

A COST BENEFIT ANALYSIS OF BCG VACCINATION AS A CONTROL MEASURE AGAINST TUBERCULOSIS AS COMPARED TO TREATMENT OF INFECTIOUS CASES BY K. NAGANNA	4
RESULTS OF TESTING WITH RT XXII, PPD-S AND PPD-B IN SYMPTOMATIC PERSONS ATTENDING A TUBERCULOSIS CENTRE BY D.C. PANDE, K.D. GAUTAM AND M.L. MEHROTRA	9
PLEURAL BIOPSY (ANALYSIS OF 81 CASES) BY R.K. TANDON AND S.R.P. MISRA	18
KIDNEY CHANGES IN PULMONARY TUBERCULOSIS—A STUDY BY KIDNEY BIOPSY BY P.K.D. SHAH, M.K. JAIN, H.N. MANGAL AND N.M. SINGHVI	
LIVER FUNCTION IN EXTRA-PULMONARY TUBERCULOSIS BY V.K. JHA, K. KOTILINGAM, D.C. RAY, P.K. SHUKLA AND M. JOSHI	28
ASSOCIATION OF PULMONARY TUBERCULOSIS AND LUNG CANCER BY A. NAFEE, S.P. MISRA, S.N. DHAR AND S.N.A. SHAH	31
TAI GOLD MEDAL	46
SUMMARIES OF PAPERS PRESENTED AT THE DELHI CONFERENCE	47
BACILLARY RESISTANCE TO DRUGS IN TUBERCULOSIS—A TREND OVER 13 YEARS BY P.K. SEN AND B.N. RAY	68
PROGRESS IN THE CONTROL OF TB DRUG—THERAPY PLAYS KEY ROLE BY ARVIND NAIR	73
COMPARATIVE STUDIES OF CULTURAL AND HISTOPATHOLOGICAL ASPECTS OF EXPERIMENTAL H37 Rv INFECTION IN GUINEAPIGS BY N.K. GANGULY AND N.L. CHITKARA	76
PERCUTANEOUS LUNG BIOPSY WITH VIM SILVERMAN'S BIOPSY NEEDLE BY B.K. KHANNA	81
R PSYCHOLOGICAL SURVEY OF TUBERCULOSIS PATIENTS BY B. LALDUBEY	
PROGRAMME FOR BIG CITIES BY D.R. NAGPAUL	96
NOTE ON URBAN TUBERCULOSIS CONTROL PROGRAMME STANDING TECHNICAL COMMITTEE	104
URBAN NEIGHBOURHOOD CLINICS IN THE MANAGEMENT OF PULMONARY TB—PRELIMINARY REPORT BY SANJAYA TANDAN, M.L. MEHROTRA AND J.R. LAKHERA	108
NEUROTUBERCULOSIS—HISTOPATHOLOGICAL STUDY OF 90 CASES BY G. CHENGAL RAJU, G. SUVARNA KUMARI, M. JAWAD ALI KHAN, D. BHASKARA REDDY AND I. DINKAR	111
PATTERN OF TUBERCULOSIS—A REVIEW BASED ON AN AUTOPSY STUDY BY D. BHASKARA REDDY, G. CHENGAL RAJU AND G. SUVARNA KUMARI	115
TOXIC PSYCHOSIS DUE TO ISONIAZID BY M.C. AGARWALA, H.M. KANSAL, R.K. GUPTA, D.K. GUPTA AND S. KUMAR	119
ALOPECIA DUE TO ETHIONAMIDE BY O.P. MITAL AND D.K. GUPTA	121
FATAL DERMATOLOGICAL HYPERSENSITIVITY REACTION DUE TO THIAZETAZONE BY S.K. JAIN, I. TEWARI AND V. SWARUP	123
MILIARY TUBERCULOSIS SIMULATING ACUTE MYELOID LEUKAEMIA—REVIEW OF LITERATURE AND REPORT OF A CASE BY C.S.V. SUBRAMANYAM, J.M. AHUJA AND M.L. SAPRA	136
ETHAMBUTOL IN RETREATMENT OF PULMONARY TUBERCULOSIS O.P. MITAL, R.K. NARANG AND A.S. SACHAN	142
A STUDY OF SERUM GLUTAMIC—OXALACETIC TRANSAMINASE AND GLUTAMIC—PYRUVIC TRANSAMINASE IN PULMONARY TUBERCULOSIS BY K. NIGAM, M.C. GUPTA, S.B. GUPTA AND K.J.B.S. GAUR	147
TOXICITY OF THIAZETAZONE (WHEN USED IN COMBINATION WITH ISONIAZID) A STUDY AMONG 1225 PATIENTS BY K.C. MATHUR	151
SPINAL SUBDURAL TUBERCULOMA BY I. DINAKAR, B.C. REDDY, D. BHASKARA REDDY, G. SUVARANA KUMARI AND M. JAWAD ALI KHAN	158

INDEX TO CONTENTS VOL. XXIII

iii

MASS VACCINATION CAMP	174
TB CAMP: KAKINADA, ANDHRA PRADESH	174
REFRESHER COURSES IN UTTAR PRADESH	174
MEXICO CONFERENCE	174
XTH EASTERN REGION CONFERENCE	175
AMRUT MODY RESEARCH FOUNDATION AWARDS—RS. 10,000 EACH	175
MEMORIAL PRIZES	175
INDIAN COLLEGE OF ALLERGY AND APPLIED IMMUNOLOGY... ..	175
OBITUARY	175

INDEX

Agarwala M.C. et. al. , Toxic psychosis due to Isoniazid	119
Ahuja J.M. et. al. , "Miliary Tuberculosis simulating acute myeloid leukaemia—Review of Literature and report of a case	136
Alopecia due to Ethionamide	121
Amrut Mody Research Foundation Awards	175
Annual Meetings	86, 125
Anti-TB Shibirs	174
Association of Pulmonary Tuberculosis and Lung Cancer	31
Asthma, Bronchitis Foundation	38
Autopsy study, — Pattern of Tuberculosis — a review based on an	115
Awards	125
Bacillary resistance to drugs in tuberculosis — a trend over 13 years	68
B.C.G. Vaccination	1
B.C.G. Vaccination, A cost-benefit analysis of, as a control measure against Tuberculosis as compared to treatment of infectious cases	4
"BEAT TB" — incentive for students	38
Chairman, Technical Committee	86
Chanchal Singh Memorial Award	37, 86, 126
Chandna R.S. et al , TB of the Tongue	163
Cheagal Raju G. et. al , Neurotuberculosis — Histopathological study of 90 cases	111
Cheagal Raju, G. et. al , Pattern of Tuberculosis—A review based on an Autopsy study	115
Chitkara, N.L. et. al , Comparative studies of Cultural and histopathological aspects of experimental H37RV infection in Guineapigs	76
Comparative studies of cultural and histopathological aspects of experimental H37RV infection in Guineapigs	76
Conference/Seminars/Shibirs	87
Conjunctiva, primary tuberculosis of the	160
Cost benefit analysis of BCG vaccination as a control measure against Tuberculosis as compared to treatment of infectious cases.	4
D'Arcy Cowan Memorial Prize—1975	87
Dermatological Hypersensitivity reaction due to thiacetazone, Fatal	123
Deshmukh, M.D. Report on TB control programme in Libya	168
Dinkar, I. et. al , Neurotuberculosis, Histopathological study of 90 cases	111
Dinkar, I. et. al , Spinal subdural Tuberculoma	158
Drugs, Bacillary Resistance to, in TB	68
Dubey, B. Lal , Psychological survey of TB patients	83
Essay Competition	37, 86, 126
Ethambutol in retreatment of pulmonary TB	142
Ethionamide, Alopecia due to	121
Excerpta Medica Foundation Congress	87
Expert Committee	174
Fatal dermatological hypersensitivity reaction due to thiacetazone	123
Gandhewar, R.N. et al , Primary TB of the conjunctiva	160
Ganguly, N.K. et al , Comparative studies of cultural and histopathological aspects of experimental H37RV infection in Guineapigs	76
Gaur, K.J.B.S. et. al , A study of serum Glutamic Oxalacetic transminase and Glutamic-Pyruvic transminase in pulmonary tuberculosis	147
Gautam, K.D. et. al , Results of testing with RT XXIII, PPD-S and PPD-B in symptomatic persons attending a tuberculosis centre	9
General Practitioners & TB	133
Glutamic-Oxalacetic transminase, a study of serum,	147
Gupta, D.K. et. al , Toxic psychosis due to Isoniazid.	119
Gupta, D.K. et. al , Alopecia due to Ethionamide	121
Gupta, M.C. et. al , A study of serum Glutamic-Oxalacetic transaminase and Glutamic-Pyruvic transaminase in pulmonary tuberculosis	147
Gupta R.K. et. al , — Toxic psychosis due to Isoniazid	119
Gupta S.B. et. al , A study of serum Glutamic-Oxalacetic transaminase and Glutamic-Pyruvic transaminase in pulmonary TB	147
Health Visitors Course	86, 125
Histopathological study of 90 cases, Neurotuberculosis	111
Hypersensitivity, fatal dermatological, reaction due to Thiacetazone	123
Indian College of Allergy & Allied immunology	175
International Conference in Mexico	126
Iraqi, A.A. et. al, Tuberculosis of the Mandible	162
Isoniazid, Toxic psychosis due to,	119
Jain, M.K. et. al , Kidney changes in pulmonary TB — a study in Kidney biopsy	23
Jain, S.K. et. al , Fatal Dermatological hypersensitivity reaction due to Thiacetazone	123
Jawad Ali Khan, M. et. al , Neurotuberculosis Histopathological study of 90 cases	111
Jawad Ali Khan, M. et. al , Spinal subdural tuberculoma	158
Jha, V.K. et al. , Liver function in extra-pulmonary TB	28
Joshi, M. et. al , Liver function in extra-pulmonary TB	28
Kansal, H.M. et al , Toxic Psychosis due to Isoniazid	119
Kasauli Sanatorium	37
Khan, A.A. et al , TB of the Mandible	162
Khan, Ansar A. et al , TB of the Mandible	162
Khanna, B.K. , Percutaneous lung biopsy with Vim Silverman's biopsy needle	81
Khushi Ram Shield	87
Kidney changes in pulmonary TB — a study by Kidney biopsy	23
Kotilingam K. et. al , Liver function in extra-pulmonary tuberculosis	28
Kumar, S. et. al , Toxic psychosis due to Isoniazid	119
Lakhera, J.R. et al , Urban neighbourhood clinics in the management of pulmonary TB — preliminary report	108
Leukaemia, Miliary TB simulating acute myeloid review of literature and report of a case	136
Libya, Report on TB control Programme in	168

