all Strategies

(A) DEMOGRAPHIC		
Population in 1986		1672944
Birth rate in 1986		3.2%
Rate of decrease in birth rate		1.2%
Death rate in 1986		1.1%
Rate of decrease in death rate		2.5%
(B) HIV RELATED		
Prevalence of HIV infection among TB in 1986		0.5%
HIV infection among low risk		1%
Proportion of population at high risk		8%
(C) TB RELATED		
(i) Common to HIV+ves and HIV-ves		
Case finding coverage		31%
Compliance		45%
(ii) HIV negative		
Cure rate among regulars		80%
Cure rate among defaulters		30%
Cure rate among untreated		10%
Death rate among regulars		4%
Death rate among defaulters		12%
Death rate among untreated		16%
(iii) HIV positive		
Cure rate among regulars		25%
Cure rate among defaulters		0%
Cure rate among untreated		0%
Death rate among regulars		30%
Death rate among defaulters		50%
Death rate among untreated		80%

Table 1B: Varying parameters

Parameter	Value	Source
Coverage of chemo-prevention	0-31-100%	Jagota et al ⁴ (for 31%) (Vide Annexure)
Efficacy of chemo-prevention	60-80%	Ferebee ⁵
Breakdown rate	5-8%	Narain et al ¹

final prevalences would be 4.33-4.53 per thousand for breakdown rate of 8% (chemoprophylaxis efficiency (60-80%)). (fig. 4A)

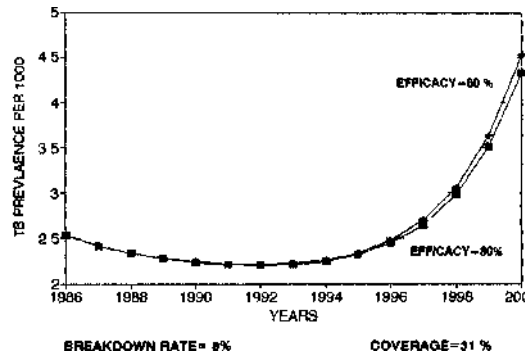


FIG. 4A. Impact of Chemoprevention on TB Prevalence (Low Coverage)

If 100% coverage of the dually infected could be achieved, the final prevalence would be 2.51-3.18 per thousand provided the breakdown rate is 8% (fig.4B).

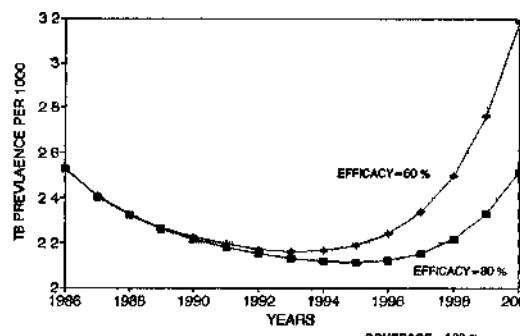


FIG. 4B. Impact of Chemoprevention on TB Prevalence (High Coverage)

It is seen that even if 100% of the dually infected are offered preventive chemotherapy, the upsurge in prevalence after 7 years cannot be prevented, if chemoprophylaxis efficiency is only 60%.

Impact of Breakdown Rate on Trend

All the above outputs are based on the assumption of 8% breakdown among the dually infected. Calculations were also made assuming

a breakdown rate of 5%. Fig. 5 shows that with chemoprevention efficiency of 60%, tuberculosis prevalence in the year 2000 will be 3.5 per thousand if the coverage is 31%, and 2.7 per thousand with a coverage of 100%.

Sensitivity Analysis of the Model

A perusal of the figures shows that in all simulations the prevalence predictions for the first seven years do not show any appreciable difference, with variation in input parameters. Fig. 4 and Fig. 5 could also be given a sensitivity analysis interpretation. It is seen that when chemoprevention coverage is kept at 31% and the efficiency is varied between 60 and 80 per cent there is no appreciable change in the predicted trends. However, the model is sensitive to changes in chemoprevention efficiency at higher coverages. (Fig. 4B)

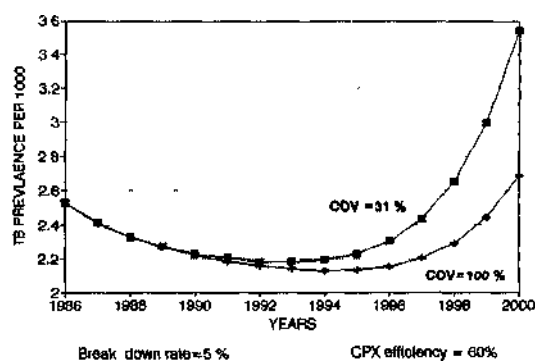


FIG. 5. TB Prevalence trend with assumption of lower breakdown rate

Discussion

In some developed countries tuberculosis chemoprophylaxis has been officially used for the last twenty years in special groups. However, such chemoprophylaxis has not so far been included in control programme of the developing countries, including India. Interest in chemoprophylaxis is being revived in view of the upsurge in tuberculosis due to the spread of HIV infection.

This paper has focussed attention on the likely time trend of tuberculosis in the context of HIV infection. How far the introduction of a

hypothetical chemoprevention programme will lessen the upsurge, has been examined. A high coverage of the dually infected by NTP appears crucial but unlikely to be achieved. If the present level of case finding in DTP is maintained for dually infected, the results are also likely to be poor. In a report from WHO⁶, it is suggested that as and when 60-65% overall coverage and cure rate is reached in less developed countries, "we will be able to introduce chemoprophylaxis to the infected who have a high risk of developing tuberculosis". In 1991, the Centres for Disease Control, Atlanta, USA advised that 1 year of Isoniazid prophylaxis be considered for HIV infected patients who are either PPD positive (≥ 5 mm) or who are anergic to control recall antigens and who come from a group with $\geq 10\%$ prevalence of active or latent tuberculosis infection⁷. In 1994, the American Thoracic Society statement on treatment of tuberculosis and tuberculosis infection in adults and children recommended that persons with positive tuberculin test and with HIV infection and persons with risk factors for HIV infection whose HIV infection status is unknown but who are suspected of having HIV infection should be considered for Isoniazid preventive therapy regardless of age⁸.

In India, a policy decision has to be taken on the desirability of inclusion of chemoprevention in the National Tuberculosis Programme. Such a decision will take into consideration the

- (1) Likely epidemiological impact
- (2) Toxicity
- (3) Acceptability to the community
- (4) Operational feasibility.

The present model provides a useful methodological framework for pinpointing the factors which will determine the epidemiological outcome of the strategy. We are handicapped by the lack of data applicable to Indian conditions. This has been overcome by assuming a range of values within which the Indian values may lie.

The model underscores the importance of covering a substantial proportion of the dually infected, if any appreciable impact is desired.

The operational feasibility is not within the

scope of the present paper; Perhaps establishment of HIV testing and tuberculin testing centres and collaboration between National Tuberculosis Programme and AIDS programme may be essential.

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Appendix I

Appendix III

HYPOTHESIS USED

(a)	Population of an average Indian/district	1.9 million
(b)	Prevalence of all cases 5+ age 4/1000 population viz	7600
(bj)	Prevalence of smear positive cases 40% of b viz	3040
(c)	Cases found	936
(d)	Coverage ((c) as percentage of b ₁)	31%

Source: Case holding in Tuberculosis Programme: Epidemiological Priorities and Operational Alternatives

Appendix II

BASIC DATA ON HIV SEROPREVALENCE IN PONDICHERY IN SUCCESSIVE YEARS

Year	Total Done	+ve	Cumulative Total	Cumulative Positive	Cumulative Pos%
(1)	(2)	(3)	(4)	(5)	(6)
1986	3166	6	3166	6	0.1895
1987	1291	21	4457	27	0.6058
1988	1046	33	5503	60	1.0903
1989	1046	40	6549	100	1.5270
1990	1021	60	7570	160	2.1136
1991	981	78	8551	238	2.7833
1992	1277	95	9828	333	3.3883

Column 6 is Column 5 as a percentage of Column 4

STATISTICAL METHODOLOGY USED FOR FITTING EXPONENTIAL CURVE

(Year)	Observed	Estimated
(1)	(2)	(3)
1986	0.1895	0.32191376
1987	0.6058	0.50059715
1988	1.0903	0.77846161
1989	1.5270	1.2105592
1990	2.1136	1.88249947
1991	2.7833	2.92741096
1992	3.3883	4.5523173
1993	-	7.07915394
1994	-	11.0085517
1995	-	17.1190247
1996	.	26.6212136
1997	-	41.3977446
1998	-	64.3762258
1999	-	100.109281
2000	-	155.676541

Regression Output:

Constant	-1.5749896
Std Err of Y Est	0.34283311
R Squared	0.90279877
No. of Observations	7
Degrees of Freedom	5
X Coefficient (s)	0.44151793
Std Err of Coef.	0.06478937

$$Y = \text{EXP}(0.441518 * X - 1.5749896)$$

N.B.: The calculations were done using a spreadsheet software

RAPID RECOVERY AND DRUG SUSCEPTIBILITY TESTING OF MYCOBACTERIA FROM CLINICAL SPECIMENS USING AUTOMATED RADIOMETRIC TECHNIQUE

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Summary: The time required for the isolation and drug susceptibility testing of mycobacteria from different clinical samples was determined by using BACTEC rapid radiometric technique. The results showed that mycobacteria could be isolated from most of the smear positive specimens within 6 days. The average detection time ranged between 3 and 15 days in the smear negative specimens. And the drug susceptibility test results became available within 7 days,

(POES), a growth promoting substance, and 4% CO₂ growth promoting environment are used. Mycobacteria utilise a ¹⁴C isotope labelled substrate (fatty acid) present in the medium and release ¹⁴CO₂ into the atmosphere above the medium. The amount of ¹⁴CO₂ thus released is determined quantitatively by its radioactivity and is expressed in terms of numbers on a scale from 0 to 999, designated as Growth Index (GI)⁶.

This article gives the results of the efficiency evaluation of this radiometric (BACTEC 460 TB system) technique using 1000 clinical specimens,

Introduction

The conventional method of isolating *M. tuberculosis* is on Lowenstein Jensen's (L J) medium. Primary cultures of tubercle bacillus take between 4 and 8 weeks. Once isolated, species identification or drug susceptibility testing can take another 4-8 weeks and during subculturing the isolates could be lost or get contaminated. Under the circumstances, culture and susceptibility studies are often not ordered and considering the extent of the disease in the country, the laboratories for performing isolation of mycobacteria are few.

Radiometric BACTEC method of isolation of tubercle bacillus offers a different solution to the time problem. True, there is the high initial investment of 2 million rupees and the high cost of culture medium (Rs.60 per patient as compared to Rs.20 for L J medium) but this method offers certain advantages like speed, higher success rate and, as a result, the prospect of more frequent use of essential drug susceptibility studies.

Several studies have demonstrated the high sensitivity and time saving offered by the BACTEC technique^{1,5}. In this technique, the BACTEC TB medium (128) containing polyoxyethylene stearate

Material and Methods

Clinical specimens: The clinical specimens tested included 375 sputa, 269 urines, 124 broncho-alveolar lavages (BAL), 84 body fluids, 75 biopsies/tissues, semen, stool, etc. and 73 pus (all totalling 1,000) collected from patients attending various hospitals in and around Baroda. The specimens were received over a period of 2 years for susceptibility testing. Around 80 per cent of the cases had received or were receiving treatment for tuberculosis.

Processing of specimens: Sputum specimens were digested and decontaminated by the N-acetyl-L-cysteine (NALC)-NaOH method⁷. Specimens other than sputum and volume over 10 ml were concentrated by centrifugation (2000-3000xg) for 15-20 minutes before digestion and decontamination by the NALC-NaOH method. Specimens having less than 10 ml volume were directly digested and decontaminated with NALC-NaOH. The treated specimens were neutralised with phosphate buffer (pH 6.8-7.0) and centrifuged. The sediment, thus obtained was suspended in 1.0 ml of normal saline using a tissue grinder and

the suspension was processed as for other specimens.

Culture: In each case, 0.5 ml of the suspension was inoculated into the Middlebrook 7H12 Medium (BACTEC 12B Becton Dickinson). As recommended, 0.1 ml of PANTA supplement (Polymixin B 50u/ml, Amphotericin B 5ug/ml, Nalidixic acid 20ug/ml, Trimethoprim 5ug/ml and Azlocillin 10ug/ml, Becton Dickinson) was added to 12B medium to deal with contamination. BACTEC 460 system was used to establish a 5-10% CO₂ atmosphere in the 12B vials, which were incubated at 37°C and read on 3, 6, 15 and 45th day. The amount of 14 CO₂ flushed out from the head space of the vials at the time of reading was quantitated and expressed as Growth Index (GI) on a scale of 0-999. When the GI reached 20, the culture was considered as positive and a smear was prepared and examined by acid fast staining⁸.

Initially, commercially available LJ slants were used but later we prepared our own LJ medium. Simultaneously, 2 LJ slants along with 1 BACTEC medium were inoculated.

Drug susceptibility tests: One hundred positive cultures were tested for susceptibility to Streptomycin (SM), Isoniazid (INH), Ethambutol (EMB) and Rifampin (RIF) using the BACTEC system. The drug concentrations used in the 12B medium were SM: 6.0 meg/ml, INH : 0.1 meg/ml, EMB: 7.5 meg/ml and RIF: 2.0 meg/ml. Al: (0.1 ml) dilution (diluent: fatty acid-poor albumin 0.2% and tween 80 0.02% in distilled water, filter-sterilized) of the positive culture was inoculated into the control vial (without any drug) to determine the conventional 1% level of resistance by comparing the growth in the control and the drug containing vials. The rest of the test was carried out as described by Middlebrook et al⁹.