Liver function in extrapulmonary TB	28	Pulmonary, Report on terminology for, physical signs	165
Lung cancer, Association of pulmonary TB and Mandible, TB of the	31 162	Pulmonary TB	
Mangal, H.N. et al. , Kidney changes in pulmonary TB—a study of Kidney biopsy	23	Association of, and lung cancer	31
Mary Clubwala Jadav	87	Ethambutol in retreatment of,	142
Mass vaccination Camp	87	Kidney changes in,	23
Mathur, K.C. Toxicity of Thiacetazone (when used in combination with Isoniazid) a study among 1225 patients	151	Liver function in extra,	28
Mehrotra, M.L. et al. , Results of testing with RT XXIII, PPD-S and PPD-B in symptomatic persons attending a TB Centre	9	A study of serum Glutamic-Oxalacetic transaminase and Glutamic-Pyruvic transaminase in,	147
Mehrotra, M.L. et al. , Urban neighbourhood clinics in the management of Pulmonary TB — preliminary report	108	Urban neighbourhood clinics in the management of, preliminary report	108
Memorandum	87	Raj, B.N. et al., Bacillary resistance to drugs in TB—a trend over 13 years	68
Memorial Prizes	175	Rajasthan	38
Mexico Conference	174	Ray, D.C. et al., Liver function in extra-pulmonary TB	28
Miliary TB simulating acute myeloid Leukaemia—review of literature and report of a case	136	Reddy, B.C. et al. , Spinal subdural tuberculoma	158
Misra, S.R.P. et al. , Pleural biopsy (analysis of 81 cases)	18	Reddy, D. Bhaskara, et al. , Neurotuberculosis—Histopathological study of 90 cases	111
Misra, S.P. et al. , Association of pulmonary TB and lung cancer	31	Reddy, D. Bhaskara et al. , Pattern of TB — a review based on an autopsy study	115
Mital, O.P. et al. , Alopecia due to Ethionamide	121	Reddy, D. Bhaskara et al. , Spinal subdural tuberculoma	158
Mital, O.P. et al. , Ethambutol in retreatment of pulmonary TB	142	Refresher courses	126, 174
Nafae, A. et al. , Association of Pulmonary TB & Lung cancer	31	Report on terminology for pulmonary physical signs	165
Naganna, K. A cost benefit analysis of BCG vaccination as a control measure against TB as compared to treatment of infectious cases	4	Report on TB control Programme in Libya	168
Nagpaul D.R. , A TB programme for big cities	96	Resistance, bacillary, to drugs in TB — a trend over 13 years	68
Nair, Arvind , Progress in the control of TB drug — therapy plays key role	73	Results of testing with RTXXIII, PPD-S & PPD-B in symptomatic persons attending a TB Centre	9
Narang, R.K. et al. , Ethambutol in retreatment of pulmonary TB	142	Sachan, A.S. et al., Ethambutol in retreatment of pulmonary TB.	142
National Conference	86, 174	Sapra, M.L. et al., Miliary TB stimulating acute myeloid Leukaemia—review of literature and report of a case	136
Neurotuberculosis — histopathological study of cases	90 111	Seal Sale Campaign	37, 87
Nigam, R.K. et al. , A study of serum glutamic-oxalacetic transaminase and glutamic-pyruvic transaminase in pulmonary tuberculosis	147	Sen P.K. et al., Bacillary resistance to drugs in TB—a trend over 13 years	68
Note on urban TB Control programme	104	Shah, P.K.D. et al. , Kidney changes in pulmonary TB—a study by kidney biopsy	23
Obituary	175	Shah, S.N.A. et al. , Association of Pulmonary TB and Lung cancer	31
Open air TB Sanatorium	174	Spinal subdural tuberculoma	158
Pande, D.C. et al. , Results of testing with RT XXIII, PPD-S & PPD-B in symptomatic persons attending a TB Centre	9	S.T.C. members	86
Patel, C. et al. , Tuberculosis of the Tongue	163	Summaries of papers presented at the Delhi Conference	47
Pattern of TB — a review of, based on an autopsy study	115	Suvarna Kumari G. et al., Neurotuberculosis—Histopathological study of 90 cases	111
Percutaneous lung biopsy with Vim Silverman's biopsy needle	81	Suvarna Kumari G. et al., Spinal subdural tuberculoma	158
Physical signs, report on terminology for pulmonary	165	Swarup, V. et al., Fatal dermatological hypersensitivity reaction due to Thiacetazone	123
Pleural Biopsy	18	Study of serum Glutamic-Oxalacetic transaminase and Glutamic-Pyruvic transaminase in pulmonary tuberculosis.	147
Pondicherry	38	Tandon, R.K., et al. , Pleural biopsy (analysis of 81 cases)	18
PPD-S & PPD-B, results of testing with RT XXIII, in symptomatic persons attending a TB Centre	9	Tandon, Sanjaya, et al. , Urban neighbourhood clinics in the management of pulmonary TB—preliminary report	108
Primary TB of the conjunctiva	160	Tewari, I. et al. , Fatal dermatological hypersensitivity reaction due to Thiacetazone	123
Prime Minister inaugurates Seal Campaign	173	Thiacetazone, Fatal dermatological hypersensitivity reaction due to,	123
Psychological survey of TB patients	83		

Thiacetazone, Toxicity of, (when used in combination with Isoniazid) a study among 1225 patients	151	A, programme for big cities	96
Third National Congress in diabetes	126	Psychological survey of, patients	83
Toxic Psychosis due to Isoniazid	119	Results of testing with RTXIII, PPD-S and PPD-B in symptomatic persons attending a Centre	9
Toxicity of Thiacetazone (when used in combination with Isoniazid) a study among 1225 patients	151	A study of serum glutamic-Oxalacetic transaminase and Glutamic-Pyruvic transaminase in pulmonary,	147
Tuberculoma, Spinal subdural	158	Urban neighbourhood clinics in the management of pulmonary, preliminary report	108
Tuberculosis		Tuberculosis of the Mandible	162
Association of pulmonary, and lung cancer	31	Tuberculosis of the Tongue	163
Bacillary resistance to drugs in, a trend over 13 years	68	Report on, control programme in Libya	168
A cost benefit analysis of BCG vaccination as a control measure against, as compared to treatment of infectious cases	4	Urban, Control Programme	93
Ethambutol in retreatment of pulmonary,	142	General Practitioners and,	133
Kidney changes in pulmonary, a study by kidney biopsy	23	Twentysixth TB Seal	125
Liver function in extra-pulmonary,	28	TB Detection Camp	126
Miliary, simulating acute myeloid Leukaemia, review of literature & report of a case	136	TB Camp, Kakinada	174
Note on urban, control programme	104	Urban neighbourhood clinics in the management of pulmonary TB — preliminary report	108
Pattern of, a review based on an autopsy study	115	Urban TB Control Programme	93
Primary, of the conjunctiva	160	Urban, TB Control programme. Note on	104
		Vim Silverman's biopsy needle. Percutaneous lung biopsy with,	81

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B C.G. VACCINATION

Although BCG was introduced to prevent tuberculous disease in human beings over half a century ago, it was adopted as a mass immunization measure much later in the wake of the Second World War in war-torn countries of Europe and developing countries in Asia and Africa with high prevalence of disease and paucity of traditional requisites of control. Millions of children have been vaccinated but the controversy regarding its utility still continues.

It is to be remembered that BCG vaccination was introduced without prior controlled trials. Even without BCG every infected individual does not develop disease. Chances of developing disease also depend on several factors. The time-lag between infection and disease may extend to several years. Consequently a very large and relatively static population has to be followed up for a long time before valid conclusions could be drawn about the effectiveness of BCG. Obviously such trials are extremely difficult, if not impossible, to organise.

The few pre-planned controlled trials of acceptable scientific merit have been carried out only recently. Some like Hyge's study in Danish children were purely fortuitous. All these, with the solitary exception of the USPHS study, have proved significant advantage in favour of the vaccinated children though the quantum of protection afforded varies considerably. This discrepancy has been attributed to several factors such as quality of the vaccine used, strength of the tuberculin used to sort out the uninfected from the infected, low grade non-specific sensitivity etc. in the USPHS study. It is almost universally accepted that BCG confers protection against development of disease.

The utility of a measure like mass BCG vaccination has also to be judged in terms of its contribution towards the overall control of tuberculosis on the basis of cost-benefit analysis. Elsewhere in this issue, Naganna, on the basis of Frimodt-Moller's study¹, reports that the impact of BCG on control of tuberculosis in the South Indian population is very insignificant and it is cheaper to find and treat a bacillary case of pulmonary tuberculosis than to prevent it by BCG vaccination. It is common knowledge that most of the cases prevented by BCG are abacillary. Why should these be ignored and cost-benefit analysis based only on the bacillary cases? Even the WHO Expert Committee on Tuberculosis² recognizes that the problem of tuberculosis is "sum total of individual suffering caused by disease" and this includes not only abacillary pulmonary disease but also disease of organs other than the lung. Is miliary and meningeal tuberculosis, which BCG prevents, less important than

bacillary pulmonary disease ? And if total tuberculous disease is taken as the basis of comparison between vaccinated and unvaccinated tuberculin negatives even Frimodt-Moller's study³ shows significant advantage in favour of the vaccinated. The meticulously conducted B.M.R.C. study⁴ has shown that even after 15 years, the vaccinated groups enjoy considerable advantage over the unvaccinated.

Apart from this, there are other flaws too in Naganna's analysis. He bases his calculations on a group of population where only 52% were tuberculin negative. Would the impact not have been bigger if the tuberculin negatives were, say 80% or 90%? Springett⁶ has shown that the benefit from BCG gets considerably reduced if more than 25% are tuberculin positive. Then, there are some other factors the contribution of which may be immeasurable but, nevertheless, is very pertinent to the cost-benefit analysis and which Naganna has ignored. What about the chain of transmission which a case (which has not been prevented) starts before the disease is diagnosed and treatment started? What about the psychological trauma? The loss in production on grounds of tuberculosis calculated by Naganna appears to be grossly under-estimated. Even a house-wife suffering from tuberculosis who, because of illness, cannot attend to her household chores is an economic loss to the family. Then again the cost of treatment is calculated on the basis of one year's treatment. Every clinician knows that one year's treatment for pulmonary cases, with sputum positive by direct smear, is usually not enough. Treating such cases with INH alone is, today, unthinkable. Cases treated for one year are likely to have a higher relapse rate. What about the economic and other implications of increased relapse rate? And, lastly, BCG vaccination is easier to organise than large-scale case-finding. In short, the over-simplified analysis on the basis of which Naganna questions the value of BCG vaccination is too superficial and entirely unconvincing.

Waler and Rouillon⁶ in a much more elaborate cost-benefit analysis of the impact of BCG in countries with very low prevalence of disease have proved significant advantage in favour of vaccination at school-leaving age even if the annual risk of infection is as low as 0.02%. BCG vaccination of new-borns, according to them, is advantageous only if the annual risk of infection is 0.3% per year or more. Every one knows that the annual risk of infection in our country is many times more than 0.3 %. Endo and Aoki⁷ basing their cost-benefit analysis on BCG vaccination in Japan have come to the conclusion that even if the cost of BCG vaccination was 10 times more, vaccination would still be a profitable investment. If that is so in a country like Japan, where the incidence and prevalence of disease are lower than in our country, the opportunities for infection are diminishing rapidly and the socio-economic condition is much better than ours, how much more beneficial would BCG be in our country?

Sutherland⁸ has shown a good relationship between the degree of protection from BCG and the incidence of tuberculosis in the unvaccinated groups. In the USPHS trial in Georgia the protection was only 14% when the incidence of disease amongst the unvaccinated was 0.13% per 1000 per year. On the other hand, the protection in British school-children was 78% when the incidence amongst the unvaccinated was 1.3% per 1000. Comstock and Edwards⁹

Of the USPHS (the USPHS study is often quoted as evidence against the protective value of BCG) also, by and large, corroborate Sutherland's remarks. According to them the primary determinant of the utility of BCG vaccination is the risk of becoming infected with tubercle bacilli. If this is low as in the USA to-day, there is little need for the kind of protection that BCG can give but where the risk of becoming infected is high (as in India) the need for the kind of protection that BCG could give becomes far greater.

Thus, the contribution of BCG vaccination to the overall control of tuberculosis anywhere depends on the epidemiology of the disease there. There is ample and weighty evidence to show that as long as environmental factors remain unfavourable in our country and the risk of infection is high even in small children, it will be inexcusable to deny them the protection of BCG. No authentic evidence to the contrary is available so far.

REFERENCES

1. Frimodt-Moller, J. et al; *Bull Int. Union. Tub.*; 1972, 48, 40.
2. WHO Expert Committee on Tuberculosis, 8th Report; 1964,
3. Frimodt-Moller, J., et al; *Ind. J. Tub.*; 1964,11, 114.
4. Fourth Report of the Tuberculosis Vaccines Clinical Trial of B.M.R.C; *Bull. Wld. Hlth. Org.*; 1972, 46, 371.
5. Springett, V.H.; *Tubercle*; 1965, 46, 76.
6. Waaler, H. & Rouillon, A.; Paper presented at the IUAT 22nd International Tuberculosis Conference, Tokyo; 1973.
7. Endo, S. & Aoki, K.; *Kekkaku*; 1972, 47, 215.
8. Sutherland, I.; *Post-graduate Medical Journal*; 1971, 47, 759.
9. Comstock, G.W. & Edwards, P.Q.; *Scand. Rev. Resp. Dis.*; 1972, 53, 207.