Sensitivity and specificity: For determining sensitivity and specificity of the method, the following definitions were used¹⁰.

$$\text{Sensitivity} = \frac{\text{True positive}}{\text{True positive} + \text{False negative}} \times 100$$

$$\text{Specificity} = \frac{\text{True negative}}{\text{False positive} + \text{True negative}} \times 100$$

$$= \frac{\text{SNCN}}{\text{SNCN} + \text{SPCN}} \times 100$$

S=. Smear, C=Culture, N=Negative, P=Positive

Results

Of the total 1,000 specimens processed, 399 were culture positive and results in respect of 304 (76%) were obtained in the first 15 days, as shown in Table 1. Out of the 304 positive cultures, results of 193 were available in the first 6 days and 111 between 6-15 days. More than 15 days were required for the remaining specimens.

Table 1: Culture results reported from 1000 specimens processed according to nature of specimen and time

Specimens Total	Positive Cultures (in days)				Total
	<6	6-15	>15		
Sputum	375	146	34	29	209
Urine	269	14	23	15	52
BAL	124	16	23	22	61
Fluids	84	7	12	11	30
Pus	73	8	11	9	28
Others	75	2	8	9	19
Total	1000	193	111	95	399

Note: Others include biopsies, semen, stools etc.

Of the 137 smear positive cases who were also culture positive, the culture results of 125 (91%) were obtained in the first 6 days (Table 2)

Out of 830 smear negative specimens, 262 (31.6%) were positive by culture compared to 137 (80.6%) of 170 smear positive specimens (Table 3). The average detection time by culture in the smear negative specimens was around 3 to 15 days.

Table 2: Number of days required for reportable culture results from smear positive specimens

Specimens	DAYS							Total
	2	3	4	5	6	15	45	
Sputum	23	21	24	12	26	4	3	113
Urine	1				2			3
BAL	2	1		1	7			11
Pus			1	2		2	1	6
Fluids		2					1	3
Biopsy							1	1
Total	26	24	25	15	35	6	6	137

Using above definition (Material and Methods), and data from table 3 the sensitivity and specificity of the BACTEC system were found to be 92% and 94%, respectively.

Table 3: Smear and culture status

Specimens	SPCP	SNCP	SPCN	SNCN	Total
Sputum	113	96	12	154	375
Urine	3	49	15	202	269
Others	21	117	6	212	356
Total	137	262	33	568	1000

S=Smear, C=Culture, P=Positive, N=Negative

Table 5 presents comparative data of success rate of isolation and average isolation time on 124 positive cultures on LJ slants and BACTEC medium.

From the positive cultures, 100 were tested for drug susceptibility to SM, INH, RIF and EMB (Table 4) by the BACTEC method. All the

Table 4: Drug susceptibility in 100 cultures

Antibiotic	Resistant	Sensitive
Streptomycin	54	45
Isoniazid	53	45
Rifampin	49	50
Ethambutol	48	47

Only unequivocal results are included in above table.

above 100 positive cultures were from different patients.

The average detection time to report drug susceptibility was 5-6 days by radiometric method. Many of these specimens were from patients on therapy. Out of these 100 cases, 79 were known to have taken previous anti-tuberculous treatment. One was known to have taken no treatment. In the case of the other 20 cases we have no history but they also may have taken treatment as in this part of the country, in cases of tuberculosis, doctors ask for susceptibility studies only when treatment has equivocal response.

Discussion

The radiometric method has been reported to have several advantages over other culture methods which use Middlebrook 7H10 medium,

Table 5: Comparison of isolation success and isolation time for 124 combined mycobacterial positive cultures.

Method	No. of Positive Cultures	Average Isolation Time
Only BACTEC	57 (45.69 %)	2.00 Weeks
Only L J	15 (12.09 %)	4.40 Weeks
BACTEC+L J	52 (41.93 %)	3.00 Weeks
Total	124	
BACTEC	109 (87.90 %)	2.16 Weeks
L J Medium	67 (54.00 %)	3.87 Weeks

selective Middlebrook 7H11 and LJ medium (which are currently in use). In the present study the isolation efficiency of BACTEC method and the conventional method using LJ media was not compared. There are many such excellent data available (3,4,10). Previous studies have shown that the BACTEC system has higher isolation rate (91%) as compared to LJ medium (73%) (1,10). Radiometric BACTEC method is now also included in many standard microbiology and laboratory medicine text books (6,15). In the present study, the cultures which remained negative were examined every week for 8 weeks and no culture became positive after 45 days. Therefore, 45 days was used as the cut off time for reporting cultures as negative. In the case of sputum, 70% of positive culture results were available in the first 6 days itself. A further 15% were available by another 7-8 days.

In the case of the 137 specimens positive by smear, results of 125 were available in 6 days and the results of sensitivity tests to therapeutic agents were available in another 6-7 days. Park et al (2) observed that the average detection time on BACTEC system was 20 days (range 12-31) for smear negative samples compared to 28 days (range of 20-34) using Lowenstein Jensen or Grafts slants. Our study (Table 5) also shows similar trends i.e. of 15 days and 27 days respectively. Out of 399 total positive cultures in the present study, 262 were negative by smear examination.

For the purpose of this study we are defining smear negative as smear made from concentrated pre-inoculated samples. The difference between smear and culture positivity was even more pronounced in extra-pulmonary materials such as urine samples and body cavity fluids. Smear examination has to be augmented with culture and sensitivity tests which can be done in a short time using the BACTEC method. Drug susceptibility testing of *M. tuberculosis* can be reported within a week with radiometric method as against the 4 weeks needed for the conventional testing (11). This will enable more efficient treatment by avoiding the use of ineffective drugs. The sensitivity and the specificity of the BACTEC method in the present study were 92% and 94% respectively.

In urine cultures, smear positive-culture negative cases were more. One of the reasons could be false positive smears. Such cases can be reduced by collecting urine samples on two separate days and inoculating them into two separate vials. Also, first morning samples are preferable because 24 hour samples lead to increased contamination problems.

Earlier studies have shown that the radiometric method is comparable to the conventional method for testing the susceptibility of *M. tuberculosis* strains to drugs (9, 11, 12, 16). In the present study, the incidence of drug resistance for INH, SM, RIF, EMB is high, because most of these patients (80%) had taken prior treatment or were under treatment. Though we have presented only the data for resistance to single antibiotics, we did find 29 cases resistant and 4 cases susceptible to all four antibiotics. In addition 13 were resistant to HR, 1 resistant to SR and 2 resistant to RE.

BACTEC detection procedures can also differentiate between *M. tuberculosis* complex and Mycobacteria Other Than Tuberculosis (MOTT) i.e. non tuberculosis mycobacteria (NTM) by using NAP (p-nitro-alpha-acetylamino-beta-hydroxypropylphenone) based on selective growth inhibition of the *M. tuberculosis* complex in the presence of NAP. A concentration of 5ug/ml of NAP in 7H12 medium effectively separates *M. tuberculosis* complex from 35 MOTT (NTM) species within 4-6 days compared to 20 days by conventional methods (13, 14). The NAP selective inhibition test, performed in the present study on 15 clinical specimens by the BACTEC method identified 13 cultures as belonging to *M. tuberculosis* and 2 cultures as belonging to MOTT (NTM) group (results not shown). The NAP selective inhibition test used as an early screening test, identified members of *M. tuberculosis* complex in 4 days and differentiated most cultures of MOTT (NTM) in 24 hours. One hopes that introduction of radiometric facilities will also increase the use of both MOTT (NTM) differentiation and antibiotic sensitivity tests.

Thus, we conclude that the BACTEC system is efficient and accurate in the diagnosis of pulmonary and extrapulmonary tuberculosis and in carrying out drug sensitivity tests.

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COMPARATIVE EFFICACY OF RAPID SLIDE CULTURE OF *M. TUBERCULOSIS* AND CONVENTIONAL LJ MEDIUM CULTURE IN DIAGNOSIS AND MANAGEMENT OF PULMONARY TUBERCULOSIS CASES*

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Summary: Rapid slide culture (RSC) method using human blood medium (HBM) was compared with the conventional culture method using Lowenstein Jensen (LJ) medium for primary culture of *Mycobacterium tuberculosis* (MTB) in fresh, untreated cases of pulmonary culture results in 7 days with RSC method compared to 6-8 weeks on LJ medium is a distinct advantage in favour of the former method.

Out of the 336 patients of pulmonary tuberculosis studied, smear (3 specimens) was positive in 91 patients, RSC (1 specimen) method in 105 and LJ culture (3 specimens) in 137 patients. Early availability of MTB growth was possible in 27 smear negative cases. There were 14 cases having drug resistant organism, of which 10 could be picked up by RSC and 4 more by LJ method.

methods, culture is the more sensitive one with ability to give positive results on a clinical specimen containing as low as 10-100 bacilli per ml. The conventional culture method using Lowenstein Jensen medium takes 6-8 weeks for primary isolation of the organism. This prolonged period has prompted many workers to look for quicker methods of culture, such as the rapid slide culture (RSC) technique.

Robert Koch was the first to use RSC technique¹. Using coagulated human serum, he was successful in obtaining the growth of *M. tuberculosis* in seven days but contaminations hindered further success. Dickinson and Mitchison employed RSC in sensitivity testing by using outdated citrated human blood as the medium². Their procedure, however, required a fluorescent microscope. Gupta et al. substituted fluorescent microscope with bright light microscope³. The RSC is a rapid, simple and safe method and culture results are available in seven days. This method has also been successfully employed by Purohit et al⁴.

Introduction

Tuberculosis, with a world wide prevalence of over 40 million cases and 10 million new cases added every year, is probably the most important infectious disease of human beings. Its early detection and effective treatment, therefore, are essential for controlling this problem. Confirmation of diagnosis is based on microscopy examination for acid fast bacilli (AFB) and culture for growth of *M. tuberculosis*. Of the two

In the present study, both RSC using human blood medium (HBM) and conventional culture technique using LJ medium have been used for the primary isolation of MTB. The results of both the culture methods along with the results of smear examination have been compared.

Material and Methods

Patients with clinical and radiological evidence of pulmonary tuberculosis, and not on

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any anti-tuberculosis therapy, were asked to collect their morning sputum specimens in sterile McCartney bottles. The collected samples were processed by the modified Petroff's method⁵. From the centrifuged deposit, duplicate LJ slopes were inoculated and two thick smears were made, one over the middle 1/3 of a 75x25 mm glass slide (A) and another over the lower 1/3 of glass slide (B), using one half of a longitudinally cut glass slide. Smear A was air dried, heat fixed and stained by Ziehl Neelsen (ZN) method, and results of microscopy examination were recorded. The paired inoculated LJ slopes were incubated at 37°C. For each patient the smear examination and culture on LJ slopes were done on three consecutive days, whereas only one of the specimens was subjected to RSC using HBM.

Human Blood Medium. Outdated but not more than 4 weeks old citrated human blood was used for preparing the medium as described by Gupta et al.³. Such blood was diluted with an equal volume of sterile deionized water to cause haemolysis. The medium was made selective by adding polymixin-B (2,00,000 units/L), carbenicillin (100 mg/L), trimethoprim (10 mg/L) and amphotericin-B (10 mg/L). The pH of the medium was adjusted to between 6.5 and 7.5. Seven ml of this mixture put in a sterile screw capped McCartney bottle constituted one unit of HBM.

Slide B was air dried and put into a McCartney bottle containing HBM in such a way that the smear on the slide remained dipped in the medium. The inoculated bottle was incubated at 37°C for seven days. On the seventh day, the slides were taken out with a pair of forceps and dipped, individually, in separate 10 ml aliquots of sterile distilled water to enable washing off of the excess HBM on the smears. The slides were then placed in an oven at 80°C for 30 minutes, stained by ZN method and examined under oil immersion objective for microcolonies of AFB.

Readings on LJ slopes were taken weekly and results recorded. Subsequently, all the isolates were identified and drug sensitivity tests were put up⁵.

Results

Smear and culture results of a total of 336 patients were analysed. Of these, 161 (47.9%) were positive by one or more tests and 175 (52.1%) were negative by all the tests. Of the 161 patients who were positive by at least one of the tests, smear was positive in 91 cases (56.5%), RSC was positive in 105 (65.2%) cases whereas LJ medium culture was positive in 137 (85.1%) (Table 1).

Table 1: Distribution of positive results according to test used

Test	Positive	Percentage
Smear (3 specimens)	91	56.5 %
RSC (1 specimen)	105	65.2 %
LJ (3 specimens)	137	85.1 %
All the 3 tests	70	43.5 %
One or more tests	161	100 %

The correlation between the results of RSC and LJ medium cultures in total patients studied is shown in Table 2. Eighty three patients showed positive results by both the culture methods, 22 had positive culture only by the RSC method whereas 54 showed positive only on LJ medium. In all 177 cases were culture negative.

Table 2: Overall correlation between RSC and LJ culture results

	LJ medium culutre		
	Positive	Negative	Total
RSC Positive	83	22	105
RSC Negative	54	177	231
Total	137	199	336

$\chi^2=12.64, p<0.001$

Among the 366 patients included in the study, only 91 (24.9%) were positive by smear. Among the 91 smear positive cases, 78 were RSC positive and 81 were LJ positive on culture (Table 3). Of these, 70 were positive by both RSC and LJ, and 2 were negative by both methods. Of the 78 positive by RSC, 8 were

negative on LJ. Similarly of the 81 positive on LJ, 11 were negative in RSC.