A COST BENEFIT ANALYSIS OF BCG VACCINATION AS A CONTROL MEASURE AGAINST TUBERCULOSIS AS COMPARED TO TREATMENT OF INFECTIOUS CASES

K. NAGANNA

(From Tuberculosis Prevention Trial, Bangalore).

Introduction

Since the advent of BCG vaccination it has been advocated as a measure of control against tuberculosis. Various controlled studies have been conducted around the world to measure its protective effect. The protection offered by BCG vaccination against Tuberculosis is still under dispute as the protection offered by it varied from zero to eighty percent. One of the factors which is of considerable importance in advocating BCG vaccination as a measure of control against tuberculosis is, the epidemiology of tuberculosis particularly, the incidence of disease. However, BCG vaccination has been advocated, in the words of D'Arcy Hart 'Pragmatic WHO line', particularly for developing countries as a measure of control against tuberculosis. But this practice has to be reviewed with epidemiological findings available at present.

The Indian Journal of Tuberculosis in its editorial of June 1962, while summarising salient points agreed upon by the panel of tuberculosis experts on the subject of tuberculosis control listed that 'The first attempt should be to detect the infective cases (Sputum positive)...'. However, it appears that no cost benefit analysis of preventing a case by BCG vaccination and converting a case by treatment seems to be available then. Now it is possible to say which method either BCG vaccination programme or programme of detecting and treating infectious cases is economical after comparing the costs of prevention of a case and treatment of a case.

Effect of BCG Vaccination

In India a BCG trial has been carried out by Fridmodt-Moller et al (1972). This trial was started in 1950 and results of follow-up of this trial over a period of 20-21 years are available now.

The findings of this trial are important in two respects viz., the protection offered by BCG vaccination and how much such a protective measure will have its impact over the total tuberculosis problem specifically in an Indian community.

The findings of this trial are very important for the study of the latter aspect for the following

two important considerations. The first point is that this trial has been conducted as an epidemiological study which gives incidence of tuberculosis disease also among tuberculin positives, the group which usually is excluded for vaccination, apart from the BCG vaccinated and control groups. The second point is that as suggested by WHO Expert Committee on Tuberculosis (1964) only 'Bacteriologically confirmed' cases are considered as cases of tuberculosis.

This study has shown that the incidence of disease is considerably greater among those who were initially reactors to the tuberculin test. This finding is also in line with the findings in a study conducted in another part of South India by Raj Narain et al (1973).

Table 1 shows number of cases found among BCG vaccinated, control and tuberculin positive groups after a follow-up period of 20-21 years in a sample of South Indian rural population as reported by Fridmodt-Moller et al (1972). Further, it also shows the percentage of cases that would have been prevented by BCG vaccination if BCG had been given to the entire tuberculin negative group. It could be seen that only about 7.6 % of the new cases would have been prevented had BCG vaccination been given to all tuberculin negatives. This finding compares well with the findings by Palmer et al (1958) in Puerto Rico and Muscogee-Russell trials which were 7.9 percent and 9.3 percent respectively. Thus, BCG vaccination would have very small impact over the tuberculosis problem in India, particularly and specifically so in South India.

Cost of Prevention by BCG Vaccination

(i). Testing and then vaccinating only Tuberculin Negatives :

Naganna and Ramesh (1973) estimated the 'Cost of Pulmonary Tuberculosis Prevalence Surveys' which included cost of vaccination also based on the data collected in the year 1969. Cost of BCG vaccination programme alone as in a routine programme, which reduces the cost of vaccination as compared to a research programme could be worked out.

In a routine vaccination programme regular

TABLE I

*Number of 'Bacillary' cases found during 20-21 years of follow-up of a population (in South India)**

Category	Number of persons	Person years	Number of cases observed	Incidence Rate per thousand persons per year	Number of cases that would have been observed if BCG had not been given	Number of cases that would have been observed if BCG had been given to all Tuberculin negatives
BCG vaccinated (Tuberculin negatives)	5069	61175	33	0.539	41	33
Controls (Tuberculin negatives)	5808	70208	47	0.669	47	38
Tuberculin positives	9979	114576	135	1.178	135	135
Total	20856		215		223	206

* Source, Frimodt-Molleretal (1972)

- (i) Total percent of tuberculin negatives is 52.2
- (ii) Protective effect of BCG upto the end of 20-21 years is 20 percent
- (iii) Number of cases that would have been prevented had BCG been given to all tuberculin negatives is 17
- (iv) Percent of cases that would have been prevented by BCG if BCG had been given to all tuberculin negatives is

$$\frac{(223-206) \times 100}{223} \text{ i.e. } 7.6$$

census taking is not required and secretaries for testers, readers and vaccmators are also not required. Further, in a BCG programme only the non-reactors to a tuberculin test are vaccinated which reduces the work load by 50 percent for the vaccinators. However, in a BCG vaccination programme the vaccination would be done by house-to-house visit following tuberculin test reader which would slow down the efficiency of vaccinators. Ultimately, it is expected that about 25 percent of the work load for the vaccinators could be reduced. After considering all these aspects in a routine BCG programme to vaccinate 52.2 percent of one lakh which is the proportion of tuberculin negatives (Frimodt Moller et al 1972), the amount required is Rs. 147.6 thousands (see Appendix A(i)). Therefore, to vaccinate only 10,877 tuberculin negative persons (as in Frimodt-Moller, et al 1972) the amount required is Rs. 30,756/-.

Number of cases prevented thus, by BCG

vaccination is 17 cases. Therefore, to prevent a case the amount required is Rs. 1,809/-.

Direct Vaccination

In the direct vaccination programme by house-to-house visit no testing and reading teams are required. However, no work load would be reduced for vaccinators rather the efficiency of them would be reduced due to house-to-house visit. However, this effect for estimating the cost has not been considered. Thus, to vaccinate one lakh persons the amount required is Rs. 51.1 thousands (see Appendix A(ii)). To vaccinate a total of 20,856 persons (as in Frimodt-Moller et al 1972) or to prevent 17 cases the amount required is Rs. 10.7 thousands. Thus, the amount required to prevent a case is Rs. 629/-.

Cost of Conversion by Treatment

From the available data it is possible to work

out the total cost of finding a case and cost of treatment with a suitable drug regimen. For this, loss due to loss of economic productivity during the period of treatment, though not a part of treatment, could also be added. Andersen (1962) has shown that only in about 13 percent of the cases the economic loss was not fully recovered and average annual loss for a tuberculosis case was estimated to be about Rs. 30/-. Nagpaul (1963) in his paper presented to the 17th International Tuberculosis Conference (1963) Rome, has given cost of finding a treatment-case by various methods. However, the method 'Sputum case-finding on the basis of symptoms' has been considered. The methodology is described briefly as follows :

'An agent motivates the community and collects sputum from those who have symptoms. Sputum is examined by simple microscopy'. This method has been justified for developing countries, in the words of Nagpaul (1963) "As long as the means are not sufficient to treat at first those who are already infecting others, early treatment of bacillary cases is meaningless in developing countries. This will emphasise what should be the primary concern of all developing countries namely, find all or nearly all the infectious cases and provide them with adequate treatment...Sputum case finding should, therefore, become the backbone of case finding, especially for rural areas in most developing countries." By this method the cost of finding a treatment case was given as Rs. 95/- in 1963 which works out to Rs. 129.20/- in 1972.

Further, treating such a case for one year by INH alone (400-450 mgs) daily for one year was given as Rs. 20/- in 1963 which works out to Rs. 27.20/- in 1972. This regimen will give a sputum conversion rate of 70 percent at 9 months and cavity closure to an extent of 52 percent and further this regimen has been recommended for mass chemotherapy for the following reasons by Nagpaul (1963).

"Sputum conversion may be 60-70 percent instead of 90 percent and some cases may become drug resistant in the face of clear advantages namely, isoniazid perhaps the most acceptable of all anti-tuberculosis drugs and the only one which is known to be capable of being applied on a mass scale For developing countries as a class Isoniazid alone appears to be the only practical regimen for all intents and purposes."

Thus, total cost of finding a treatment case, cost of actual treatment and loss incurred due to loss of economic productivity which is 13 percent (Andersen 1962) of per capita income of Rs. 542.30 in 1968-69 (Khanna 1972) works out to

Rs. 227/- (Rs. 129.30 + Rs. 27.20 -f Rs. 70.49 — Rs. 226.89). Even after considering conversion rate of 70 percent by this regimen the cost works out to about Rs. 325/-.

Even if one uses the highly successful regimen of SM = INH for six months and then INH = PAS for another six months which gives a conversion of above 85 percent the cost would be only Rs. 554/-.

Cost Benefit of Treatment Programme

The amount spent to prevent a case by BCG vaccination programme having tuberculin test to vaccinate only tuberculin negatives is Rs. 1809/- and by direct vaccination method is Rs. 629/- whereas to convert a case which includes finding, treating and loss due to economic productivity is only Rs. 325/- and this amount is only Rs. 554/- even when SM = INH and then INH = PAS regimen is adopted.

Whatever investment is made the aim should be to derive maximum benefit to the community. In the field of public health in the words of Nagpaul (1963) "The investment of resources has to be on health and not on disease that is the long term goal should not be alleviation of human suffering (at best, a short term objective) but *the epidemiological conquest of disease**... Success in this task should be measured not by the increase in per capita expenditure on health, but in terms of dividends from the investments made."

Case finding and chemotherapy programme has economic benefit besides attacking the tuberculosis problem in the right place as the prevalence of disease is always more among tuberculin positives. Incidence of disease is greater among tuberculin positives and particularly among household contacts of culture positive cases (Raj Narain et al 1973). It has been also shown that infectiousness of bacteriologically proved cases is greater to their household contacts particularly so among contacts of 'Microscopy positive cases' (Raj Narain et al 1966, Raj Narain et al 1971). These findings question one of the basis on which BCG vaccination programme is advocated. Palmer and associates (1958) have said "... It was widely believed that, if tuberculosis disease were to occur, it would generally do so within the first few years after infection; and that most of the new cases were.... therefore destined to arise in those not yet infected. Indeed one of the principal arguments for the use of BCG was predicated on that concept of the pathogenesis of Tuberculosis.*"

* Underlining is by the present author.

* The authors have quoted, Holm J, Pub. Health Rep. 1946, 61, 1298.

The Tuberculosis control programme primarily based on case finding and treating such cases not only from economic point of view but also from epidemiological point of view is beneficial as compared to the benefits derived by the BCG vaccination programme. Further, according to Frimodt Moller et al (1972), "...The main effect of vaccination in man is the same as observed in experimental animals, namely, to suppress the multiplication of the bacilli after primary infection. In many cases this is sufficient to prevent the development of demonstrable tuberculosis but in others it delays the onset of the disease."

Summary

BCG vaccination as a measure of control of Tuberculosis has been advocated particularly for developing countries. A controlled study conducted in South India suggests that BCG vaccination would have an impact of only about 8 percent on the total tuberculosis expected during 20-21 years.

It is estimated that to prevent a case by BCG

vaccination after testing and by direct BCG vaccination without testing the amounts required are about Rs. 1,810/- and Rs. 630/- respectively.

Further, it is estimated that the cost of finding and treating an infectious case, including the loss due to loss of economic productivity, with INH alone and with the highly successful regimen of SM and INH and then INH and PAS, the amounts required are about Rs. 325/- and Rs. 554 respectively.

Thus, it appears that case finding and chemotherapy programme to treat infectious cases is economical besides, attacking the tuberculosis problem epidemiologically at the right place.

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APPENDIX — A

Cost of Vaccination Programmes (From Data Provided in Table II and Appendix — lofNaganna and Ramesh, 1973).

(i) Testing and Vaccinating Tuberculin Negatives:

(ii) Direct Vaccination:

	<i>Rs in thousand</i>	<i>Persons</i>		<i>Rs in thousands</i>	<i>Persons</i>	
Testing team	69.4	12		Vaccination team	67.3	12
Reading team	61.9	13	12			
37 of 63.3 i.e. Field Administration	28.9	—	81	of 63.3 i.e. Field Administration	9.4	—
81				Total	76.7	12
Total	227.5	37				

4 tester's secretaries, 4 Reader's secretaries, 4 vaccinator's secretaries and 1 vaccinator are not required out of 37 persons in the simplified vaccination programme.

Therefore the cost works out to Rs (thousand)

$$\frac{227.5 \times (37-13)}{37} \text{ i.e. Rs. 147.6 thousands.}$$

4 Vaccinator's secretaries are not required out of 12 persons in the direct vaccination : rog-remme.

Therefore the cost works out to Rs (thousand)

$$\frac{76.7 \times (12-4)}{12} \text{ i.e. Rs. 51.1 thousands.}$$

K. NAGANNA

REFERENCES

- Andersen, S., 1962; *Ind. J. Tub.* IX, 3,176-180.
- Competition Success Review*, March 1974. (Annual issue) 48/4, East Patel Nagar, New Delhi, p. 23. Not quoted but consulted.
- D'Arcy Hart, P., 1967; *Brit. Med. J.* 1, 587.
- Editorial, June 1962. Control of Tuberculosis in India. *Ind. J. Tub.* IX, 3, 145-146.
- Frimodt-Moller, J., Acharyulu, G.S. and Keshava Pillai, a K., 1972; Observations on the protective effect of BCG vaccination in a South Indian Rural population (Fourth Report). *Bull. Int. Union Tub.* Vol. 48.
- Khanna, O.P., 1972; *General Knowledge*, IV Revised edition: Khanna Bros., Ambala, India, p. 183.
- Nagpaul, D.R., 1963; Chemotherapy Programme and drug regimens related to the economic resources in developing countries. Paper presented to the XVII International Tuberculosis Conference, Rome. (Personal communication). Summary of this paper has been published in XVIIe CONFERENCE INTERNATIONALE DE LA TUBERCULOSE. Rome. September 1963.
- Naganna, K., and Ramesh, A.S. 1973; *Indian J. Med. Res.* **61**, 1233-1242.
- Palmer, C.E., Shaw, L.W., and Comstock, G.W., 1958, *Amer. Rev. Resp. Dis.*, 77, 6, 877-907.
- Raj Narain, Nair, S.S., Ramanatha Rao, G., and Chandrasekhar, P., 1966; *Bull. Wld. Hlth. Org.*, 34, 639-654.
- Raj Narain, Subba Rao, M.S., Chandrasekhar, P., and Pyarelal, 1971; *Amer. Rev. Resp. Dis.*, 103, 761-773.
- Raj Narain, Naganna, K., and Murthy S.S., 1973; *Amer. Rev. Resp. Dis.*, **107**, 992-1001.
- WHO Expert Committee on Tuberculosis (1964); Eighth Report, WHO Technical Report Series No. 290, WHO, Geneva.

RESULTS OF TESTING WITH RT XXIII, PPD-S AND PPD-B IN SYMPTOMATIC PERSONS ATTENDING A TUBERCULOSIS CENTRE

D.C. PANDE, K.D. GAUTAM AND M.L. MEHROTRA
(From T.B. Demonstration and Training Centre, Agra.)

Definition of tuberculous infection by a tuberculin test has never been satisfactory. Several workers have given different definitions for estimating population having tuberculous infection (1-6). The reason is that there are other infections than infection with myco-bacterium tuberculosis which also lead to a 'Positive' reaction to a tuberculin test (7-9).

Palmer and Edwards (10) in their study among Naval recruits followed over a long period showed that two tests one with a standard tuberculin and another with an antigen prepared from an atypical myco-bacterium, may be more accurate, in defining tuberculous infection, especially for the intermediate (6-11 mm) range of reactions to the standard tuberculin.

Raj Narain et al (11) later showed that dual testing with PPD-S and PPD-G (antigen prepared from scotochromogen called Gause bacillus) was a very promising method of defining the infected and uninfected and -also suggested that even large reactions to a single tuberculin test (PPD-S) may not be a conclusive evidence of infection.

The present study was carried out to find out the value of such dual testing in persons attending a Tuberculosis Centre because of their symptoms suggestive of Pulmonary Tuberculosis.

Methods and Material

The study was started at Tuberculosis Demonstration and Training Centre, Agra, on 28th October 1971. Persons attending the centre because of their symptoms either voluntarily or being referred by medical practitioners or other agencies were interviewed before registration. The persons were interrogated regarding duration of symptoms if any.

Eligibility

Persons, 15 years and above in age regardless of their sex, who had symptoms suggestive of Pulmonary tuberculosis (viz. Haemoptysis, cough, Fever, and Chest pain) of 4 weeks and/or above duration, were eligible for registration.

Registration

Eligible persons were registered on pre-

numbered individual cards having provision to record all relevant data.

Investigations

1. Tuberculin Testing :- Every registered person was given three tuberculin tests at the same time by a tester in the following way.

a. Tuberculin test with 1 TU RT XXIII in 0.1 ml phosphate buffer containing 0.005 per cent tween 80 on the volar aspect of the left forearm.

b. Tuberculin testing with PPD-S (5 IU) and PPD-B (10 TU) was done with blind techniques. The tester (standardised) and reader (standardised) had no knowledge of the antigens used. The vials were labelled with code name only. The antigens were allocated to the mid-dorsal aspect of the right and left forearms in a random order by making use of the last digit of the individual number being odd or even.

c. The reactions to all the three antigens were read by a reader at the same time on the 3rd day and in a few on 4th day of testing. The same tester and reader were used throughout the study.

2. Radiographic Examination: All the registered persons were offered a 70 mm photofluorogram on the day of registration. The films were read by two readers independently.

3. Sputum Examination : All persons with any abnormal radiographic shadow in the lungs were eligible for examination of two specimens of sputum. As the results of X-ray readings were available on the day of registration, a 'Spot' specimen of sputum was obtained between 12.30 p.m. to 2.30 p.m. on the same day. In addition a sterile bottle was given to these persons and they were asked to bring early morning specimen of sputum next day. Both specimens were examined by direct microscopy and culture (on two slopes of Lowenstein-Jensen medium without potato starch). Cultures that yielded bacilli were identified by sub-culturing and observing growth at room temperature, production of pigment in the dark and after exposure to day light, rate of growth at 37° C, catalase reaction and Niacin production.

Study Population

A total of 500 persons were registered from

28th October 1971 to 8th November 1971 481 (95.3 per cent) persons were available for reading of reactions.

Thus the study population consisted of 481 persons having symptoms suggestive of pulmonary tuberculosis and aged 15 years and above.

Distribution of the size of reaction to RT XXIII

In fig. 1, the basic histogram is that of the size of reaction to RT XXIII in symptomatics i.e., if we neglect the different shadings to each column, the histogram shows distribution of the size of reaction to RT XXIII. The histogram shows a bimodal distribution and suggests a dividing point at 8 mm, therefore 8 mm and bigger size of reactions to RT XXIII could be taken as indicative of tuberculous infection.

In figure 2, the histogram is that of the size of reaction to RT XXIII in culture positive cases detected amongst the symptomatics. The histogram shows dividing point at 8 mm.

Considering 8 mm and bigger size of reactions to RT XXIII as the evidence of infection, 430 (89.4 per cent) of the 481 symptomatics and 96 (95 per cent) of the 101 culture positive cases could be classified as infected with myco-bacterium tuberculosis (table 1).

The mean sizes of reaction in the symptomatics and culture positive cases were 18.3 mm and 18.9 mm respectively. The modal class for 'Symptomatics classified as infected and culture positive cases classified as infected was (20-21) mm.

Distribution of the size of reaction to PPD-S :

In fig. 3, the basic histogram is that of the size of reaction to PPD-S in symptomatic persons. The histogram shows a bimodal distribution and suggests that 12 mm and bigger size of reactions could be taken as evidence of tuberculous infection.

Size of reactions to PPD-S in culture positive cases detected amongst symptomatics are shown in fig.4. The histogram suggests a dividing point at 10 mm.

Considering 10 mm and bigger size of reactions as evidence of infection, 444 (92.3 per cent) of the 481 symptomatics and 100 (99 per cent) of the 101 culture positive cases could be classified as infected with myco-bacterium tuberculosis (table 1).

The mean sizes of reaction in symptomatics and culture positive cases were 21.0 mm and 21.67 mm respectively. The modal class for symptomatics classified as infected and culture positive cases classified as infected was (22-23) mm.

Distribution of the size of reaction to PPD-B

Histogram in fig. 5 shows distribution of the size of reaction to PPD-B. The histogram shows almost an unimodal distribution i.e. all the symptomatics may be considered as having atypical infection. The modal class was (18-19) mm and the mean size of reaction was 18.9 mm.

Distribution of the size of reaction to RT XXIII and relative size of reaction to PPD-B.

In fig. 1, the different shadings in each column give relative size of reaction to PPD-B. Dark shadows represent those in whom size of reaction to RT XXIII is bigger than that of PPD-B, continuous slanting lines represent those in whom size of reaction to RT XXIII and PPD-B is equal, and white shadings represent those in whom size of reaction to PPD-B is bigger than that of RT XXIII. The study of histogram shows that with 8 mm and bigger size of reactions to RT XXIII, the dark area represents those possibly infected with myco-bacterium tuberculosis. If so, what about those whose size of reactions to RT XXIII, is equal or smaller than that of PPD-B. Do they have infection with myco-bacterium tuberculosis only or infection with atypical myco-bacteria only or both? To seek an answer, distribution of the size of reaction to RT XXIII and relative size of reaction to PPD-B in culture positive cases detected amongst the symptomatics was studied (fig. 2). Out of the 101 cases, 46 had size of reaction to RT XXIII, bigger than that of PPD-B, 23 had size of reaction to RT XXIII equal to size of reaction to PPD-B and 27 had size of reaction to PPD-B bigger than that of RT XXIII. The histogram suggests that the size of reaction to RT XXIII equal or smaller than the size of reaction to PPD-B also represents infection with myco-bacterium tuberculosis perhaps with the presence of atypical infection.

Distribution of the size of reaction to PPD-S and relative size of reaction to PPD-B.

In fig. 3 the different shadings in each column give size of reaction to PPD-S and relative size of reaction to PPD-B. The different shadings are as described for fig. 1, but for the different specific antigen used i.e. PPD-S instead of RT XXIII. The study of the histogram reveals that with 10 mm and bigger size of reactions to PPD-S; the dark shadow represents (304 persons) those possibly infected with myco-bacterium tuberculo-

TABLE I
Distribution of Symptomatics and number found Culture Positive for Myco-bacterium Tuberculosis by the size of reaction to dual tuberculin test.

Dual Test Reaction (mm)	Symptomatic tested.	Number Culture positive	Tuber- culosis case rate %	Dual Test Reaction (mm)	Sympto- matic tested	Number Culture positive	Tuber- culosis case rate %
PPD-S	37	1	2.7	RT XXIII	51	5	10.0
0-9				0-7			
PPD-10+	92	15	16.3	RT XXIII } R < B	172	27	15.7
	48	8	16.7	8+ } R = B+1	82	23	28.0
	304	77	25.3	} R > B	176	46	26.1
Sub Total	444	100	22.5	Sub Total	430	96	22.3
Total	481	101	21.0	Total	481	101	21.0

S is code for PPD-S, R is code for RT XXIII and B is code for PPD-B.

Percentages in brackets are based on less than 25 observations.

1 TU RT XXIII in 0.1 ml phosphate buffer containing 0.005 percent Tween 80.

TABLE 2
Distribution of culture positive cases, classified as infected with Mycobacterium Tuberculosis according to bacterial content in cultural and dual tuberculin test reaction

Sl. No.	Dual Test reaction (mm)	Number culture positive	Bacterial content in culture*			Dual Test reaction (mm)	Number culture positive	Bacterial content in culture*				
			+	++	& +++			No.	%	+	++	& +++
1	S<B	15	8	(53)	7	(47)	11	40.7	16	59.3		
2	S=B (+1)	8	2	(25)	6	(75)	10	(43.5)	13	(56.5)		
	Sub Total (1+2)	23	10	(43.5)	13	(56.5)						
3	S>B	77	27	35	50	65	16	34.8	30	65.2		
	Sub Total (2+3)						26	37.7	43	62.3		
	Total	100	37	37	63	63	37	38.5	59	61.5		

Note : 1 Size of reaction to PPD-S 10 mm. Size of reaction to 1 TU RT XXIII in 0.1 ml. phosphate buffer containing 0.005 percent tween 80 8mm.
 S refers to reaction to PPD-S, B. refers to reaction to PPD-B and R refers to reaction to RT XXIII. Percentage in bracket depends upon less than 25 observations.
 * (a) + plus 20 to 100 colonies.
 (b) ++ plus innumerable colonies but growth not confluent.
 (c) +++ plus confluent growth.

sis. The other two shadings, analogous to the earlier discussion of figure 1 & 2, represents (140 persons) those infected with mycobacterium tuberculosis perhaps with the presence of atypical infection.