Table 3: Correlation between RSC and LJ culture results in smear positive cases

		LJ medium culture		
		Positive	Negative	Total
RSC	Positive	70	8	78
	Negative	11	2	13
	Total	81	10	91

$\chi^2=0.21, p > 0.05$

Among the 245 smear negative cases, 27 were RSC positive and 56 were LJ positive in culture (Table 4). Of these, 13 were positive by both RSC and LJ, and 175 were negative by both methods. Of the 27 positive RSC, 14 were negative on LJ. Similarly, of the 56 positive on LJ, 43 were negative in RSC.

Table 4: Correlation between RSC and LJ culture results in smear negative cases

		LJ medium culture		
		Positive	Negative	Total
RSC	Positive	13	14	27
	Negative	43	175	218
	Total	56	189	245

$\chi^2=13.7; p < 0.001$

All the 137 isolates on LJ were identified as *M. Tuberculosis*.

Discussion

Definitive laboratory diagnosis of tuberculosis still revolves around the smear examination and culture confirmation for *M. Tuberculosis*. Conventional culture confirmation using LJ medium has the inherent disadvantage of time required to observe the growth. This, on many occasions, can delay the start of treatment, facilitating spread of the disease, or lead to unnecessary treatment for non-specific pulmonary infections. In our study, out of 336 cases of clinically and radiologically diagnosed pulmonary tuberculosis,

161 (47.9%) cases were either smear, RSC or LJ medium culture positive. The Military Hospital, Pune, being a tertiary referral hospital, receives service personnel from all over the country. Some of them having been found smear positive at the periphery are started on anti-tuberculosis drugs before transfer. Care was taken that those having received such treatment for more than 7 days were not included in the study. Besides, most of them are early cases. These factors could explain 24.9% smear positivity among the study population.

The RSC was found to be more sensitive than smear examination and LJ medium culture the most sensitive for establishing the diagnosis as well as for primary isolation of MTB (Tables 1 and 2) in this study. There was significant difference between the results of LJ medium culture and RSC ($p < 0.001$). The difference between RSC (65.2%) and LJ medium culture (85.1%) positivity rates could most probably be due to the fact that RSC was performed only on a single sputum specimen whereas 3 consecutive morning specimens from each patient were subjected to smear as well as LJ medium culture. The eleven smear and LJ culture positive cases found negative by RSC (false negatives - Table 3) could also be due to single specimen processing and or procedural shortcomings like (i) wet smear inoculation leading to washing off of the AFB from the slide into the HBM, (ii) overdrying the smear before inoculation leading to death of AFB and (iii) use of very cold HBM. In 14 smear negative and 8 smear positive cases (Tables 3 and 4) MTB could be cultivated only by the RSC method. Taking into consideration the fact that only clinically and radiologically diagnosed and untreated pulmonary tuberculosis cases were included in the study, RSC has shown better results in these 22 cases in comparison to LJ medium culture (Table 2). Thus, it can be inferred that had multiple specimens been processed by RSC, the results of RSC could have been much better and much more comparable with the results of LJ medium culture. This aspect needs further study.

The correlation between RSC and LJ culture results in 91 smear positive cases did not show any significant difference ($P > 0.05$) (Table 3) whereas in the 245 smear negative patients there

was a significant difference ($P < .001$) with better result obtained by the LJ method than RSC (Table 4). This difference emphasises the importance of culture in arriving at a definitive diagnosis in smear negative, paucibacillary pulmonary tuberculosis cases.

We could not locate an identical analytical report, in literature, including a large number of patients, without confining the study to smear positive cases only. We also did not find a single case of culture contamination, unlike the 5.5% contamination rate reported by Purohit et al⁴.

An advantage of RSC is that it only involves picking up microcolonies with an ordinary bright light microscope, without the need of sophisticated equipment or complicated procedures, besides the precaution of eliminating rapid growers by concurrent observation of the same inoculum on corresponding LJ slants. A controlled study was also carried out, with a known rapid grower, utilizing RSC. It was observed that much larger microcolonies could be seen even as early as within 24 hours of incubation.

RSC proved to be a rapid, cheap and effective method for obtaining culture confirmation of tuberculosis. The recurring cost of the procedure in an ongoing laboratory is about Rs 4/-per test, without requiring sophisticated equipment. Nevertheless, LJ medium remains the gold standard for culture and sensitivity testing of MTB. RSC is useful for (1) early confirmation of viable MTB, (2) monitoring response to therapy, and

(3) monitoring treatment response in multi drug resistant tuberculosis. Therefore, RSC is strongly recommended for a country like ours.

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INVOLVEMENT OF LUNG AND LUNG FUNCTION TESTS IN STONE QUARRY WORKERS

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Summary: The workers employed in stone quarries, which is an unorganised sector of industry, are exposed to variable silica dust concentration at their work place. A Very large extent of respiratory morbidity and lung function impairment is observed in this group of employees. A cross-sectional study was carried out to study the respiratory morbidity and lung function involvement in this group. This study has found 32.5% prevalence of respiratory morbidity In stone quarry workers, on the basis of radiological appearance. However, no case of silicosis was detected. The impairment of lung function was significantly associated with increasing age, duration of dust exposure, smoking status and presence of chronic obstructive airways disease on radiological appearance. However, the measured dust concentration levels were found to be in permissible range. Thus, It can be concluded from this study that even low dust level exposure for longer duration can result In lung and lung function involvement. Hence, stone quarry workers, because of their occupational exposure to silica dust, are at increased risk of lung and lung function Involvement.

Introduction

Stone quarry workers form an unorganized sector of industry scattered all over India. Various procedures and operations are involved in this work viz. stone cutting, loading and crushing. Based on these operations, the workers are employed at different places as per the nature of work and are exposed to silica dust of different concentrations. The health impact of the working conditions and environmental factors in stone

quarry industry have been well documented^{1,4}. And therefore, a very high degree of respiratory morbidity is associated with this industry. Moreover, as the workers are exposed to silica dust over a long term, a considerable lung function impairment in this group of workers is reported in the literature^{5,7}. The present study was, therefore, designed to evaluate the respiratory effects of occupational exposure to silica dust in stone quarry workers.

Material and Methods

A cross sectional study was carried out at stone quarries situated in Pachgaon area 26 kms east of Nagpur. There are about 285 such unorganised stone quarries situated in this area. However, three quarries from this area were selected for the study as these were run by the same proprietor and employed workers from the same ethnic group belonging to Orissa. The subjects for this study consisted of 80 workers from these stone quarries.

A detailed health status appraisal was done for all the workers included in the study. It included personal details through history taking and clinical examination. All the workers were brought to Govt. Medical College and Hospital, Nagpur for roentgenologic examination and pulmonary function testing. Reading of radiographs was done by two experts at Western Coalfields Limited Dispensary, Coal Estate Nagpur and Govt. Medical College, Nagpur. Every postero-anterior chest radiograph was searched for evidence of pneumoconiosis as per ILO classification, 1980⁸. Twenty four hours sputum collection of every worker was screened for acid fast bacilli at Tuberculosis Control and Training Centre, Nagpur.

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Pulmonary function parameters such as FEV₁, FVC, FEV₁/FVC%, PEF_R and FEF₂₅₋₇₅ were recorded by using Jaeger's Ultrascreen waterless spirometer corrected to BTPS along with age, height (cm), weight (kg) and sex⁹⁻¹⁰. Each individual performed three tests. The best result was chosen. The respirable dust sampler was used for the measurement of dust concentration at three different work sites viz. cutting, loading and crushing, during actual work time¹¹⁻¹².

To study the statistical significance of difference between various parameters of lung function, mean values and their standard errors were calculated. Whenever indicated non-parametric Mann Whitney 'IT test was used.

Results and Discussion

Table 1 describes the type of radiological appearance detected in workers. Twentysix (32.5%) workers were found to have one or another radiological abnormality. Out of 7 workers whose chest radiographs were suggestive of pulmonary tuberculosis, 4 were bacteriologically confirmed cases of pulmonary tuberculosis. However, tin's study could not detect any worker suffering from silicosis. The variation in the prevalence of various respiratory morbid conditions in different studies could be because of different dust concentration levels and mechanization processes^{2,4,13-14}.

Table 1: Radiological Appearance in Stone Quarry Workers

Radiological Appearance	Number	Percentage
Normal	54	67.50
COAD	15	18.75
Pulmonary Tuberculosis	7	8.75
Bacterial Pneumonitis	1	1.25
Cardiomegaly	2	2.50
Calcified Hilar Lesion	1	1.25
	80	
Total		100.00

In this study the respirable dust concentration level at stone cutting loading and stone crushing was found to be 23.42 ug/m³, 20ug/m³ and 15.38j.g/m³ respectively, i.e. the workers were exposed to very low levels of respirable dust.

Tables 2 and 3 reveal that there was statistically significant decrease in PEF_R of male workers and FEV₁ and FVC of female workers after the age of 40 years.

There was no significant difference in mean pulmonary function values in workers engaged in different aspects of quarrying as there was no significant difference in dust concentration at different work places.

Table 2: Mean values of pulmonary function (Males)

Age Group (Years)	Mean FEV ₁ X±2SE	Mean FVC X±2SE	Mean FEV ₁ /FVC% X±2SE	Mean PEF X±2SE	Mean FEF ₂₅₋₇₅ X±2SE
11-20	2.54	2.92	87.43	5.92	3.53
(15)	2.21-2.87	2.51-3.33	84.45-90.41	5.11-6.73	3.04-4.02
21-30	2.68	3.13	85.62	6.97	3.93
(16)	2.38-2.98	2.83-3.43	81.41-89.83	5.99-7.95	3.31-4.55
31-40	2.40	2.84	84.34	5.78	3.26
(18)	2.13-2.67	2.57-3.11	80.65-88.03	4.95-6.61	2.75-3.77
>40	2.31	2.98	76.43	4.54	2.29
(8)	2.02-2.60	2.64-3.32	68.08-84.78	4.16-4.92	1.44-3.14
Total	2.50	2.96	84.40	5.98	3.38
-(57)	2.35-2.65	2.78-3.13	82.10-86.70	5.51-6.45	3.06-3.70

Table 3: Mean values of pulmonary function (Females)

Age Group (Years)	Mean FEV ₁	Mean FVC	Mean FEV ₁ /FVC%	Mean PEF _R	Mean FEF ₂₅₋₇₅
	$\bar{X} \pm 2SE$	$\bar{X} \pm 2SE$	$X \pm 2SE$	$\bar{X} \pm 2SE$	$\bar{X} \pm 2SE$
11-20 (3)	2.04 1.58-2.50	2.79 1.98-3.60	73.69 68.18-79.20	4.09 3.14-5.04	1.70 1.59-1.81
21-30 (17)	1.59 1.48-1.70	1.89 1.76-2.02	85.08 81.09-89.07	3.89 3.34-4.41	2.75 2.39-3.11
31-40 (1)	0.80	0.84	95.24	2.54	1.36
>40 (2)	1.41 1.39-1.43	1.50 1.50	94.00 92.66-95.34	3.95 3.95	3.07 3.07
Total (23)	1.60 1.46-1.74	1.93 1.71-2.15	84.81 80.45-89.17	3.87 3.46-4.28	2.58 2.25-2.91

Table 4 shows the relation of mean pulmonary function values of male workers with duration of dust exposure in years. It appears from this table that male stone quarry workers showed a significant decrease in FEV₁/FVC% PEF_R and FEF 25-75 when they were exposed to dust for more than 20 years. Table 5 shows

the relation of mean pulmonary function values of female workers with duration of dust exposure. This table shows the decrease in pulmonary function with increasing years of dust exposure but this finding is not statistically significant. From Tables 4 and 5, it can be concluded that pulmonary function impairment is associated

Table 4: Mean Values of pulmonary functions in relation to years of dust exposure (Males)

Dust Exposure (Years)	Mean FEV ₁	Mean FVC	Mean FEV ₁ /FVC%	Mean PEF _R	Mean FEF ₂₅₋₇₅
	$X \pm 2SE$	$X \pm 2SE$	$X \pm 2SE$	$X \pm 2SE$	$X \pm 2SE$
<05 (24)	2.41 2.18-2.64	2.78 2.48-3.08	87.37 84.63-90.11	5.82 5.12-6.52	3.64 3.20-4.08
06-10 (17)	2.78 2.49-3.07	3.19 2.92-3.46	86.56 83.96-89.16	6.81 5.88-7.74	3.66 3.17-4.15
11-15 (5)	2.54 2.27-2.81	3.15 2.93-3.37	80.77 72.80-88.74	6.02 4.59-7.45	2.69 1.88-3.50
16-20 (6)	2.28 1.73-2.83	2.85 2.38-3.32	77.13 65.48-88.78	5.65 4.35-6.95	3.15 1.60-4.70
>20 (5)	2.25 1.86-2.64	3.02 2.49-3.55	75.16 67.70-82.62	4.27 3.56-4.98	2.19 1.31-3.07
Total (57)	2.50 2.35-2.65	2.96 2.78-3.13	84.40 82.1-86.70	5.98 5.51-6.45	3.38 3.06-3.70

with the duration of dust exposure. As in case of females, if the duration of dust exposure was less than 15 years, the decrease in pulmonary function was not statistically significant. However, in male population this decline was significant. Thus, it is observed in this study that workers exposed to even low level of respirable dust for more than 20 years, showed significant decrease in FEV₁/FVC% PEER and FEF₂₅₋₇₅, suggesting overall obstructive change in ventilatory function as an effect of silica dust⁷.

It was found in the present study that for all the parameters of pulmonary function except

mean FEF₂₅₋₇₅, there was no significant difference between mean values of pulmonary function of non-smoker and smoker male workers but the mean FEF₂₅₋₇₅ in smoker males was significantly decreased¹⁵, $p < 0.05$ (Table 6).