Tuberculosis case rate

Among 51 symptomatics with (0-7) mm size of reaction to RT XXIII, 5 cultures positive cases were detected, which gives tuberculosis case rate of 10 percent (Table 1).

Among 430 symptomatics with 8 mm and bigger size of reaction to RT XXIII, 96 culture positive cases could be detected, which gives tuberculosis case rate of 22.3 per cent. These 430 symptomatics could be further classified into undermentioned three categories according to the relative size of reaction to PPD-B.

Category A : 176 persons in whom reaction to RT XXIII was greater than that of PPD-B.

Category B : 82 persons in whom reaction to RT XXIII was equal to that of PPD-B.

Category C : 172 persons in whom reaction to RT XXIII was smaller than that of PPD-B.

The tuberculosis case rate was 26.1 per cent in category A, 28.0 percent in category B and 15.7 per cent in Category C (Table 1).

Amongst 37 symptomatics with (0-9) mm size of reaction to PPD-S, only one culture positive case was detected, which gives tuberculosis case rate of 2.7 per cent (Table 1).

Among 444 symptomatics with 10 mm and bigger size of reaction to PPD-S, 100 culture positive cases could be detected, which gives tuberculosis case rate of 22.5 percent. These 444 symptomatics could be further classified into undermentioned three categories according to the relative size of reaction to PPD-B.

Category X : 304 persons in whom reaction to PPD-S was greater than that of PPD-B.

Category Y : 48 persons in whom reaction to PPD-S was equal to that of PPD-B.

Category Z : 92 persons in whom reaction to PPD-S was smaller than that of PPD-B.

The tuberculosis case rate was 25.3 percent in category X, 16.7 per cent in category Y and 16.3 percent in category Z (Table 1).

Discussion

Distribution of the size of reaction to RT XXIII in the study population and in culture positive cases amongst the study population (fig. 1 and 2) suggested that 8 mm and bigger size of reaction could be considered evidence of infection with myco-bacterium tuberculosis. Thus 430 (89.4 per cent) out of 481 symptomatics could be classified as infected, whereas 96 (95 per cent) of a total of 101 culture positive cases could be classified as infected and 5 (5 per cent) as non-infected. Raj Narain et al (2,12) had also reported that about 4 to 6 percent of culture positive cases had less than 8 mm size of reactions to RT XXIII. Tuberculosis case rate (22.3 per cent) was quite high among 430 symptomatics classified as infected and was substantially low (10 percent) amongst 51 symptomatics with (0-7) mm size of reaction. However the number of symptomatics with (0-7) mm size of reaction was quite small and no significance can be attached to it. Hence the definition of infection with myco-bacterium tuberculosis (induration of 8 mm and above to 1 TU RT XXIII) seems to be rather satisfactory.

Distribution of the size of reaction to PPD-S in 101 culture positive cases detected amongst the study population, showed that 10 mm and bigger size of reaction to PPD-S (fig. 4) could be considered as evidence of infection with myco-bacterium tuberculosis. Thus 100 (99 per cent) out of a total of 101 culture positive cases and 444 (92.3 percent) out of 481 symptomatics could be classified as infected. Tuberculosis case rate was quite high (22.5 per cent) among 444 infected symptomatics and substantially low (2.7 per cent) among 37 symptomatics with (0-9) mm size of reaction; however the number with (0-9) mm size of reaction to PPD-S was too small to be of any significance. Thus the definition of infection with Myco-Tuberculosis (induration of 10 mm and above to 5 TU PPD-S) seems to be rather satisfactory.

Raj Narain and others (12) in their study in general population showed that only those with 12 mm and bigger size of reaction (as also suggested in present study among symptomatics, fig. 3) to PPD-S; size of reaction to PPD-S being greater than that of PPD-B may be considered as infected with myco-bacterium Tuberculosis. The basis for such a conclusion was that more than 95 per cent of culture positive case could be classified as infected with such a definition; but in the present study only 77 per cent of culture

positive cases could be classified as infected, if 10 mm and bigger size of reaction to PPD-S size of reaction to PPD-S being greater than that of PPD-B was considered as evidence of infection. Obviously such a definition may not be suitable for our study population.

Palmer and Edwards (11) in their study among Naval recruits showed that in addition to those with 12 mm bigger size of reaction to PPD-S (as also suggested by fig. 3) also those with (6-11) mm size of reaction to PPD-S, reaction to PPD-S being greater than that of PPD-B, may be considered as infected. However we could not achieve such a division of (6-9) mm size of reaction to PPD-S with the help of the size of reaction to PPD-B. This might be due to small number of such reactors in our study or due to the high strength of PPD-B (10 TU). Palmer et al used 5 TU PPD-B and 5 I.U. PPD-S in their study.

It would be worthwhile to mention here that if we had taken 12 mm and bigger size of reactions to PPD-S as positive and divided (6-11) mm size of reaction as done by Palmer, the results would have remained the same except that infection rate of 92.3 percent as given by 10 mm and bigger size of reactions got reduced by one.

Different definitions of infection by RT XXIII and PPD-S might be due to difference in their strength. PPD-S was stronger than RT XXIII. Comstock et al (13) reported that 2.5 TU of RT XXIII was approximately equivalent to 5 TU of PPD-S.

Dual Testing with RT XXIII and PPD-B

430 infected symptomatics (with 8 mm and bigger size of reaction to RT XXIII) were further divided into the following three categories with the help of relative size of reaction to PPD-B. (Table 1).

Category A : 176 persons in whom reaction to RT XXIII was greater than that of PPD-B.

Category B : 82 persons in whom reaction to RT XXIII was equal to that of PPD-B.

Category C : 172 persons in whom reaction to RT XXIII was smaller than that of PPD-B.

Tuberculosis case rate was 26.1 per cent, 28.0 percent and 15.7 per cent in category A, Category B and Category C respectively. Thus it varied and was not of the same high order in all the three categories. The difference in the case

rate between A and B categories was not substantial. Amalgamating the results in Category A and Category B, Tuberculosis case rate (26.7 per cent) was significantly higher in comparison to Tuberculosis case rate (15.7 percent) in category C ($P < 0.1$). Hence the categories A and B may be classified as higher risk group and category C as lower risk group.

Dual testing with PPD-S and PPD-B.

444 infected symptomatics (with 10mm and bigger size of reaction to PPD-S) were further divided into the following three categories with the help of relative size of reaction to PPD-B (Table 1).

Category X : 304 persons in whom reaction to PPD-S was greater than that of PPD-B.

Category Y : 48 persons in whom reaction to PPD-S was equal to that of PPD-B.

Category Z : 92 persons in whom reaction to PPD-S was smaller than that of PPD-B.

Tuberculosis case rate was 25.3 per cent, 16.7 percent and 16.3 per cent in category X, Category Y and Category Z respectively. Thus it was almost of a similar order in category Y and Category Z. Tuberculosis case rate (25.3 per cent) in category X was significantly higher than tuberculosis case rate (16.4 percent) in Category Y and Category Z put together. ($P < 0.5$). Hence category X may be classified as higher risk group and categories Y and Z as lower risk group. This finding was also supported by Table 2, which showed that 65 per cent of the 77 culture positive cases belonging to category X had high bacterial content in sputum culture (2-plus or 3-plus) as against 56.5 per cent of the 23 culture positive cases belonging to category Y or Z. A substantial difference though statistically not significant.

Comparison of dual testing with PPD-S and PPD-B and dual testing with RT XXIII and PPD-B.

Definitions of higher and lower risk groups brought forth by dual testing with PPD-S and PPD-B were different than those brought forth by dual testing with RT XXIII, and PPD-B. Out of 444 infected symptomatics (10 mm or bigger size of reaction to PPD-S) 48 in whom the reaction to PPD-S was equal to that of PPD-B (Category Y) entered in the lower risk group on the basis of low Tuberculosis case rate (16.7 percent) in their category Y whereas out of 430 infected symptomatics (8 mm and bigger size of

reaction to RT XXIII) 82 in whom the reaction to RT XXIII was equal to that of PPD-B (category B) entered in the higher risk group on the basis of high Tuberculosis case rate (28.0 per cent) in their category B.

Dual testing with PPD-S and PPD-B classified 304 (Category X) out of 444 infected symptomatics (10 mm and bigger size of reaction to PPD-S) forming higher risk group whereas dual testing with RT XXIII and PPD-B classified 258 (Category A and B) out of 430 infected symptomatics (8 mm and bigger size of reaction to RT XXIII) forming higher risk group.

Amongst 444 infected symptomatics (10 mm and bigger reaction to PPD-S) 48 in whom reactions to PPD-S and PPD-B were equal (Category Y), were considered as having infection with mycobacterium tuberculosis perhaps with the presence of atypical myco-bacterium infection (Fig. 3). This finding was supported by the fact that these symptomatics (Category Y) entered in the lower risk group.

Amongst 430 infected symptomatics (8 mm and bigger reaction to RT XXIII) 82 in whom reactions to RT XXIII and PPD-B were equal (Category B), were considered as having infection with mycobacterium tuberculosis perhaps with the presence of atypical myco-bacterial infection (fig. 1). But in contrast to the finding with dual testing with PPD-S and PPD-B in above paragraph they (Category B) entered in the higher risk group.

It appears from the above findings that dual testing with PPD-S and PPD-B was relatively more specific than dual testing with RT XXIII and PPD-B in classifying the infected population into higher and lower risk groups.

Influence of non-specific sensitivity on Tuberculosis case rate.

The tuberculosis case rate (25.3 percent) among 304 reactors to PPD-S; the size of reaction to PPD-S being greater than that of PPD-B: the so-called higher risk group, was significantly higher ($P < .05$) than the Tuberculosis case rate (16.4 percent) among 140 reactors to PPD-S; the size of reaction to PPD-S being smaller than or equal to that of PPD-B: the so-called lower risk group. (Table 1).

The Tuberculosis case rate (26.7 percent) among 258 reactors to RT XXIII; the size of reaction to RT XXIII being greater than or equal to that of PPD-B: the so-called higher risk group, was significantly higher ($P < .01$) than the Tuberculosis case rate (15.7 per cent) among 172 reactors

to RT XXIII; the size of reaction to RT XXIII being smaller than that of PPD-B: the so-called lower risk group (Table 1). A plausible explanation is that non-specific sensitivity (indicated by the size of reaction to PPD-B bigger than or equal to the size of reaction to PPD-S, as also by size of reaction to PPD-B bigger than the size of reaction to RT XXIII) might have offered protection against Pulmonary Tuberculosis. Well planned experimental studies in animals have shown that infection with some of the so-called atypical myco-bacteria offers a considerable degree of protection against a later challenge with myco-bacterium Tuberculosis (14). In a retrospective study by Raj Narain et al (15), non-specific sensitivity showed a high protection against development of tuberculosis in children (0-14 years of age) among non-reactors to RT XXIII. In the present study it is assumed that the higher and lower risk groups were comparable i.e. no significant initial difference between these two groups existed, the risk of tuberculous infection was similar in both the groups and the social and economic conditions in the two groups were similar. With this hypothesis, protection offered by non-specific sensitivity against Pulmonary tuberculosis was of the order of 35 to 41 per cent (see appendix 1).

Summary

Concurrent testing with 1 TU RT XXIII with 5 IU PPD-S and 10 TU PPD-B in North Indians aged 15 years and above attending a Tuberculosis Centre because of their symptoms suggestive of pulmonary tuberculosis was undertaken to find out the value of dual antigen testing with a standard tuberculin and an antigen prepared from an atypical myco-bacterium. Dual antigen testing was found to be helpful in deciding higher and lower risk groups amongst persons classified as infected by a standard tuberculin test. For such a purpose dual testing with 5 IU PPD-S and 10 TU PPD-B appears to be more specific than dual testing with 1 TU RT XXIII and 10 TU PPD-B. Significantly lower tuberculosis case rate was observed among symptomatics having infection with myco-tuberculosis perhaps with the presence of atypical infection, as compared to those possibly infected with myco-tuberculosis alone; this might be due to the protection offered by non-specific sensitivity against myco-bacterium tuberculosis.

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APPENDIX 1

(1) Dual testing with PPD-S and PPD-B.

Persons with 10 mm and bigger size of reactions to PPD-S were classified as having Tuberculous infection. They were divided into following two groups with the help of the size of reaction to PPD-B.

a. Persons with the size of reaction to PPD-S greater than that of PPD-B. i.e. those with presence of tuberculous infection (higher risk group).

b. Persons with the size of reaction to PPD-S smaller than or equal to that of PPD-B i.e. those with presence of Tuberculous infection as well as atypical infections (lower risk group).

Let f_1 and f_2 be the tuberculosis morbidity rate in a and b respectively. If P is the protection offered by non specific sensitivity, then the estimate of P is given by

$$P = \frac{f_1 - f_2}{f_1} \times 100 \quad \text{--- (1)}$$

In the present study $f_1 = 25.3$ per cent and $f_2 = 16.4$ percent.

$$P = \frac{25.3 - 16.4}{25.3} \times 100 \\ = 35.2 \text{ per cent.}$$

(2) Dual testing with RT XXIII and PPD-B.

8 mm and bigger size of reaction to RT XXIII was taken as the evidence of tuberculous infection. The reactors formed the following two distinct groups with the help of PPD-B reaction.

1. Persons with the size of reaction to RT XXIII greater than or equal to that of PPD-B (higher risk group)
2. Persons with the size of reaction to RT XXIII smaller than that of PPD-B (Lower risk group).

$$\text{No. } P = \frac{f_1 - f_2}{f_1} \times 100 \quad \dots (1)$$

In the present study $f_1 = 26.7$ percent and $f_2 = 15.7$ percent.

$$P = 41 \text{ per cent.}$$

REFERENCES

1. Medical Research Council, Tuberculosis Vaccines Clinical Trial Committee: BCG and vole vaccillis vaccines in the Prevention of Tuberculosis in adolescence and early adult life, *Br. Med. J.*, 1963, 1973.
2. Raj Narain, Geser, A., Jambunathan, M.V., and Subramanian, M., some aspects of a tuberculosis prevalence survey in a south Indian district, *Bull. Wld. Hlth. Org.* 1963, 29, 641-644.
3. Edwards Lydia B., and Smith, David, T., Community-wide tuberculin testing study in Pamlico county, *Ame Rev. Resp. Dis.*, 1965, 92, 43.
4. Keay, A.J., and Edmund, E.: Differential Mantoux testing in the diagnosis of Atypical Mycobacterial infection in children, *Lancet*, 1966, 2, 1425.
5. Hsu, Katharine H.K., Fonges Jen and Jenkins, Danial, E.; Studies on the specific tuberculin reaction, *Ame. Rev. Res. Dis.* 1964, 90, 36.
6. Comstock, G.W., and Palmer, C.E., Long-term results of BCG Vaccination in the Southern United States, *Ame. Rev. Resp. Dis.*, 1966, 93, 171.
7. Palmer, C.E., Ferebee, S.H., and Patersen, O.S.: Studies of Pulmonary findings and antigen sensitivity among student nurses: Geographic differences in sensitivity to tuberculin as evidence of non specific allergy, *Public Health Rep.* 1950, 65, 1111.
8. Nyboe, J.: The efficiency of the tuberculin test, *Bull. Wld. Hlth. Org.* 1960, 22, 5
9. Palmer, C.E.: Tuberculin sensitivity and contact with tuberculosis: Further evidence of non-specific sensitivity, *Tubercle*, 1953, 68, 678.
10. Palmer, C.E., and Edwards Lydia B.; Identifying the tuberculous infected: The dual test technique, *J.A.M.A.*, 1968, 205, 167,

11. Raj Narain, Mayurnath, S., Bagga, A.S., Naganna, K., Subha Rao, M.S., and Rangaswamy, K.R.; Results of testing with PPD-S and PPD-G. 24th TB and Chest Diseases Workers Conference, Trivandrum (India) Jan. 1969, 90-99.
12. Raj Narain, Nair, S.S., Naganna, K., Chandra Sekhar, P., Ramanatha Rao, A, and Pyare Lal: problem of defining a case of Pulmonary Tuberculosis in Prevalence surveys, *Bull. Wld. Hlth. Org.*, 1968, 39, 701-729,
13. Comstock, G.W., Edwards, Lydia, B., Philip, Robert, N., and Winn, W.A.; A comparison in the United states of America of two tuberculins PPD-2 and RT XXIII, 1964, 31, 161-170.
14. Palmer, C.E., and Long, M.W.; Effects of infection with atypical mycobacteria as BCG Vaccination Tuberculosis, *Ame. Rev. Res. Dis.* 1966, 74, 553.
15. Raj Narain, Naganna, K., and Pyare Lal: Non-specific sensitivity and its influence on incidence of Pulmonary tuberculosis, *Ame. Rev. Resp. Dis.* 1972, 105, 4, 578-585,

PLEURAL BIOPSY (ANALYSIS OF 81 CASES)

R.K. TANDON AND S.R.P. MISRA
(From S.N. Medical College, Agra)

Inflammation of the pleura with or without effusion is a common disease. The aetiological diagnosis of effusion is of paramount importance. Needle or open biopsy of the pleura offers the means for aetiological diagnosis.

Laggat (1959) used Vim-Silverman's needle for percutaneous pleural biopsy in 22 cases. Overall impression was that the specimen was not satisfactory. Pollar (1958) performed percutaneous pleural biopsy and obtained 228 specimens from 200 patients. He established the diagnosis in 80 % of the tuberculous and 60 % of the malignant effusions and his impression was that this is the most reliable diagnostic technique when effusion of a tuberculous nature is suspected. The present paper reports 81 cases of pulmonary lesions with pleural involvement who underwent pleural biopsy by Abrams punch or open pleural biopsy in selected cases.

Material and Methods

The present study was carried out in 81 cases admitted in the Thoracic Unit of S.N. Medical College, Agra. Their detailed medical history, physical findings and laboratory investigations were recorded. Mantoux test was done in 37 patients. All patients had X-ray chest (PA and lateral views) and bronchogram wherever indicated. All cases were bronchoscoped and specimen of sputum was taken for bacteriology or cytology study. Percutaneous pleural biopsy was taken by Abrams Needle with the technique employed by Abrams (1958) in his series. Out of these 81 cases chest was opened in 22 cases

and specimen of pleura was taken to confirm the diagnosis and to compare the results with percutaneous pleural biopsy.

Techniques of Pleural Biopsy by Abrams Needle

After selecting the site, a small intradermal wheal was raised by injecting 1 % xylocaine solution in skin, subcutaneous tissue and intercostal muscles right upto the pleura. A tiny incision was made with scalpel, the pleural punch was introduced and the notch closed in which state it is straight. After withdrawing the stilette, the aspiration apparatus was attached to the mount on the inner tube, the back hexagonal grip was twisted anticlockwise to open the notch of the punch and the aspiration carried out to remove as much fluid as possible. At the end of the aspiration, the notch was directed along the intercostal space by means of the indicator knob on the hexagonal grip and the punch slowly withdrawn. Sideways pressure in the direction of the notch was maintained, until it was felt to engage in the chest wall. The punch was then held firmly against the chest wall. The back hexagonal grip was twisted sharply clockwise and the punch withdrawn. The biopsy specimen was found either in the hollow point or inside the cutting cylinder. Pleural tissue was immediately transferred in a bottle containing ten percent formal saline and sent for histological examination.

Observations

The age distribution of the cases in the present series is shown in Table I.

Table I

Showing age distribution

S. No.	Age	No. of cases	Percentage
1.	0—20 years	24	29.6
2.	21—30 years	30	37.0
3.	31—40 years	8	9.8
4.	41—50 years	12	14.8
5.	51—60 years	5	6.1
6.	60 years and above.	2	2.7

Table II

Duration of clinical symptom

S.No.	Duration of symptom	No. of cases	Percentage
1.	Below 1 month	6 cases	7.4
2.	1—6 months	19 cases	23.5
3.	7 months—1 year	30 cases	37.0
4.	1—2 years	6 cases	7.4
5.	2—3 years	10 cases	12.2
6.	3—4 years	3 cases	3.7
7.	4—5 years	3 cases	3.7
8.	Above 5 years	4 cases	5.1

Table III

Types of pleural involvement

Types of Disease	Left	Right	Bilateral	Total	Percentage
Cases with effusion	21	24	—	45	55.5
Pleural involvement without effusion	6	6	15	27	33.3
Hydropneumothorax	5	1	—	6	7.5
Pneumothorax	3	—	—	3	3.7

Sex : There were 60 males and 21 females with ratio 2.8 : 1.

Duration of Clinical Manifestation

The patients at the time of admission had symptoms for 1 month to 5 years but in the majority (60%) the symptoms and signs of pulmonary disease had lasted from 1 month to 1 year as shown in Table II.

Out of 81 cases studied, 45 cases had pleurisy with effusion, 3 had pneumothorax and six hydropneumothorax. The remaining 27 cases showed signs of pleural involvement which presented in the X ray as thickened pleura. In

these 27 cases, 12 had unilateral pleural thickening and 15 bilateral pleural involvement. Table III shows the types of pleural reaction seen.

The main presenting symptoms in these cases were cough with expectoration, pain in the chest, fever, loss of appetite and breathlessness. Their frequency is shown in Table IV.

A total of 93 biopsies were done in 81 cases. Adequate tissue was obtained in 88 biopsy specimens only. Biopsy was repeated in the remaining five cases to obtain adequate tissue. The piece of pleura obtained with Abrams needle was 2-4 mm. The histological diagnosis is shown in Table V.

Table IV

Clinical manifestation of pleural involvement of the present series

S.No.	Symptom	Male	Female	Total	Percentage
1.	Cough with expectoration	45	13	58	72.2
2.	Pain in Chest	42	12	54	66.6
3.	Fever	36	15	51	63.0
4.	Loss of appetite	32	13	45	55.5
5.	Breathlessness	34	8	42	51.8
6.	Haemoptysis	16	5	21	25.6
7.	Ankle Oedema	9	—	9	11.1

Table V

Pleural histology

S.No.	No. of cases	Clinical	Tuberculous	Malignancy	Chronic non-specific inflammation	Total
1.	63	Tuberculosis	27(42.9%)	—	36	63
2.	15	Malignancy	—	12	3	15
3.	3	Amoebic	—	—	3	3

In the present series 63 were cases of tuberculosis of the lung involving the pleura. The histological diagnosis was positive in only 27 cases while the remaining 36 cases showed signs of chronic inflammation though there were cases of tuberculosis as diagnosed by positive sputum in 16 cases while clinical and X-ray findings were suggestive of tuberculosis in remaining 20 cases. This is probably because the small specimen of pleura obtained by the needle biopsy was not involved with the scattered tubercle over the parietal pleura. Similarly out of 10 cases of malignant pleura involved secondarily to the bronchogenic carcinoma of lung only 4 cases were confirmed by pleura biopsy as secondaries in the parietal pleura.

The amoebic empyema cases showed chronic inflammation of the parietal pleura without any specific change to suggest or indicate the

amoebic nature of empyema. Entamoeba could not be demonstrated in these cases either in the pleural fluid or in the pleural biopsy material.

There was no serious complication following percutaneous pleural biopsy with Abrams needle. The minor complications encountered were bleeding from the site of the biopsy, local cutaneous emphysema, surgical emphysema spreading over the chest and abdomen with or without pneumothorax. These are shown in Table VI.

The two cases who developed pneumothorax with widespread surgical empyema were treated by intercostal drain connected to under water seal for 24 hours.