It appears from Table 7 that, in 12 male workers with COAD on radiological appearance, there was impaired pulmonary function based on mean FEV₁ and mean PEFR. However for other parameters of pulmonary function, the difference was marginally non-significant statistically. This kind of analysis for females could not show any statistical association between abnormal radiological

Table 5: Mean Values of pulmonary function in relation to years of dust exposure (Females)

Dust Exposure (Years)	Mean FEV ₁ X±2SE	Mean FVC X±2SE	Mean FEV ₁ /FVC% X±2SE	Mean PEFR X±2SE	Mean FEF ₂₅₋₇₅ X±2SE
<05 (8)	1.67 1.40-1.94	2.19 1.73-2.65	77.84 70.65-85.03	3.67 2.96-4.38	2.12 1.58-2.66
06-10 (10)	1.70 1.55-1.85	1.91 1.73-2.09	89.26 84.83-93.69	4.21 3.52-4.90	2.94 2.52-3.36
11-15 (5)	1.29 1.03-1.55	1.53 1.13-1.93	87.06 75.83-98.29	3.49 2.96-4.02	2.61 1.90-3.32
Total (23)	1.60 1.46-1.74	1.93 1.71-2.15	84.81 80.45-89.17	3.87 3.46-4.28	2.58 2.25-2.91

Table 6: Mean values of pulmonary function in relation to smoking habits (Males)

Smoking Habit	Mean FEV ₁ X±2SE	Mean FVC X±2SE	Mean FEV ₁ /FVC% X±2SE	Mean PEFR X±2SE	Mean FEF ₂₅₋₇₅ X±2SE
Non smoker	2.6071 2.4-2.82	3.0304 2.81-3.25	86.03 83.70-88.99	6.2454 5.7-6.79	3.8539 3.48-4.23
Smoker	2.4148 2.19-2.64	2.8969 2.64-3.15	82.8303 79.38-86.28	5.7121 4.94-6.48	2.9286 2.48-3.38
Total	2.50 2.35-2.65	2.96 2.78-3.13	84.4 82.1-86.70	5.98 5.51-6.45	2.38 3.06-3.70
W	909.0	844.5	913.5	871.0	988.5
P	0.1234	0.6094	0.1069	0.3503	0.0050

Table 7: Relation of radiological appearance and mean lung function values (Males)

Radio- logical Appearance	Mean FEV ₁	Mean FVC	Mean FEV ₁ /FVC%	Mean PEFR	Mean FEF ₂₅₋₇₅
	X±2SE	X±2SE	X±2SE	X±2SE	X±2SE
Normal	2.71	3.15	86.14	6.44	3.67
(37)	2.57-2.85	3.00-3.30	83.93-88.35	5.94-6.94	3.36-3.98
COAD	2.08	2.66	78.56	4.84	2.63
(12)	1.87-2.29	2.30-3.02	71.51-85.61	4.12-5.56	1.80-3.46
Pulmonary Tuberculosis	2.24	2.63	84.23	6.05	3.39
(6)	1.61-2.87	2.03-3.23	76.50-91.96	3.86-8.24	2.33-4.45
Bacterial Pneumonitis	0.92	1.09	84.40	1.91	1.00
(1)					
Cardio- megaly	3.33	3.53	94.33	5.98	4.65
(1)					
Total	2.50	2.96	84.40	5.98	3.38
(57)	2.35-2.65	2.78-3.13	82.10-86.70	5.51-6.45	3.06-3.70

appearance and pulmonary function impairment. This could be because of lower prevalence of respiratory morbidity in females as compared to males.

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RESPIRATORY DISORDERS AMONG WORKERS IN A RAILWAY WORKSHOP*

S.K. Gupta¹

Summary; In all, 400 full-time workers - engaged in various sections of a railway workshop and exposed to dust, smoke and irritant fumes and 100 matched controls from local administrative staff were surveyed for prevalence of respiratory disorders. Of them, 100 (25%) workers and 12 (12%) controls were found to have respiratory disorders, **Eosinophils were elevated in 20% of workers and 8% of controls. Radiological evidence of pulmonary tuberculosis was noted in 6(1*5%) among workers and 2(2%) in control subjects. Sputum cytology revealed bronchial infection in 42 (10.5%) of workers and 5(5%) in controls, PEFV less than 300L/min. was observed in 63% of workers and 8% in controls, A significantly higher prevalence of chronic bronchitis, bronchiectasis and respiratory allergies was seen in workers. Advancing age, smoking and duration of exposure: had significant influence on prevalence of respiratory disorders.**

in workers exposed to smoke and fumes in a railway workshop.

Material and Methods

The present study was conducted on 400 full-time workers in units involved in industrial processes exposing them to dust, smoke and fumes. The workers were selected irrespective of their age. To serve as controls, 100 matching subjects (not exposed but having similar socio-economic profile and living in the same environment) were also selected. Each worker/control was subjected to detailed history taking questions based on BMRC questionnaire, physical examination, relevant hematological investigations (total leucocyte count and absolute eosinophil count), sputum cytology and chest MMR. Peak flow rate was recorded in sitting position with the help of a simple peak flow meter and best of three readings was recorded. Smoking habit was graded according to smoking index. Smoking index was calculated as per the number of bidis or cigarettes smoked per day multiplied by the number of years smoked and classified as following:-

Introduction

Due to increasing industrialisation and urbanisation, the prevalence of respiratory disorders has increased. Occupational respiratory disorders have been recognised for centuries¹. Industrial dust, smoke and fumes and poor working environment have been recognised as important causative factors in increasing the prevalence of chronic bronchitis among industrial workers. Age, smoking habit, duration and type of exposure at working sites, nutritional and socio-economic status, etc. are contributory factors^{3,4}. The present study is an attempt to study the prevalence of various respiratory disorders and to evaluate the role of some important factors in their development

Habit	Smoking Index (Frequency x Duration)
Non smokers	0
Light smokers	1-200
Moderate smokers	201-600
Heavy smokers	600 and more

Observations

Tables 1 and 2 give prevalence of respiratory disorders according to age and smoking status¹. The prevalence of respiratory disorders increased with advancing age in both workers and controls, and difference was highly significant (Table 1) in smokers in both workers and controls.

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Table 1: Prevalence of Respiratory Disorders by Age

Age Group	No. of Workers	Workers With Resp. Disorders	%	No. of Controls	Controls With Resp. Disorders	%
21-30	118	16	13.55	33	2	6.06
31-40	152	22	14.47	38	3	7.89
41-50	89	28	31.46	20	3	15.00
51 & above	41	34	82.92	9	4	44.44
Total	400	100	25	100	12	12

The frequency of respiratory disorders was more in moderate to heavy smokers (Table 2).

Table 2: Respiratory disorders related to extent of smoking

Smoking status	Workers			Controls		
	Total	With Resp. Disorders	%	Total	With Resp. Disorders	%
Non-smokers	148	4	2.7	50	3	9.4
Light Smokers	200	62	31.0	32	3	30.0
Mod.Smokers	37	19	51.3	10	6	75.0
Heavy Smokers	15	15	100.0	8		
Total	400	100	25.0	100	12	12.0

None of the subjects gave history of worm infestation or cutaneous allergy. Specific questions were directed to elicit rhinitis or bronchospasm (wheezing) amongst workers and controls.

Respiratory disorders were more common in workers as compared to controls (Table 3), chronic bronchitis being the commonest.

Table 3: Respiratory Disorders Among Workers And Controls

	Workers (N=400)		Controls (N=100)	
	No.	%	No.	%
Chronic Bronchitis	68	17.0	8	8.0
Bronchial Asthma	14	3.5	2	2.0
Pulmonary Tuberculosis	6	1.5	2	2.0
Bronchiectasis	2	0.5	-	-
Respiratory Allergies	10	2.5	-	-
Total	100	25.0	12	12.0

There was a significant rise in prevalence with advancing exposure also. A positive correlation could be observed between prevalence of respiratory disorders and duration of exposure to dust and smoke as shown in Table 4.

Table 4: Relation between Duration of Exposure and Respiratory Symptoms among Workers

Duration of Exposure in years	Number	Symptomatics	
		No.	%
0-5	244	42	17.2
6-10	84	20	23.8
11-15	34	16	47.0
16-20	26	22	84.6
21 & Above	12	10	83.3
Total	400	100	25.0

Increase in eosinophil counts (counts above 440/mm³) was detected in 20% subject among workers as compared to 4% in control group which is a significant finding (Table 5).

Table 5: Absolute Eosinophil count in the two Groups

Absolute Eosinophil Count	Workers		Controls	
	No.	%	No.	%
Normal (upto 440/mm ³)	320	80.0	96	96
Elevated Eosinophil Count (>440/mm ³)	80	20.0	4	4

Mean values of PEFR were lower in smokers as compared to non-smokers in both workers and controls. Mean PEFR less than 300 L/min. was noted in 252 (63%) workers and in only 8 (8%) controls suggesting additional role of working environment in lowering ventilatory function (Table 6).

Table 6: Peak Expiration Flow Rate Related to Smoking in the two Groups

Category	Workers	PEFR +se (L/Min.)	Controls	PEFR +se (L/Min.)
Non Smokers	148	304±5	50	472±4
Light Smokers	200	294±4	32	382±4
Mod. Smokers	37	285±5	10	322±3
Heavy Smokers	15	276±4	8	288±7

Workers-252 (63%)
PEFR <300L/Min.
Controls-8 (8%)

Discussion

The workers in railway workshop under study had exposure to a variety of irritants and smoke containing carbon particles, metal fumes from antimony, tin, lead, oxides of iron and nitrogen, aldehydes, sulfur dioxide, hydrogen chloride etc., which cause widespread bronchial narrowing by directly injuring the airway mucosa and causing inflammatory swelling and excessive secretions and/or by stimulating rapidly adapting

irritant receptors¹. In the present study a significantly higher prevalence of chronic bronchitis has been observed in workers. Our findings are in conformity with those of Vishwanathan et al³ who found chronic bronchitis in 14.06% of industrial workers. Higher prevalence of respiratory disorders with advancing age may be due to longer duration of exposure. This is in conformity with the observations of others^{3,4}. Smoking is related to respiratory disorders, especially chronic bronchitis, in both workers and controls but

significantly higher prevalence rates were observed in smokers as compared to non smokers. The longer duration of exposure increases the risk. It may partially be due to advancing age as well.

The observation of a higher incidence of elevated eosinophil count among workers may indicate some allergic reaction between dust, smoke and respiratory mucosa.

As far as pulmonary tuberculosis is concerned, a higher incidence was not found among exposed workers. It can thus be concluded that exposure to dust, smoke and irritant fumes, advancing age, tobacco smoking, would all contribute to pathogenesis of respiratory disorders. The use of protective devices, forbidding smoking, engineering measures to make working environment safe, periodical health check up of workers, and health education are mandatory in checking progression of respiratory disability among workers.

Otherwise, the work will no more remain worship but hardship to them⁵.

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HAEMATOLOGICAL CHANGES IN DISSEMINATED TUBERCULOSIS

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Summary: Various types of haematological changes observed in 39 cases of disseminated tuberculosis such as different types of anaemia including refractory anaemia, high erythrocyte sedimentation rate, mononuclear cell preponderance with transformed and atypical forms, hypocellular bone marrow with depressed normoblastic erythropies, unremarkable megakaryopies, increased lymphomononuclear cell, plasma cell and RE cell population and defective ferrokinetics are described. None showed abnormal haemoglobin.

Introduction

Haematologic changes associated with disseminated tuberculosis (active tuberculosis in two or more sites but without continuity) are varied. Pancytopenia, leukoerythroblastic anaemia, leukaemoid reaction, polycythemia, disseminated intravascular coagulation, anaemias of different types and even myelofibrosis have been reported^{1,2,3,4}. Subramanyam et al had reported a case of acute myeloid leukaemia which showed disseminated tuberculosis but no leukaemia on autopsy.⁵ Jadhav et al described blast cells with Auer bodies in disseminated tuberculosis.¹ The anaemias in disseminated tuberculosis are often refractory to iron and vitamin therapy but are reversible when the primary cause is eliminated⁴. Again, concomitant blood loss, nutritional deficiencies and short erythrocyte life span may either contribute or modify the different haematologic changes found at presentation, amongst cases of disseminated tuberculosis at

Culcutta National Medical College & Hospital, Calcutta are analysed.

Material and Methods

A total of 39 cases of disseminated tuberculosis were found amongst the tuberculosis patients admitted to the Calcutta National Medical College & Hospital and S.S.K.M. Hospital, Calcutta between 1988 and 1990. A detailed history was taken with particular emphasis on the onset and duration of illness, symptomatology, history of contact with a tuberculosis case, previous immunization, any addiction including smoking, the associated diseases, history of blood loss, previous treatments received (including vitamins and minerals) and significant past and family history. A meticulous clinical examination was undertaken. Clinical evidence of tuberculosis in different systems (skin, genitourinary, meningeal, osteoarticular), in addition to lungs was looked for in all the cases. Initial investigations included tuberculin skin test, chest roentgenogram, examination of sputum or aspirated material from lymph nodes or CSF or ascitic or pleural or other aspirated fluids for acid fast bacilli (by conventional Ziehl Neelsen stain and culture on Lowenstein Jensen and Middlebrook's 7H9 media) and fine needle aspiration cytology and resection biopsy (undertaken in a few cases). Blood sugar (post-prandial), urea, creatinine estimation and liver function tests were also done.

All the 39 cases were then subjected to different haematologic investigations such as haemoglobin, TLC, DLC, PCV, MCV, MCHC,

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reticulocyte count, platelets count, peripheral blood film, ESR, bone marrow examinations (in 25 cases) with Perl's stain for iron, serum iron and TIBC, Haemoglobin electrophoresis was done in 4 cases who had severe anaemia with hepatosplenomegaly. Culture for acid fast bacilli was done on bone marrow in 12 cases. All the investigations were performed prior to therapy according to standard procedures^{6,7}. The patients were followed up carefully.

Table 1: Age and sex distribution of 39 cases of disseminated tuberculosis

Age (Years)	Male (Percent)	Female (Percent)	Total cases
0-9	2 (5.12)	1 (2.56)	3
10-19	0	4 (10.25)	4
20-29	4 (10.25)	11 (28.20)	15
30-39	4 (10.25)	2 (5.12)	6
40-49	4 (10.25)	1 (2.56)	5
50 or more	3 (7.69)	3 (7.69)	6
Total	17	22	39

Results

Out of the 39 cases of disseminated tuberculosis, 23 (58.9 per cent) had miliary tuberculosis. Table 1 shows details of age and sex distribution. Most cases were in the age group 20-29 years.

The salient haematologic features are given in the Tables 2 & 3, Severe anaemia (Hb 5-8 G percent) was present in 12 cases, leucopenia in 5 cases and leucocytosis in 9 cases. One patient had leucocyte count of 29,000 per cmm with mild shift to the left. Erythrocyte sedimentation rate was raised in all the cases and lymphomononuclear cell preponderance with transformed

and atypical forms with nucleoli and basophilic abundant cytoplasm were found in the differential counts in 21 cases. Thrombocytopenia (7 cases) was associated with leucopenia (5 cases) and together with decreased haemoglobin leading to pancytopenia in 5 cases. These 5 cases had been refractory to vitamin and iron therapy at presentation and also during follow up till the antituberculosis treatment had been continued for 8-10 weeks. Thrombocytosis was present in one case. Evidence of enhanced erythroid regeneration was not marked and reticulocyte count was less than 2 per cent in 30 cases. Erythrocytes were mostly normocytic normochromic; dimorphic anemia was found in 3 cases.

Bone marrow examination in 25 cases revealed : hypocellular marrow in 14 cases, depressed normoblastic erythropoiesis in 18 cases; mononuclear leucopoiesis with mild to moderate atypicity in 14 cases; increased plasma cell population in 18 cases and hyperplastic reticulo-endothelial cell with increased stainable iron in 16 cases. There was no typical tuberculosis granuloma in the few aspirated bone marrow materials examined and the culture was positive in 3 cases only. Serum iron and total iron binding capacity were diminished in 24 cases; low serum iron with increased binding capacity was seen in 6 cases and the rest were within normal range. Haemoglobin electrophoresis in 4 cases showed Hb A only. Blood sugar and other biochemical parameters were unremarkable.

Discussion

Haematologic changes in disseminated tuberculosis are protean and reversible only when tuberculosis is treated adequately.⁴ The predominant variations are: (i) different degrees of anaemia (morphologically normocytic normochromic, hypochromic and dimorphic) with some apparently refractory, (ii) high erythrocyte sedimentation rate, (iii) lymphomononuclear cell preponderance with atypicity in peripheral blood films, (iv) hypocellular marrow and depressed normoblastic erythropoiesis, lymphomononuclear cell preponderance with atypicity and increased plasma cells and RE cells and (v) defective ferrokinetics.

The mononuclear phagocytic system under the circumstances of chronic inflammation becomes hyperplastic and is responsible for the trapping of free iron and also for the extravascular haemolysis. The iron transfer to developing erythroid cells in bone marrow is decreased leading to increased iron storage in phagocytic cells and, simultaneously, decreased stainable iron in erythrocytes (hypochromia)^{8,9}. Again, chronic inflammation itself depresses the erythropoiesis (normal or depressed reticulocytes), leucopoiesis (leucopenia) and megakaryopoiesis (thrombocytopenia), ultimately developing pancytopenia.¹⁰ In this study, five cases presented as refractory anaemia, mimicking "Myelodysplastic Syndrome"¹¹ (MDS): Atypical and transformed mononuclear cells in peripheral blood and also in bone marrow with depressed megakaryopoiesis gave the impression of possible MDS. They also responded to hematinics, but after a long period (of 8-12 weeks) when treated along with antituberculosis therapy. So, in our country, where undiagnosed refractory anaemia and

tuberculosis are quite common, and can coexist, a proper search for tuberculosis becomes mandatory in all cases of apparent refractory anaemia.

Thrombocytosis in one patient was found following profuse bleeding.¹² Nutritional deficiencies were thought to be an additional factor leading to dimorphic anaemia in three patients. Atypical mononuclear cells with nucleoli may be an expression of chronic antigenic challenge.

Reports vary on the involvement of bone marrow in disseminated tuberculosis^{14,15,16} and show a minor role of bone marrow examination in the diagnosis of tuberculosis. We also did not find any suggestive granuloma in bone marrow materials but AFB culture showed positive results in 3 cases.

Lastly, none of these patients showed an abnormal haemoglobin disorder, a common cause of anaemia in this part of our country.

Table 2: Salient haematological findings in 39 case of disseminated tuberculosis

Haemoglobin (G%)	10-12.5 (16); 8-10 (11); 5-8 (12)
Erythrocyte Sedimentation Rate (mm in 1st hour)	20 (5); 20-50 (9); 50-100 (15); 100 (10)
Total leucocyte count (per cubic mm)	4000 -11000 (25); 4000 (5); 11000 (9)
Differential leucocyte count	Normal (14); Lymphomononuclear preponderance with neutrophilia (4); Transformed and atypical forms (21)
Peripheral blood film (erythrocytes)	Normocytic normochromic (19); Nonnocyctic hypochromic (13); Microcytic hypochromia (4); Dimorphic (3)
Platelets (per cubic mm)	1,50,000 (7); 1,50,000-4,00,000 (31); 4,00,000 (1)
Reticulocytes (per cent)	2 (30); 2 (9)
Packed cell volume (percent)	37 (34); 47 (0); 37-47 (5)
MCV (fl)	83 (4); 97 (3); 83-97 (32)
MCHC (Percent)	32 (4); 36 (0); 32-36 (35)
Serum Iron (ug%)	75 (24); 100 (0); around 100 (15)
TIBC	300 (24); 300 (6); around 300 (9)
Haemoglobin electrophoresis (done 4 cases)	Normal

*Figures within parentheses are number of cases

Table 3: Salient bone marrow findings in 25 cases of disseminated tuberculosis*

Bone marrow	(a) Normocellular (8); Hypocellular (14); Hypercellular (3)
	(b) Megakaryocyte - Adequate (19); Depressed (5); Increased (1)
	(c) Erythropoiesis - Normal (4); Depressed normoblastic (18); Nomomegaloblastic (3)
	(d) Leucopoiesis: - Normal (16); Depressed (3); Increased (6); Differential count. Dysplasia (6); LMC Preponderance (14); Transformed and atypical LMC (dysplasia) (6)
	(e) Plasma cells - Normal (7); Increased (18)
	(f) Macrophages - Normal (9); Increased (16)
	(g) Perls stain - Normal (8); Increased (16); Decreased (1)
	(h) Granuloma - None found
	(i) AFB culture - Positive (3)

* Figures within parentheses are number of cases

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OPPORTUNISTIC PULMONARY ASPERGILLOMA TREATED WITH SURGICAL RESECTION

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Summary: A 47 year old male with diabetes mellitus, which predisposed him to infection first with *Mycobacterium tuberculosis* followed by aspergilloma is reported. Recurrent haemoptysis necessitated the resection of the right upper lobe. Some of the issues involved in the management of pulmonary aspergilloma, especially those in with tuberculosis, are discussed.

Introduction

Pulmonary tuberculosis has been reported to be the commonest antecedent disease leading to the development of aspergilloma¹⁻⁴. In fact tuberculosis cavity provides the nidus for its development on the characteristic Monod's sign⁵ which shows a cavity containing a mobile mass surrounded by an air crescent. In spite of pulmonary tuberculosis being common in our country, very few cases of aspergilloma have been reported from India. Sporadic case reports have appeared giving the suggestive radiological profile. Identification of aspergillus species from different samples and sites, including sputum, bronchial aspirates, and presence of serum precipitins against aspergillus have been reported⁶⁻¹². However, as aspergillus is a very common contaminant, histological evidence is desirable for confirmation of etiology. A case of aspergilloma with supportive histological evidence in a diabetic patient with pulmonary tuberculosis is presented.

Case Report

A 47 year old male presented with 3 years'

history of cough and recurrent haemoptysis gradually increasing in quality. A week previously, he had coughed out about 150 ml of fresh blood. He was diagnosed elsewhere to have bilateral apical pulmonary tuberculosis three years ago and had been continuously taking various antituberculosis drugs including parenteral Kanamycin. He complained of general weakness, but no other symptoms like plentiful sputum, fever or chest pain. He was found to have diabetes mellitus 4 years ago, and controlled with 40 units of lente insulin a day. On examination, his height was 166 cm and body weight 63 kg. Pulse was 90/minute, regular, BP 140/80 mm Hg. General examination was non-contributory and he had no clubbing. On examination of the chest, vocal fremitus percussion note and vocal resonance were impaired in right apical region where bronchial breath sounds were also heard. There were occasional crepitations audible over both the apices. Routine investigations showed: Hb 11 Gm%, total leucocyte count 84,00 per cumm with polymorphs 70% lymphocytes 27%, eosinophils 1%, and monocytes 2%, blood urea 25 mgm% and ESR 58 mm in 1st hour. Random blood sugar level was 170 mg%. Gastric juice smear and culture for AFB were negative. Chest radiography showed bilateral apical infiltrations with haziness and cavity in right apex radiologically suggestive of aspergilloma. Bronchogram showed evidence of right upper lobe bronchiectasis and an aspergilloma with air space above was seen (Fig 1): movements with change of position were also observed during the bronchographic procedure.

Patient underwent right thoracotomy and had right upper lobectomy. Histology of the

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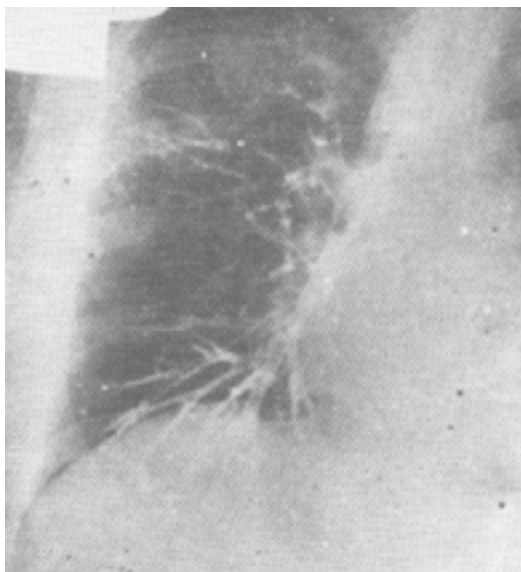


Fig. 1. Bronchogram showing evidence of right upper lobe bronchiectasis: aspergilloma with air space above is well seen.

biopsy material was consistent with aspergilloma (Fig 2). The diagnosis was further confirmed by growth of *Aspergillus fumigatus* in culture of lung tissue. Postoperatively he made an uneventful recovery. He was discharged on maintenance dose of 60 units of lente insulin a day. During a two year follow up period the patient remained free from any major symptoms and there was no radiological deterioration or recurrence of aspergilloma.

Discussion

Pulmonary mycetomas appear in cavities, cysts or spaces as saprophyte infection. It has been observed that the clinical course of fungal growths depends on the underlying disease⁷ Eastridge¹⁴ described a cavitory pulmonary infarct which healed as a solid scar inspite of a mycetoma complicating the cavitory phase. In contrast, in tuberculosis, bronchiectatic spaces remain open even without fungus contamination. Mycetomas can spontaneously resolve without closure of the space and this may be related to

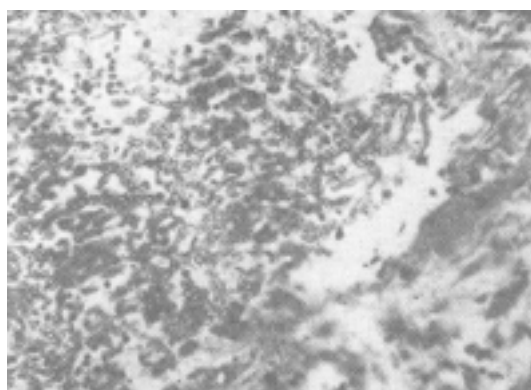


Fig. 2. Sections of colony of aspergillus with uniform septate branching hyphae

other organisms infecting the cavity The treatment of mycetomas, therefore, should be directed to specific pulmonary disease complicated by myceloma. Pulmonary tuberculosis complicated by a fungus growth is such an entity Haemoptysis is the symptom most commonly associated with aspergilloma The British Survey¹ of tuberculous cavities measuring 2.5 cm or larger found 11 per cent with definite aspergilloma. On resurvey 3 years later, it was found that 5 per cent of the 59 patients with aspergilloma had died with bleeding, 5 per cent had required pulmonary resection and 12 per cent had died of other causes¹⁵ Faulkner et al¹³ have stated that tuberculous cavities are more apt to bleed and mortality in series with fewer cases of tuberculosis is significantly lower. Although haemoptysis poses a real hazard in patients with tuberculosis with cavities who have mycetomea, Butz et al⁴ found that haemoptysis was not the most common cause of death for such patients: respiratory failure most often contributed to death They concluded that the treatment of mycetoma in patients of tuberculosis was treatment of tuberculosis, and if the patient had massive or recurrent haemoptysis or if a new growth could be excluded, resection of the destroyed lung should be undertaken with every effort to preserve pulmonary tissue

Our patient illustrates certain elementary yet highly interesting points The diabetic status of the patient was obviously the basic cause which led to both mycobacterial and fungal infections. However, it was tuberculosis which made the first inroad on apparently previous

healthy lung tissue. Chronic tuberculosis and resultant bronchiectasis, with damaged lung tissues, provided the nidus for aspergilloma to grow secondarily. The recurrent haemoptysis was the main indication for undertaking resective surgery. Though the aim of surgery should be to preserve as much of lung tissue as possible, the preoperative bronchographic evaluation showing the extent of underlying bronchiectasis favoured a lobectomy rather than segmental resection.