Out of these 81 cases, 22 cases had thoracotomy and open pleural biopsy. Out of these 22 cases 14 cases showed tuberculosis, 2 cases malignancy

Table VI

Complications during and after pleural biopsy

S.No.	During Biopsy	No. of cases	Percentage	S.No.	After Biopsy	No. of cases	Percentage
1.	Bleeding from biopsy site	5	6.2	1.	Pain	8	9.9
2.	Cutaneous Emphysema	3	3.7	2.	Local sepsis	6	7.5
3.	Wide spread surgical emphysema with pneumothorax	2	2.5	3.	Abscess in Chest	2	2.5

Table VII

Results of open pleural biopsy

S.No.	Histology of Pleura	No. of cases	Percentage
1.	Tuberculosis	14	63.6
2.	Malignancy	2	9.1
3.	Non-specific Chronic Inflammation	6	27.3

and 6 cases non-specific chronic inflammation. These findings are shown in Table VII. Three cases showing non-specific chronic inflammation on percutaneous pleural biopsy, proved to be tubercular in 2 cases and malignancy in one case in histology of the pleura biopsy which was taken at the time of thoracotomy.

Discussion

Leyden (1833) was first to introduce needle biopsy of the lung and pleura by aspirating organism from a case of pneumonia. Aspiration biopsy for cytological examination was introduced by Martin and Ellis (1930). Aspiration is usually acceptable in localised lung or pleural pathology; it is not useful when a large amount of tissue is needed for diagnosis in diffuse parenchymal disease.

The second phase of lung or pleural biopsy began with the introduction of Silverman's cutting biopsy needle. Manfredi and co-workers (1960) reported the use of Vim Silverman cutting needle for percutaneous biopsy of the pleura and lung.

Some pathologists have pointed that the tissue obtained through the needle may not be representative of the disease process. Essentially for the reason biopsy in diffuse lung lesion or pleura has usually been performed by open thoracotomy. It is a major surgical procedure and is subject to the usual complications of thoracotomy.

In the present series, Abrams Needle was used for percutaneous biopsy and open biopsy of pleura was undertaken in selected cases.

The percutaneous biopsy was attempted in 81 cases and out of these, 63 cases were suspected cases of tuberculosis. Of these 63 cases, 27 cases were positive for tuberculosis (positive result 42.9 %). Open biopsy was done in 22 cases and out of these 14 cases were positive for tuberculosis giving 63.6% positive result.

Fifteen out of the 81 cases were of malignancy of the lung involving the pleura presenting as recurrent pleural effusion. Percutaneous pleural biopsy was positive in 12 cases (60%). The

remaining 3 cases had open thoracotomy and out of these 2 cases showed evidence of malignancy.

The amoebic empyema showed evidence of chronic inflammation with percutaneous biopsy in 3 cases. The pleura was thickened and the endothelial lining was destroyed. There was fibrosis with lymphocyte and round cell infiltration. Similar findings were obtained on open biopsy of pleura. No specific changes due to amoebic involvement of pleura could be identified on histological examination.

Smaller number of positive results are reported in present series as compared to those reported by Mestitz (1958) using the Abrams needle for percutaneous pleural biopsy. He was able to establish the diagnosis in 80 % of cases of tuberculosis while in present series positive results were obtained in 42.9 % which could be due to the fact that our cases were referred fairly late and they had received considerable amount of chemotherapy before the biopsy was performed. Mestitz (1958) reported positive result in 60% of malignant pleural effusion while in the present series, result was positive in 80% of cases. These cases by the time they came to us, were too far advanced with multiple seeding of malignant deposits on the parietal pleura, which were easily hit by the Abrams needle. Moreover, the specimen obtained by the Abrams needle were satisfactory for histological study. Our study regarding open pleural biopsy gave better results. Positive diagnosis was obtained in 63.6% of tuberculosis cases as compared to 42.9 % by the percutaneous method. In malignancy, positive results were 66.6%.

Better results obtained with open biopsy could be due to following reasons

- (a) Good specimen of pleura was obtained.
- (b) Site of pleura which was felt to be diseased was taken for histological confirmation of diagnosis.

- (c) Lung was palpated to study the nature of lesion.

Previously open biopsy was considered to be risky in chronically ill patients but due to advancement in technique of anaesthesia and better surgical care, it carries no risk as seen in the present series. For cases in which needle biopsy is inconclusive, this is the method of choice.

Summary

Comparative account of the result of needle biopsy with Abrams Needle and open pleural biopsy has been discussed. Needle biopsy was done in 81 cases while open biopsy was done in selected 22 cases where percutaneous biopsy was inconclusive. The positive results were obtained in 42.9% with percutaneous pleural biopsy, and 66.7 % with open pleural biopsy.

REFERENCES

1. Abrams, L.D., A Pleural Biopsy Punch, *Lancet* 1 : 30, 1958.
2. Benjamin, P.K., Needle biopsy of the parietal pleura. *J. Ass. P. Ind.* 18, 275, 1970.
3. Laggat, P.O., Study of pleural biopsy by Vim Silverman and Abrams Needle. *B.M.J.* 2: 378, 1959.
4. Leyden, H., Neber infactisce Pneumonia *Disch. Med. Wschr.*, 9, 52, 1883 as quoted by 3.
5. Martin, H.E., and Ellis, E.B., Biopsy by needle puncture and aspiration. *Ann. Surg.* 92, 169, 1930.
6. ManFredi, F. and Bwckley, C.E., Lung needle biopsy in the evaluation of diffuse pulmonary diseases: an experimental study. *Amar. Rev. Resp. Dis.* 82, 800, 1960.
7. Mestitz, P and Pollard A.C. Needle Biopsy of Pleura. *Lancet* 2: 1349, 1958.

KIDNEY CHANGES IN PULMONARY TUBERCULOSIS
—A STUDY BY KIDNEY BIOPSY

P.K.D. SHAH, M.K. JAIN, H.N. MANGAL AND N.M. SINGHVI
(From S. N. Medical College and M.G. Hospital, Jodhpur)

Introduction

Kidney involvement in patients of pulmonary tuberculosis has been reported in various autopsy and clinical studies (Auerbach, 1940; Medlar, 1949; Bsl, 1950 and Mittal, 1966). High oxygen tension in the cortical portion of kidney makes it a very vulnerable site for localised tubercular infection. Besides the simultaneous involvement of kidney by tubercular process, various other changes like amyloidosis, nephritis, cloudy swelling etc., have been described in such patients (Mittal et al, 1966). Whereas, it is important to recognize these structural alterations of the kidney at the earliest, the paucity of symptoms produced by such renal involvement often delays the diagnosis. Bacteriological investigation, like urine culture for acid fast bacilli also does not help to pick up the renal involvement in many cases (Chaddha et al, 1971). The present study was therefore undertaken to find out the various histopathological changes in kidney by percutaneous needle biopsy in patients of pulmonary tuberculosis.

Material & Methods

Thirty patients with confirmed pulmonary tuberculosis were included in this study. Detailed urine examination especially for albumin and presence of casts was done in a freshly voided sample. Urine culture for acid fast bacilli was done. Morning samples of urine obtained on five consecutive days were pooled and the sediment so obtained was spread on Lowenstein — Jenson culture medium.

Percutaneous needle biopsy of the kidney using Vim-Silvermann needle was done by the standard procedure (Muechrcke et al 1955). Kidney biopsy was performed on the right side with the patient in the sitting position. The approximate depth of the kidney was first judged by a lumbar puncture needle before inserting the Vim-Silvermann's needle.

Tissue obtained was fixed in 10% formaline solution. It was sectioned and stained with haematoxyline and Eosin stain, P.A.S. Stain, crystal violet stain for amyloid and Van-Gieson stain by the standard techniques.

Observations

Age and sex distribution of the thirty patients included the study is shown in table No. 1. Duration of illness in these patients at the time of study ranged between 1 month and three years. However, in about one third of them the duration of disease ranged between 5-7 Months — Table II.

At the time of study 10 patients had not received any antitubercular therapy, whereas, the rest had received antitubercular drugs in combination for varying periods of time (Table III).

Acid fast bacilli on smear examination of sputum were present in all except one patient included in the study. Extent of the pulmonary involvement was graded as mild, moderate or severe depending upon the extent and severity of lesions on chest X-Ray. Five patients had mild

Table No. 1

Age and sex distribution

Age in years	20—29	30—39	40—49	50—59	Total
Males	5	6	9	4	24
Females	1	3	2	—	6
Total	6	9	11	4	30

Table No. II

Duration of illness at the time of study

Duration of illness in months	1	2—4	5—7	8—12	Over 12
Number of cases	4	6	10	4	6
Percentage	13.3%	20.0%	33.3%	13.3%	20.0%

Table III

Duration of anti-tubercular therapy at the time of study

Duration of treatment in month	No treatment	6 months	7—12	13—18	19—24 months	Above 24
Number of Patients	10	14	1	3	1	1
Percentage	33.3	46.6	3.3	10	3.3	3.3

Table IV

Showing detailed urinary findings

Albuminuria	Nil	Trace	+	++	+++	++++
Number of cases	10	4	8	5	2	1
Pus cells Per HPF		4	5-10	11-16	16	With Microscopic Haematuria
Number of cases		18	6	3	2	1
Casts per HPF		No casts	+	++	+++	
Number of cases		16	3	7	4	
			Hyaline	Hyaline-4 Granular-3	Hyaline-3 Granular-1	

lesions, 8 had moderate lesions, whereas 15 had advanced extensive lesions. Two patients had pleural effusion only.

Urine Examination

Table No. IV shows in detail the abnormal urinary findings obtained in these patients. Two

thirds of the patients had albuminuria of varying degree mostly ranging between + to ++. Twelve patients had significant degree of pyuria, (Pus cells > 5 per high power field).

Hyaline and granular casts were present in 14 of the patients studied,

Table V

Showing histopathological changes

Renal Histopathology	Number of cases	Percentage
1. Tuberculosis of Kidney	1	3.3
2. Non specific changes		
(a) Amyloidosis with or without thickening of basement membrane	7	23.3
(b) Fibrosis	4	13.3
(c) Membranous Glomerulonephritis	2	6.6
(d) Cloudy swelling	5	16.6
(e) Focal Lymphocytic	2	6.6
3. Normal Kidney Tissue	9	30.0

In none of the patients studied positive urine culture for acid fast bacilli was obtained.

Histopathological Changes

Study of kidney biopsy revealed various types of changes in 21 (70%) patients. Nine patients had normal kidney tissue. Table V shows the various types of histopathological changes encountered.

Only one patient had typical caseous necrosis with epithelioid cells and lymphocytic infiltration, characteristic of tuberculosis (Figure 1). Amy-



Fig. 1

loidosis was present in seven patients. Two of these also had a significant thickening of basement

membrane. The distribution of the amyloid material was varying in various portions of the kidney. Four biopsies revealed evidence of mild to moderate infiltration by the fibroblasts. These patients with fibrosis did not have any other significant histological changes in the kidney (Fig. 2). Membranous glomerulonephritis was observed in two patients (Fig. 3). Other non-specific changes observed were cloudy swelling, focal infiltration of lymphocytes.