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RIFAMPICIN INDUCED THROMBOCYTOPENIA

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(Received on 19.9.94: Accepted on 8.12.94)

Summary: A case of Rifampicin induced thrombocytopenia developing petechial haemorrhages all over the body along with haemorrhages from multiple sites on the body is presented. The thrombocytopenia proved rapidly progressive and fatal.

Introduction

None of the anti-tuberculosis drugs is without adverse reactions but only rarely are the adverse reactions life threatening. Thrombocytopenia (TCP) is a well known complication following the administration of certain drugs and is characterized by rapid lowering of the platelet count whenever the offending drug is taken by the sensitized individual. Rifampicin induced TCP is a rarely reported adverse reaction^{1,2}. Drugs known to cause TCP are Quinine, Quinidine, Chloroquine, Sulfonamides and related drugs (tolbutamide and chlorothiazide), Digoxin, Meprobamate, sedatives, anticonvulsants, Methylidopa, Penicillamine, Amphotericin, Aspirin, etc.³.

We report a case of Rifampicin induced TCP which proved fatal. The patient developed TCP on the third exposure to the drug after an initial gap of one year and a subsequent gap of seven days after which TCP progression was rapid.

Case Report

G.S., a 35 year old male, cushion maker, was admitted to the Department of TB and Chest Diseases, Medical College, Goa with chief complaints of low grade fever, cough with expectoration, loss of appetite and breathlessness for 2 months. The patient was on anti-tuberculosis

treatment from Belgaum, till date. He had received Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E) daily in standard doses for initial three months, followed by Isoniazid and Ethambutol for twelve months, till admission. Blood examination revealed haemoglobin of 11 gm. %, TLC of 14,000 per cmm., DC, N-70%, L-24%, E-6%, RBC count of 3 million per cmm., total bilirubin 0.35 mg.%, SGPT 28 I.U., Alkaline phosphatase 12 KAU and platelet count of 0.21 million per cmm. Chest skiagram revealed fibro-cavitary disease in the right lung and patchy fluffy opacities in the left lung. His sputum smear was positive for acid fast bacilli by Ziehl Neelsen staining. The patient was administered Streptomycin (S), Isoniazid (H), Rifampicin (R) and Pyrazinamide (Z) in standard doses. Seven days later, the patient complained of anorexia and vomiting. Total bilirubin rose to 1.9 mg.%, SGPT was 102 I.U. and alkaline phosphatase 23 KAU. A diagnosis of drug induced hepatitis was made. All the antituberculosis drugs were stopped till liver function tests returned to normal, which took seven days. S, H, E, & Z were then re-started in standard doses, and three days later 300 mg. of Rifampicin was added to the regimen. Seven days later, the patient developed a bout of haemoptysis which was attributed to the disease. Three days after this episode, the patient complained of bleeding from the gums. A detailed clinical examination revealed purpura on the skin of both upper and lower limbs and on the anterior abdominal wall. Sub-conjunctival haemorrhage was noted in the left eye. Anti-tuberculosis treatment was withdrawn. The patient continued getting severe haemoptysis. Haemoglobin dropped to 6 gm.% and the platelet count was 80,000 per cmm., bleeding time was 2 mins. and clotting time was 3 min. 30 seconds. Two days later, the platelet count dropped to 40,000 per cmm. The

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patient developed left sided hemiplegia due probably to an intracerebral haemorrhage and went into comatose state. Intracerebral haemorrhage could not be confirmed due to non-availability of CT Scan. Three units of fresh blood transfusion and other supportive measures were given to the patient. The patient remained in coma and finally succumbed. Because of the lack of facilities, we could not perform complement fixation test and anti - platelet antibodies estimation.

Discussion

Adverse reactions to Rifampicin are uncommon on daily regimens but are relatively common with intermittent regimens⁴. They include a cutaneous syndrome, an abdominal syndrome, a flu syndrome, a respiratory syndrome, purpura and elevated transaminase serum levels⁵. TCP is an adverse reaction associated with intermittent Rifampicin regimen. Our patient had TCP on daily Rifampicin which was re-started 12 months after he had last received Rifampicin. Rifampicin was omitted after noticing the drug-induced jaundice and re-started within ten days.

Pool et al⁶ with 1200 mg of Rifampicin given twice weekly, reported a highly significant correlation between the presence of Rifampicin dependant anti-bodies and the occurrence of adverse reactions and recorded 3 cases of TCP. The risk of purpura occurring with daily Rifampicin cannot be completely discounted.

The drugs causing TCP lead to either suppression of platelet production or immunologic platelet destruction. Most drugs induce TCP by the latter mechanism. The platelets are damaged by complement activation following the formation of drug-antibody complex. Current laboratory tests can identify the causative agent in 10% of patients with clinical evidence of drug induced TCP. The best proof of a drug induced etiology is a prompt rise in the platelet count when the suspected drug is discontinued³.

Ferguson and the Hong Kong trial reported TCP even with daily Rifampicin.^{2,3} Incidence of TCP occurred from the first to the fourteenth month of therapy on Rifampicin⁴. Most workers agree that continuous treatment with Rifampicin

results in neutralization of any of the antibodies formed, the antigen - antibody complex being continuously removed without causing allergic reaction. Discontinuation of treatment allows a sufficient quantity of antibody to be built up during the drug free interval so that when Rifampicin is re-administered, an intense reaction ensues. *In vitro* tests, for identifying circulating antibodies are not easy to perform. No single test (complement fixation test, immuno injury test) detects all the cases of drug induced TCP. Direct binding assays for IgG or complement on the platelet surface are very useful⁷.

Although most patients recover within seven to ten days and do not require therapy, occasional patients with platelet counts below 10,000 to 20,000 per microlitre have severe haemorrhage and may require temporary support with glucocorticoids, plasmapheresis or platelet transfusions. Reuse of the offending drug has to be avoided in the future since only minute amounts of drug are needed to set up subsequent immune reactions³. If purpura occurs, Rifampicin should be stopped immediately and should not be given again even in small doses⁸. We failed to observe this precaution and met with a fatal ending.

Acknowledgement

The authors thank Dr. W.K. Belokar, Dean, Goa Medical College for granting permission to publish this case report.

We also thank Mrs. Victoria Gonsalves for her secretarial assistance.

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TUBERCULOUS INFECTION IN POST-OPERATIVE WOUND

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(Received on 15.10.94: Accepted on 15.4.95)

Summary: A 60 year old Indian male presented with a sinus on the sternum in the mid-line, 9cms. Below the suprasternal notch, 4months after coronary bypass surgery. *Mycobacterium tuberculosis* was isolated from the sinus. The patient was treated with anti-tuberculosis drugs and sinus healed.

Introduction

Mycobacteria associated with skin lesions include *Mycobacterium marinum*, *M. ulcerans*, *M. fortuitum*, *M. chelonae*, *M. leprae*, and *M. tuberculosis* causing lupus vulgaris. However, wound infection due to any of these, especially *M. tuberculosis* is very rare¹. This report presents a case with post-operative wound infection due to *M. tuberculosis*.

Case Report

A 60 year old Indian male who underwent coronary bypass surgery with uneventful recovery presented 4 months after the operation with a discharging sinus on the sternum, in the mid-line, 7.5 cms below the suprasternal notch. The serous discharge was cultured on two separate occasions (not for *M. tuberculosis*), but it did not yield any aerobic bacteria.

The sinus was explored considering that discharge was due to a foreign body. The wire used for interrupted sutures placed through the sternum for closure of the median sternotomy incision was removed. The sinus was cleaned and closed and the wound healed after 10 days.

After a period of 20 days, another sinus developed on the sternum, in the mid-line, 9 cms below the suprasternal notch. Aerobic cultures did not yield any bacteria. Exploration for another foreign body was futile. A sinugram could not be done. However, the granulomatous tissue in the sinus tract was removed. Histopathological examination suggested a tuberculous granuloma. When cultured for mycobacteria on Lowenstein Jensen medium, a scanty growth of buff coloured colonies appeared by the sixth week which were characterised as *M. tuberculosis*. A close interrogation of all family members was done but no history of tuberculosis could be found in the family. The X-ray chest was normal.

Drug susceptibility test was done. The isolate was susceptible to Isoniazid, Streptomycin, Rifampicin, Ethambutol and Pyrazinamide².

Treatment with Isoniazid 300 mg, Rifampicin 450 mg and Ethambutol 800 mg daily was started. The response was dramatic. The discharge from the sinus stopped in 15 days and the sinus healed after 2 months. The treatment was continued for 7 months after the sinus healed.

Discussion

Though various mycobacteria produce cutaneous infections, surgical wound infections are very rare¹. At Virginia Department of General Services, out of 100 wounds and skin lesions, only one strain of *M. tuberculosis* was isolated. Further, there were only two *M. tuberculosis* isolates over a period of five years¹. *M. ulcerans* causes chronic indolent necrotizing ulcer due to the production of exotoxin³. *M. marinum* causes

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swimming pool granuloma which is one of the commonest mycobacterium species to cause cutaneous infection. *M. fortuitum-chelonei* complex is known to cause injection abscesses as well as sternal wound infections^{4,6}.

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NEEDS IN TUBERCULOSIS RESEARCH*

R. Prahakar¹

Tuberculosis is still a major health problem in developing countries. It is also emerging as a major infectious disease in the developed countries due to AIDS epidemic. Its pathogenesis, immunology and molecular biology are still incompletely understood. The development of new drugs to fight tuberculosis ceased over two decades ago. The variable efficacy of BCG, found in different trials, still remains an enigma. And, it is likely that its epidemiology is also different, in some aspects, in developing countries compared with the developed ones. Sometime ago, it was said that the application of current knowledge about tuberculosis was lagging so far behind its application in the field that the focus should shift from more and more research in tuberculosis. That saying appears to have lost its validity under the present circumstances, especially when the WHO has declared a global war on the "neglected epidemic". The following horizons in different aspects of tuberculosis can be recognised in respect of research needs in tuberculosis.

Epidemiology

Infection

Setting up of surveillance systems to assess the impact of control programmes. Monitoring of changes in tuberculosis infection (or prevalence of infection) (a) Sequential tuberculin testing surveys among children; (b) Surveys among sentinel populations of young adults.

Disease

Case control studies to identify the factors responsible for progression of disease. Application of new methods to characterise strains of tubercle bacilli - DNA fingerprinting. Studies to determine the impact of HIV infection on TB. Tuberculin surveys amongst close contacts of tuberculosis cases. Effect of preventive chemotherapy on the infectiousness.

Diagnosis (Case-Finding)

1. Improvement of case-finding:
 - KAP studies on tuberculosis
 - Integration of tuberculosis services into primary health care
 - Health Education
 - Active case-finding focussed on high risk populations
 - Improving the diagnosis among patients presenting at health care facilities.
 - Increased involvement of private practitioners and traditional healers
2. Improvement in currently used technologies:
 - Improvement in smear microscopy
 - Slide cultures
 - Improved culture techniques, including development of a simple non-radiometric technique of detecting mycobacteria prior to visible growth
3. Development and in-service evaluation of new technologies for the diagnosis and prediction of:
 - (a) early disease;
 - (b) relapse;
 - (c) prognosis of tuberculosis, that have potentially
 - (i) greater sensitivity
 - (ii) higher specificity
 - (iii) greater rapidity
 - (iv) greater cost effectiveness, and
 - (v) greater applicability to developing countries
4. Improved methods for diagnosis of *M. tuberculosis* infections. The criteria required for a new diagnostic test include
 - (1) Cost-should be less than US \$ 0.50 per test

* Excerpted from the Guest Lecture on "Recent Advances in Tuberculosis Research" delivered at the Indo-U.S. Conference, 11-12 February, 1995, New Delhi.

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- (2) Speed-result should be available within two hours
 - (3) Sensitivity and specificity - should be 99% when compared with culture
 - (4) Simplicity-should be adaptable to use in field conditions in developing countries
 - (5) Reliability and reproducibility
 - (6) Safety and acceptability to both users and providers
 - (7) Not invasive (short of a finger stick)
 - (8) "User friendly"
5. Approaches in development of new diagnostic test(s):
- (a) Detection of the response of the host to the bacilli. The first immunodiagnostic tuberculin test is unable to distinguish active tuberculosis from past sensitisation, BCG vaccination or environmental mycobacteria.
 - (b) Serologic tests are based on the binding of an antigen to its specific antibody in serum. ELISA test is the choicest of all serological tests.
 - (c) A very high specificity is required for any new test to be applied to the patients of mycobacterial disease. In competent laboratories, the existing methods of sputum microscopy and culture have specificities approaching 1, and this sets the standard that must be matched by new diagnostic tests. The specificity of immunodiagnosis depends on the specificity of the antigens and antibodies used. Diagnostic PCR is a technique of DNA amplification that uses specific DNA sequences to serve as markers for the presence of micro-organisms. The genetic marker most commonly used is mycobacterial insertion element - IS 6110 - DNA piece of uncertain functional sequence present in

M.tuberculosis, M.bovis, M.microtiand M.africanum.

Treatment and Case Holding

Improvement of patient adherence to treatment crucial in developing countries.

1. Studies to improve
 - the present delivery system of chemotherapy
 - alternatives to hospitalization
 - DOT (directly observed therapy) in the initial intensive phase of SCC
 - novel drug delivery (e.g. calendar, blister packs)
 - impact of participation by the private sector
 - community participation
2. Studies to
 - improve treatment adherence
 - evaluate incentives and enablers
 - select potentially non-adherent patients for supervised chemotherapy
3. Cost-effectiveness analyses of various regimens of SCC.
4. Surveys of consumer satisfaction
5. Surveillance of initial resistance to Isoniazid, Streptomycin, Rifampicin and Ethambutol
6. Development of new therapeutic modalities: New drugs like
 - Long acting Rifamycins: Rifapentene, Rifabutin
 - Quinolones: Ofloxacin, Ciprofloxacin, Sparfloxacin.
 - B lactamase inhibitors: Amoxycillin, Ticarcillin and Clavulanic acid
 - Newer Aminoglycosides
 - Clofazimine

Prevention

1. Efficacy and operational studies, including analysis of cost-effectiveness to define the

role of preventive chemotherapy in high-risk populations.

2. Revaccination with BCG vaccine
3. New forms of preventive therapy, new drugs, immunotherapeutics, depot preparations
4. Development and testing new anti-tuberculosis vaccines including understanding the immunology and molecular biology of the bacillus
5. Additional studies with BCG: Neonatal vaccination, studies of additives to BCG (e.g. killed *M. vaccae*); safety of BCG vaccine in HIV infected persons.

Economic, Social and Operational Research

1. Problems at the Tuberculosis Clinic level:
 - inadequately trained, poorly supervised and over-burdened, health manpower
 - incorrect or incomplete information available to the public on tuberculosis symptoms and risks
 - deficiencies in the quality of diagnosis, despite efficacious technology
 - inadequate cooperation and referral arrangements with private providers of services
 - Poorly designed or completed registries and notification forms
 - drug supply problems leading to intermittent shortages
 - improper prescribing patterns, and lack of follow-up
 - difficulties in motivating patients and ensuring compliance
 - lack of staff, transport and information systems to follow up all patients who do not adhere to treatment.
2. At the national or provincial control programme levels
 - increasing competition for scarce health sector financial resources
 - the low-priority status for tuberculosis

despite the continuing heavy burden of disease

- ineffective negotiations for low-priced purchase of drugs, and poorly managed distribution and quality control system
- incomplete management information system
- lack of control over prescribing and sale leading to drug resistance and chronic excreters
- poorly planned and executed integration of tuberculosis control programmes into primary health care systems, including
- lack of supervision and training
- lack of health services management

3. How to

make efficient and effective use of existing technologies
 improve the delivery system infrastructure
 increase patient and provider motivation and compliance
 appropriately adapt new technologies to operational settings
 expand programme coverage
 increase political and financial support for tuberculosis control efforts

4. Studies focussed on

cost-effective diagnostic and treatment strategies that are appropriate and feasible
 improvement of health service infrastructures for tuberculosis control
 role of hospitals in tuberculosis diagnosis and treatment
 development of strategies for enhancing the cost-effective use of hospitals
 scope of private sector involvement in diagnosis and treatment (including traditional healers)
 KAP of providers
 development of models for integrating tuberculosis control into related control services.

FALL OUT OF GENETIC RESEARCH

In some earlier issues of the *Indian Journal of Tuberculosis*, mention has already been made of the ambitious genetic research project for the comprehensive mapping of the human genome, undertaken at the National Institute of Health in Bethesda, Maryland, U.S.A. (*Ind. J. Tub.*; 1995, 42, 59) and discovery of the gene responsible for mycobacterial drug resistance (*Ind. J. Tub.*: 1994, 41, 122) and cancers such as melanoma, breast cancer, colonic and prostatic cancers, etc. Hardly had these advances been fully understood that a serious controversy has arisen because some commercial concerns have begun marketing genetic tests that can tell which persons have unsuspected cancer or are likely to develop cancer later in life. The votaries of free speech and access to information are insisting that such tests should be freely available because people have the right to know if they are at an increased risk of getting cancer while others are equally vehement that it would be unethical to tell and undesirable for the person concerned to know that they would develop cancer at an unknown future date. Undeniably, those who harbour cancer genes would be asked to undergo frequent medical check ups, indefinitely, to enable early diagnosis and treatment. The impact of such tests on the health insurance and private sector health care industries is hard to foresee clearly at present.

It is said that the test at present costs \$ 800 for first member of the family and \$ 250 for each additional family member, in the U.S.A. If the uncertainty about the ethical aspect of the tests continues, some are sure to get rich, as they make hay while the sun shines, and some others likely to die before their actual death.

PREVALENCE OF HIV INFECTION IN PATIENTS WITH TUBERCULOSIS

Dear Sir,

Tuberculosis is one of the most common infections among HIV infected persons in both developed and developing countries. Clinical manifestations of tuberculosis may be typical or atypical.

In our study a total of 369 patients with tuberculosis were screened for presence of antibodies to Human Immunodeficiency Virus, using commercially available ELISA kit; Genetic system TM HIV-1/HIV-2 EI A. 37 patients were found to be repeatedly reactive by ELISA, giving a prevalence of 10.02% in the present study. This prevalence was found to be significantly higher when compared to the prevalence of HIV infection in blood donors (1.59%) from same population group. All the samples were sent for Western Blot confirmation and 34 patients (91.90%) were confirmed to be Western Blot positive. 26 patients (70.2%) were sexually promiscuous which may be a significant factor.

Thus, the study clearly indicates that the prevalence of HIV-1 and HIV-2 antibodies is significantly higher in patients having tuberculosis. Hence, it is advisable to screen all cases of pulmonary and extrapulmonary tuberculosis for HIV infection in India. In addition to HIV screening, antituberculous drug sensitivity testing may be done in all the patients as multidrug resistant strains may infect the HIV+ve patients and pose a grave threat to effective treatment of tuberculosis both among HIV infected persons and in the general population.

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NEWS & NOTES

Ind. J. Tub., 1995, 42, 184

ANNUAL MEETINGS

The Annual General Meeting of the Tuberculosis Association of India was held on 30th March, 1995, in the Conference Hall of Hotel Imperial, New Delhi. Dr. P.K. Sen, President of the Association, presided over the meeting.

Before commencing the proceedings, the President referred to the passing away of Shri S. Ratnam, Hony. Treasurer of the Association. As a mark of respect to the departed soul, all present stood in silence for two minutes.

Dr. A.K. Mukherjee, Chairman of the Association, presented the report on the activities of the Association for the year 1993-94. In the absence of the Hony. Treasurer, the Secretary-General presented the audited accounts of the Association for the year 1993-94.

Various awards of the Association for outstanding services, activities by the State TB Associations and also for the highest collections made by them in the 43rd TB Seal Campaign were given away by Hon'ble Lt.-Governor of Delhi, Shri P.K. Dave, at the Awards function following the Annual General Meeting.

The General Body elected Drs. B.M. Soni, M.S. Agnihotri, G.P. Saxena, M.M. Singh, S. Sivaraman, I. Ranga Rao and T.K. Ravindran as members of the Central Committee of the Association for the year 1995. Dr. P.K. Sen, President, then delivered his Presidential Address. Dr. Hoimi Basu, senior TB Worker, proposed the Vote of Thanks.

Earlier, a meeting of the Standing Technical Committee of the Tuberculosis Association of India was held on 29th March, 1995, in the Association premises, with Dr. R.C. Jain in the Chair.

The Conference of the Secretaries of State TB Associations was held on 30.3.1995, in the Conference Hall of Hotel Imperial, New Delhi. It reviewed the activities of the State TB Associations with special emphasis on TB Seal Campaign.

REFRESHER COURSE ON TUBERCULOSIS & CHEST DISEASES

A Refresher Course on Tuberculosis and Chest Diseases was organised at Govt. Doctors' Association Building, Eluru, (A.P.) on 22.4.1995 under the auspices of the Tuberculosis Association of West Godavari, Eluru. The Course was inaugurated by Shri D. Rama Krishna, I.A.S., Collector and District Magistrate & President of the Dist. TB Association, West Godavari, Eluru which was presided over by Dr. T. Appa Rao, District Medical & Health Officer, West Godavari, Eluru. The Scientific Session was chaired by Dr. V.S. Prasada Rao, Medical Superintendent, A.P.V.V. Parishad, Dist. Headquarters Hospital, Eluru, which was attended by 104 doctors.

C.M.E. ON TUBERCULOSIS AND CHEST DISEASES

A Continuing Medical Education Programme on Tuberculosis and Chest Diseases was organised under the auspices of TB Association of Andhra Pradesh and TB Association of Hyderabad District on 26th April, 1995 at State TB Centre, Hyderabad. The function was presided over by Dr. B. Nandraj Singh, Director of Health, A.P., while Sri R. Subralunanyam, IAS, Collector & District Magistrate & President of the Dist. TB Association, Hyderabad was the Chief Guest. About 45 doctors attended the C.M.E. Programme.

ANTI-TB WEEK CELEBRATIONS (ANDHRA PRADESH)

In Andhra Pradesh, the anti-TB Week was celebrated in districts of Ananthapur, West Godavari, East Godavari, Guntur, Karimnagar, Kurnool, Mahaboobnagar, Ranga Reddy, Srikakulam, Vizianagar and Warangal from 17.2.1995 to 23.2.1995.

EASTERN REGION CONFERENCE

The 18th Eastern Regional Conference on Tuberculosis and Lung Disease of International

Union Against Tuberculosis and Lung Disease will be held at Dhaka (Bangladesh) from 28th to 31st October, 1995. Tuberculosis and Respiratory Diseases in the nineties, Women and Children and people with HIV would be covered during the Conference.

TEACHING AIDS AT LOW COST (TALC)

TALC has published the 1995 list of books, slides and accessories available for use by teachers and others at a cost relevant to developing countries. The list includes videos and library packs, books dealing with health care service, AIDS education and communication, mother and child care, medicine including tuberculosis, etc. Further information can be obtained from TALC, P.O. Box 49, St. Albans, Herts, Ali 5 TX, U.K.

SAARC TUBERCULOSIS CENTRE, KATHMANDU (NEPAL)

A Seminar for Tuberculosis Programme Managers of South Asian Association for Regional Cooperation (SAARC) Countries was held during 22-24 November, 1994 at the SAARC Tuberculosis Centre (STC), Kathmandu under the sponsorship of SAARC Japan Special Fund. In all, 10 persons participated which included representatives from India, Maldives, Nepal and Pakistan.

On conclusion, the group made the following recommendations:

1. This body is of the opinion that recommendations made in such seminars should be action oriented ensuring an early action and adequate priorities to Tuberculosis Control may be provided in the region.
2. Technical experts who are managing Tuberculosis Programme or have sufficient experience in Tuberculosis Control activities should be involved in such Seminars.
3. Mere introduction of Short Course Chemotherapy does not serve the purpose without simultaneous improvement in management of the treatment system. The areas of improvement in management system are:

- Regular Supply of anti-TB drugs.
- Cohort analysis of treatment outcome of sputum positive cases at District level.

4. Keeping in view the importance of cure rate, a continuous supply of anti-TB drugs is an essential component of the Tuberculosis Control Programme. For this purpose establishment of a drug bank at SAARC Tuberculosis Centre is recommended, the source of funding for this may be decided in ensuing Governing Board Meeting.
5. The flow of information from Member Countries to SAARC Tuberculosis Centre should be continuous for further dissemination on latest developments in research to Member Countries. It may be made mandatory to send such documents for publication, at least once in a year to SAARC Tuberculosis Centre by Focal Points in the Member Countries.
6. To disseminate recent advances in the art of case-finding, treatment & health education etc., an exchange of experts within Member Countries periodically will be beneficial.
7. It is recommended to develop a strong network of training & research which will encourage the simultaneous developments of appropriate programme in Member Countries.

INTERNATIONAL CONFERENCE ON MEDICAL APPLICATION OF LASERS

Organized by the Indo-Uzbek Medical Laser Therapy Centre (established in the LRS Institute of Tuberculosis and Allied Diseases, New Delhi in 1992) an International Conference on Medical Applications of Lasers was held on 22-23 April, 1995, under the sponsorship of the Department of Science and Technology, Government of India.

Uzbek scientists have done pioneering work in this field using a variety of specialized lasers. At me Indo-Uzbek Centre, two conductor lasers are available for the treatment of cases of pulmonary tuberculosis and tuberculosis glands. Lasers are also used in cardiology, ophthalmology and gynaecology. Their use could be for the purpose of diagnosis, therapy through stimulation of the human immune system and surgery either by cutting or ablation.

Ramamurthi B, Ramamurthi R, Vasudevan MC and Sridhar K. *The changing face of tuberculomas. Ann. Acad. Med. Singapore 1993, 22: 852.*

Tuberculomas of the brain continue to be prevalent in all the developing countries of Asia, Africa, South America and Europe and seem to be making a comeback in the richer nations of the West. They pose a challenge to the neurosurgeon, in spite of the advances that have been made in the diagnosis of these lesions and in the available therapeutic regimens. During the last decade, computed tomographic (CT) scan has facilitated early diagnosis of tuberculomas at a stage when the lesions are small and anti tuberculosis therapy (ATT) has been found beneficial in the majority of patients. Those lesions that do not respond, need change in the ATT regimen and addition of steroids. Some lesions tend to disappear by themselves after a few weeks and probably are not tuberculous in nature. Some continue to grow in spite of ATT, probably due to drug resistance and require surgery, and some turn out to be gliomas. As it is not possible to differentiate between glioma or tuberculoma from CT morphology alone, and as stereotactic biopsy can be expensive, a trial with ATT is worthwhile reserving surgery only for those which continue to grow in spite of ATT.

Al-Deeb SM, Yaqub BA, Sharif HS, Motaery KR. *Neurotuberculosis: a review. Clin. Neural. Neurosurg. 1992: 94 Suppl. S30*

Tuberculosis is still a major cause of serious illness in many parts of the world. CNS involvement has frequently been found secondary to tuberculosis elsewhere in the body, particularly the lungs. The disease manifests itself as meningitis, tuberculoma and /or spinal tuberculosis. The presence of tuberculosis elsewhere in the body favours the diagnosis although its absence does not exclude it. While tuberculous meningitis is

a disease of childhood, tuberculomas and spinal tuberculosis are invariably an adult manifestation. The great majority of patients with neurotuberculosis are diagnosed and treated early because of characteristic clinical, imaging and CSF findings. Clinical response to antituberculosis therapy in all forms of neurotuberculosis is excellent if the diagnosis is made early before irreversible neurological deficit is established.

Rajasekhar V, Chandy MJ. *Enlarging solitary cysticercus granulomas. J. Neurosurg. 1994, 80: 840*

Solitary cysticercus granulomas that produce seizures usually measure less than 20 mm in diameter and diminish in size spontaneously. Unlike live cysticercus cysts, they have not been known to increase in size. In a prospective follow-up study of 93 consecutive patients with epilepsy and small solitary lesions (<20 mm in diameter) enhancing on computerized tomography (CT), 91 were found to have solitary cysticercus granuloma; of these, 7 (7.7%) were diagnosed as having an enlarging cysticercus granuloma.

It is important to recognize the entity of enlarging solitary cysticercus granuloma to avoid mistaking it for a tuberculoma and treating the patient with empiric antituberculosis therapy.

Rodrigues, Laura, Diwan, Vinod K and Wheeler, Jeremy G. *Protective Effect of BCG against Tuberculous Meningitis and Millitary Tuberculosis: A meta- analysis. Internal. J. of Epid. 1993, 22: 1154.*

The protective effect of BCG against tuberculosis estimated in randomised controlled trials and observational studies ranges from negative to close to 100%. One of the many explanations offered for this is that different immunological mechanisms may be associated with protective

effect against different forms and sites of disease. In this investigation, we recalculated vaccine protective effect separately for pulmonary disease and for meningeal/miliary disease in randomised controlled trials and case control studies, tested for heterogeneity in site specific estimates of protective effect and calculated a summary measure when appropriate. We found protective effect against pulmonary disease to be heterogeneous to a statistically significant degree and thus we did not calculate a summary measure of protection. Protective effect against meningeal and miliary TB was higher than against pulmonary disease and, except for a single study with two cases only, appear to be homogeneous. Summary BCG protective effective against meningeal and miliary TB in randomised controlled trials was 86% and in case control studies 75%. The fact that protective effect appeared to be homogeneous against meningitis and miliary TB but not against pulmonary disease may result from the fact that patients with meningitis are usually younger and thus less likely or from have been exposed to atypical bacteria or from a waning of the protective effect of BCG; or from the diversity of mechanisms of pathogenesis of pulmonary disease, which can originate from reinfection, reactivation or primary progression.

Jindal SK, Gupta D, Singh A. *Indices of morbidity and control of asthma in adult patients exposed to environmental tobacco smoke. Chest 1994; 106: 746.*

A study comparing indices of morbidity and control of asthma in 100 adult patients exposed to environmental tobacco smoke (ETS) inhalation (group II) with 100 asthmatics not exposed (group I) was done. Asthma control and morbidity were assessed by enquiring into emergency department visits, hospitalizations, acute episodes, requirement of parenteral drugs at home, corticosteroids and maintenance bronchodilators in the preceding 1-year period. Lung function of both groups were recorded during this visit. Expiratory flows were lower in patients exposed to ETS. More patients in group II required daily bronchodilators and use of corticosteroids and the number of acute episodes, emergency department visits was significantly more in this group. Absence from work was more

frequently encountered in the ETS-exposed patients. The authors conclude that control of asthma was poorer and morbidity greater in adult patients with asthma exposed to ETS at home and/or workplace.

Cunningham SJ, Grain EF, *Reduction of morbidity in asthmatic children given spacer device. Chest 1994; 106:753.*

Eighty four children with asthma were divided into two groups in which the study group received inhaled p-agonist and discharged with a spacer device while the control group received inhaled/oral P-agonist without a spacer device. A baseline questionnaire was completed and a follow-up by telephone was done at 1 week, 2, 4 and 6 months. The spacer group reported significantly earlier resolution of wheezing at 2 and 4 months' follow-up assessment, fewer days of cough after asthma attack at 2 and 4 months' and significantly fewer days of school absence at 2 and 4 months. There was no difference between the two groups at 1 week and 6 months' follow-up assessment. The authors conclude that introducing a spacer device improves the functioning of asthmatic children in terms of resolution of cough and wheeze and school absenteeism.

Panchal N, Pant C, Bhagat R, Shall A. *Central bronchiectasis in allergic bronchopulmonary aspergillosis: Comparative evaluation of computed tomography of the thorax with bronchography. Eur Respir J 1994; 7: 1290.*

Demonstration of central bronchiectasis (CB) with normal distal bronchi is a *sine qua non* for the diagnosis of allergic bronchopulmonary aspergillosis (ABPA). In an attempt to find a safe and effective alternative to bronchography for the demonstration of CB, computed tomography (CT) of the thorax which was done first was evaluated against bronchography in 21 patients of ABPA; of the 378 bronchopulmonary segments available for assessment, 42 had to be excluded because of consolidation or nonfilling of dye leaving 336 segments for evaluation. CB was identified on CT in all 21 patients. CT using 8 mm contiguous scans used in 8 patients improved overall sensitivity to 82%. The authors conclude that CT of the

thorax has the potential of being the investigation of choice for the demonstration of CB in patients with ABPA.

Poe RH, Levy PC, Israel RH, Ortiz CR, Kallay MC. *Use of fiberoptic bronchoscopy in the diagnosis of bronchogenic carcinoma: A study in patients with idiopathic pleural effusion. Chest* 1994; 105: 1663.

One hundred fifteen patients with pleural effusion in whom bronchogenic carcinoma was suspected underwent fiberoptic bronchoscopy (FOB) to identify those for whom the procedure was useful. In 6 of 12 patients with hemoptysis, 8 of 12 with a mass or infiltrate and 8 of 18 with atelectasis with negative fluid cytology and 3 of 7 with cytology positive, FOB was useful in diagnosis. 66 patients had an isolated cytology-negative effusion. 7 of 18 with massive effusion had FOB detecting cancer. FOB usually was nondiagnostic in lesser-sized effusion (47 of 48). The authors conclude that FOB is useful in diagnosing bronchogenic carcinoma in such patients when there is hemoptysis, accompanying lung mass or infiltrate, atelectasis, the effusion is massive, or in cytology-positive effusion without obvious primary tumour. Due to the low prevalence of lesser size, the authors suggest that in this group FOB not be performed routinely.

Storms WW, Bodman SF, Nathan RA, Byer P. *Nocturnal asthma symptoms may be more prevalent than we think. Journal of Asthma* 1994; 31:313.

The prevalence of nocturnal asthma in a subspecialty allergic clinic was evaluated to see whether it was significantly different from the prevalence in previous studies. A questionnaire was sent to 1258 patients, of which 325 responded. Of 325, 304 patients had asthma. 204 (67%) of these had nocturnal symptoms of asthma. 11% of the total population awakened every night, 16% awakened three to six nights per week, 20% one or two nights per week, 20% one night per month, and 33% not at all. The authors discovered that patients had a rather nonchalant view of their asthma and frequently did not report nocturnal symptoms to their doctors. The authors conclude that even in a speciality allergy and asthma practice, nocturnal asthma symptoms may be

more prevalent than suspected. The reason for this is unclear but may be related to a problem with patient perception and possibility to a lack of diligence in physicians' history taking.

Van Gelder I, Damhnis RAM, Hooqsteden HC, *Prognostic factors and survival in malignant pleural mesothelioma. Eur Resp J.* 1994; 7: 1035.

The prognostic significance of age, stage of disease, gender and histological subtype was studied in 167 new cases of cytologically (15%) or histologically (85%) proven malignant pleural mesothelioma in the Rotterdam area, during 1987-89. Median survival of all patients was 242 days. Univariate analysis identified age, stage and histopathological subtype as significant prognostic factors, which was confirmed in multivariate analysis. Median survival rate for patients <65, 65-74 and >75 years were 359, 242 and 131 days respectively. Patients with stage I disease had a median survival of 359 days compared to 147 and 112 days respectively for stage II and combination of stages III and IV. Mixed histopathological subtype (190 days) was less favourable than sarcomatous (207 days) and epithelial (252 days) subtypes. Using a Cox proportional hazard model in patients with malignant pleural mesothelioma, age, histological subtype and stage were identified as independent prognostic factors. These prognostic factors should be taken into account when starting or evaluating treatment studies.

Dodge R, Cline MG, Lebowitz MD, Burrows B. *Findings before the diagnosis of asthma in young adults. J Allergy Clin Immunol* 1994; 94 : 831.

Using subject of a community-based study, the authors prospectively compared young adults destined to develop asthma with control subjects to determine differences between them before diagnosis. Subjects were participants of the Tucson epidemiological study of airways obstructive diseases and were studied between toe ages of 15 and 19 and subsequently every 1-2 years until they were at least 21 years old with questionnaires, spirometry, allergy skin testing and serum IgE testing. Logistic regression showed that "wheeze" and "attacks of shortness of breath with wheeze" were independently predictive of asthma. Positive

allergy skin tests results occurred more frequently among subjects who later received a diagnosis of asthma, and initially those subjects had higher serum IgE levels than control subjects (geometric mean IgE= 173.8 IU/ml vs. 52.5 IU/ml for control subjects; $p < 0.005$). Although initial spirometric testing did not distinguish between future asthmatics and control subjects, repeat testing after diagnosis did show significant differences in flows at low lung volumes. The data suggest that symptoms and findings suggestive of asthma may be present for many years before diagnosis.

Claman DM, Boushey HA, Liu J, Wong H, Faliy UV. *Analysis of induced sputum to examine the effects of prednisone on airway inflammation in asthmatic subjects. J. Allergy Clin Immunol* 1994; 94: 831-5.

To determine whether induced sputum samples might provide a useful means for evaluating the effects of therapy on airway mucosal inflammation, the authors examined induced sputum samples obtained before and

after 6 days of treatment with prednisone (0.5 mg/kg/day) or placebo in a randomized, double-blind study of 24 asthmatics. Induced sputum was analyzed for total and differential cell counts and for concentration of eosinophil cationic protein, albumin and mucin-like glycoprotein. The authors found that in prednisone-treated group the mean (SEM) percentage of eosinophils in sputum samples fell from $14.1 \pm 5.0\%$ at baseline to $1.8 \pm 0.8\%$ (in placebo treated group from $10.3 \pm 4.9\%$ to $11.1 \pm 4\%$; $p = 0.0002$); the absolute eosinophil count decreased significantly more ($p = 0.04$); eosinophil cationic protein levels fell from 324 ± 131 ng/ml to 144 ± 84 ng/ml (Vs. 173 ± 50 ng/ml to 188 ± 47 ng/ml in placebo-treated group, $p = 0.002$); and was associated with a significant increase in peak expiratory flow ($r_s = 0.64$, $p = 0.04$). Prednisone treatment was not associated with any significant change in the concentrations of albumin or mucin-like glycoprotein. The authors conclude that analysis of induced sputum is a useful non-invasive method for studying the effects of asthma therapy on airway eosinophilic inflammation.

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-100 001.

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 (sec 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 wherein readers can express opinions 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 for publication and to give suggestion 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 opinions 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 subject 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 table 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 of 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 a 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. 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.

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that editorial processing could be specially expedited.

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Crofton, J. and Douglas, A.: *Respiratory Diseases*, 1st Edition, Edinburgh, Blackwell Scientific Publications Ltd. 1969.

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SI No.	Location	Type of error and its correction
1	Page No. 101 in Summary	Line 2 to be read as "there in" instead of "is there",
2	Page 103 a) Third line b) Seventh line c) Para Four, 11th line d) Para Seven e) Para Nine, 4th line	> 75% should be corrected as $\geq 75\%$. > 85% should be read as $\geq 85\%$. DGH should be read as DGHS. "Table 1" in bracket should be inserted for the heading. > 80% should be read as $\geq 80\%$.
3	Page 104	Under column 7, serial no. 5 is blank. It is to be filled as 27.
4	a) Page 106, Para 2,4th line b) Para Seven	> 80% should be read as $\geq 80\%$. "Table 3" in bracket should be inserted in the heading.
5	a) Page 107, Para 2 b) Para 3, fifth line c) Page 107, Para nine, second line	Please insert "(refer table 3)" at the end of the para. > 5.0% should be read as $\geq 5.0\%$ and also insert "(Refer table 4)" at the end of para. > 35% should be changed as $\geq 35\%$.
6.	Page 109	Insert % under efficiency & delete % under Expected.
7.	Page 111, Para nine, 7th line	> 75% should be read as $\geq 75\%$
8.	Page 114	Column. 11, serial no. 1, 10 is to be changed to 18.