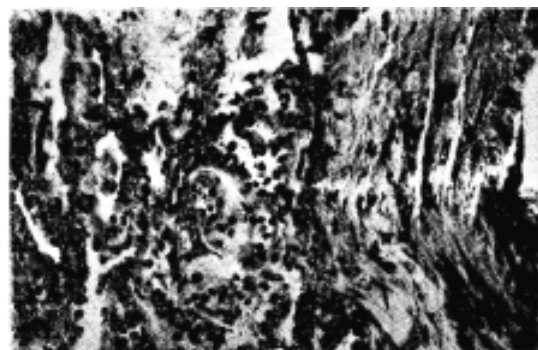


Fig. 2

Discussion

Tubercular involvement of kidney in association with pulmonary disease has been reported in as much as 28% of patients by Medlar (1949) in an autopsy study. Various clinical studies have

Table No. VI

Nature of lesion	Present study No. of pts. —30	Mittal et al. (1966) No of patients —25
(a) Normal kidney	9	12
(b) Tuberculosis of kidney	1	—
(c) Amyloidosis with thickening of basement membrane	7	2
(d) Fibrosis	4	—
(e) Membranous glomerulonephritis	2	—
(f) Cloudy swelling	5	7
(g) Focal Lymphocytis Infiltration	2	—
(h) Interstitial Nephritis	—	1
(i) Pyeleonephritis	—	3
	30	25

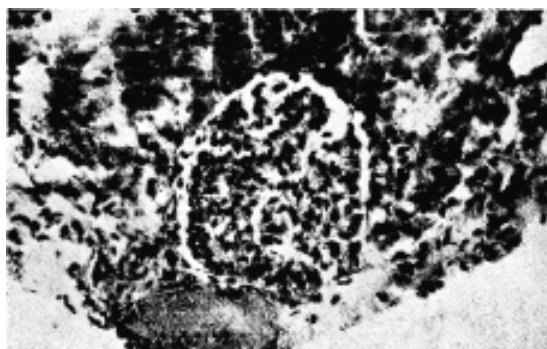


Fig. 3

reported this association in 3 % to 5 % of patients. This disparity is due to prolonged asymptomatic course of renal tuberculosis. Needle biopsy of kidney has also not been helpful in finding a greater association of renal tuberculosis in patients of pulmonary tuberculosis. In the present study of 30 patients of pulmonary tuberculosis, definite tubercular changes in the kidney could be detected in only one patient. In a similar study by Mittal et al (1966), no case of renal tuberculosis was detected out of the 25 patients of pulmonary tuberculosis studied. It is possible that the focal nature of the tubercular process in

the kidney does not make it amenable to the needle biopsy.

Needle biopsy of the kidney has, however, been helpful in picking out the wide variety of histopathological changes in the kidney. In the present study an abnormal renal histology was detected in 70 % of the patients. A comparison of the histological findings obtained in the present study and those of Mittal et al (1966) is given in Table VI.

Most of these changes except for amyloidosis or tuberculosis seem to be non-specific changes and their exact aetiological correlation with pulmonary tuberculosis is debatable. Of special interest is the presence of membranous glomerulonephritis and interstitial nephritis found in the present study and by Mittal et al (1966). It is possible that the initial damage to the kidney parenchyma produced by the tubercle bacilli or its toxins may stimulate release of auto-antigens which may perpetuate the process. Vereshchagin (1958) has incriminated hypersensitivity mediated by tubercle bacilli to be responsible for these changes.

Varying degree of fibrosis was present in four of the patients in this study and in none of these any other significant histopathological lesion was

observed. In instances where immunity dominates over the hypersensitivity reactions the essential histological change in tuberculosis may be fibrosis. It is thus possible that predominant component of the tubercular reaction in renal parenchyma is a diffuse fibroblastic reaction.

Urine findings and Histological changes

Pyuria was a significant finding in most of the patients who had histological changes in kidney. Out of the 12 patients with more than 5 pus-cells/PHF in urinary sediment, normal tissue was obtained in only 2 patients. Besides pyuria, albumin uria was the second most important urinary abnormality associated with structural changes in the kidney. Only 3 patients who had trace to ++ of Albumin in urine had normal kidney tissue, where as +++ or ++++ albuminuria was always associated with amyloidosis of kidney. Taken together, one or the other urinary abnormality was always associated with abnormal histology of kidney.

Urine for AFB culture was found to be negative in all the patients thus highlighting the failure of this investigation in picking up renal involvement. Chaddha et al. (1971) in their study of 55 patients of pulmonary tuberculosis could culture AFB in Urine in 3.8% of cases only. Kidney biopsy was not performed in these cases to confirm the renal involvement.

In the present study no definite correlation has been observed between the extent of the pulmonary disease and the changes in kidney. One patient with mild parenchymal infiltration had evidence of glomerulonephritis and another with a pleural effusion revealed evidence of amyloidosis. The duration of illness also does not appear to affect the kidney changes. The average duration of illness in patients with abnormal kidney histology was eight months, whereas the same in patients with normal kidney tissue was six month only. Mittal et al. (1966) also observed that duration of pulmonary disease has no bearing on the renal involvement.

Duration of therapy also does not seem to affect the production of renal changes. It is difficult to interpret the effect of therapy because 24 out of 30 patients included in this study had either received no treatment or were on treatment for a period of less than six months.

Summary

Kidney biopsy findings in 30 patients of pulmonary tuberculosis were studied. Abnormal renal histology was detected in 70% of these patients. These changes included the specific finding of tuberculosis, as well as other non-specific histological alterations. Urine abnormality in the form of pyuria and/or albuminuria are significant pointers to the renal involvement. Kidney involvement in pulmonary tuberculosis is not influenced by the duration of illness and severity of pulmonary lesion. Effect of anti-tubercular treatment on these lesions needs further evaluation.

REFERENCES

1. Auerbach, O. (1940), *The new international Clinic* 3, 21.
2. Medler, E.M., Spain, D.M. and Holliday, R.W. (1949) *J. Urol.* 61, 1078.
3. Bell, E.T. (1960) *Renal diseases*. Lea & Febiger. (2nd edn).
4. Merole, G. (1958) *Excerpt. Med. Surg.* p. 820.
5. Mittal, O.P., Sharma, G.S., Singh, S.K. and Agarwal, M.C. (1966) *Ind. J. Chest Dis.* 8, 20.
6. Chadha, S.K. and Sahi, R.P. (1971), *Ind. J. Tub.* 18, 54.
7. Muechrcke, R.C., Kark, R.M. and Pirani, C.L. (1955) *J. Urol.* 74; 267.
8. Vereshchagin, A.P. (1958) *Abs. Sov. Med.* 2, 469.

LIVER FUNCTION IN EXTRA-PULMONARY TUBERCULOSIS

V.K. JHA, K. KOTILINGAM, D.C. Roy, P.K. SHUKLA AND M. JOSHI
(*Institute of Medical Sciences, Banaras Hindu University, Varanasi*)

Pulmonary tuberculosis is a localised manifestation of a systemic disease with a tendency to involve organs near and far. The liver being an organ peculiar in its position, blood supply and function, it seems to be having more than its share of damaging agents. The presence of liver damage in pulmonary tuberculosis has been exhaustively worked on but only a few reports are available about the cases of extrapulmonary tuberculosis (Arora et al, 1956; Sen et al, 1966; Mukherjee et al, 1968; Mehrotra et al, 1968; Gambhir et al, 1972 and Prasad et al, 1973). This study was taken up to see the evidence of liver damage by means of a relatively wide spectrum of tests in cases of extrapulmonary tuberculosis. Most of the workers have done only the conventional liver function tests and no report is available about Pseudocholinesterase which is also a sensitive index of liver damage (Singh, D, 1969).

Material and Methods

Twelve cases of extrapulmonary tuberculosis provided material for this study. All of them were subjected to thorough clinical, radiological and bacteriological examination to exclude the presence of pulmonary tuberculosis and to establish the presence of tubercular involvement elsewhere. The findings were recorded and their blood was obtained, and the following tests were done by the methods described in Wootton's Microanalysis in Medical Biochemistry (1964).

Vanden Bergh, Serum bilirubin (Bil), Thymol Turbidity (TT), Serum Alkaline Phosphatase (Alkp), Pseudocholinesterase (Pse), Serum Glutamicoxaloacetic Transaminase (SGOT), Serum Glutamicpyruvic Transaminase (SGPT), Serum Total Protein (TP), Serum Albumin (Alb).

Liver biopsy was also performed where feasible.

Results

Out of 12 cases studied 3 were of abdominal tuberculosis, 4 of Caries spine, 2 of urogenital tuberculosis and the rest one each of tuberculosis of femur, hip and knee. The liver was found to be enlarged in 3 out of the 12 patients. It was soft, smooth, tender and 1-2 fingers below costal margin. None of the patients had clinically perceptible jaundice. The results of liver function tests and other findings are given in Table 1.

Discussion

The derangement of liver function is appreciable in the majority of the cases. The alteration of the individual liver function tests in the cases of abdominal tuberculosis showed the maximum damage, in that the highest values for Alkp, SGOT, SGPT and very low Psc values were found. Others like Gambhir et al (1972) have found varying incidence of liver damage in their cases of abdominal tuberculosis. All the three such cases in this study showed that there was hepatic involvement. For example case No. 1 who had only slight alteration in the liver function tests, showed on biopsy that there was cloudy swelling, Kupfer cell hyperplasia and round cell infiltration. Out of the remaining two cases, one had a frank caseating tuberculous granuloma and the remaining one in which biopsy was not done showed high SGOT and low Psc. Though elevated SGPT is supposed to point to liver derangement, the diagnostic specificity attributed to SGPT often fails to work in practice because the involvement of the liver may be due to the secondary effect of some other disease and the rise of SGPT in such cases is often delayed and may not become evident until SGOT activity begins to fall (Oser, 1965).

The remaining 9 cases showed only a limited degree of hepatic damage. Out of all the tests, Psc was found to be definitely lowered in 5 of them, A:G ratio was altered in 5, though Psc was not reduced correspondingly. It has been argued that Psc has a relation with Alb. (Faber, 1943). We do not feel this to be true in our cases, as can be seen in Table 1. Psc and albumin are not necessarily reduced in the same cases. There is a dissociation. This combined with other reports about the sensitivity of Psc as an index of liver damage (Singh, 1969) points to the fact that in these cases also there was an early damage to the liver.

The total proteins are in general normal or slightly increased, whereas albumin showed depression. This can be explained as tuberculosis causes hyperglobulinemia in general with simultaneous hypoalbuminemia. Mehrotra & Agarwal (1968) state that the incidence of jaundice is greater in abdominal tuberculosis (24%). The mechanism of jaundice was said to be uncertain (Prasad et al, 1973). Various factors like intrahepatic obstruction, extrahepatic obstruction by

Table I
Showing the results of liver function tests of 12 extrapulmonary tuberculosis cases studied

S.No.	Age & sex	Diagnosis	Van —den Bergh	TT	S. Bil	S. Alkp	S. Psc	SGOT	SGPT	Total protein	Serum Alb.	Liver enlargement
1.	30 F	TB Abdomen	—	2.0	0.7	10.0	45	25	35	7.5	5.0	1 finger
2.	16 F	TB Abdomen	—	3.0	0.5	18.0	40	60	35	6.3	4.0	1 finger
3.	60 M	Caries Sp.	—	1.5	0.5	17.0	30	2	18	7.3	4.8	
4.	22 M	TB Knee	—	5.5	0.4	11.0	48	18	12	7.6	4.8	
5.	18 F	Caries Sp.	—	4.5	0.5	9.4	60	10	18	7.7	4.8	
6.	21 F	Caries Sp.	—	3.0	0.7	6.0	30	20	20	6.5	3.8	
7.	62 M	Caries Sp.	—	5.0	0.5	14.0	30	15	22	7.2	3.8	
8.	16 M	TB Lt. Femur	—	1.5	0.4	9.6	50	38	18	5.5	3.0	
9.	32 M	TB Lt. hip	—	2.0	0.6	7.8	45	36	12	7.5	4.0	
10.	29 F	TB Kidney	—	2.5	0.6	11.6	65	36	12	7.3	5.0	
11.	36 F	Urogeni. TB	—	3.0	0.7	7.2	72	22	16	7.1	4.0	
12.	25 F	TB Abdomen	—	3.0	0.7	8.2	32	25	45	6.5	4.0	2 fingers
Mean				3.0	0.555	15.96	45.58	25.58	21.925	7.0	4.25	
S.D. ±				1.49	0.114	15.02	14.31	15.28	10.68	0.66	0.63	

Liver biopsy : Case No. 1 : Foamy cytoplasm and evidence of regeneration, Kupffer cell hyperplasia, Cloudy swelling, round cell infiltration around portal tract are seen.

Case No. 12 : Caseating tuberculous granuloma seen.

glands, damage to liver parenchyma by granulomatous lesions, toxins, etc. were postulated. In our cases none had manifest clinical jaundice.

As all the cases in this study were receiving first line anti tuberculous drugs, it may be argued that the liver damage is due to the same (Sherlock, 1968; Garibaldi, 1972; Meade, 1972). We do not entirely decline this statement but how can the fact be explained that the maximum damage to the liver was found in the cases of abdominal tuberculosis only? If the drugs only were responsible we could expect the presence of maximum liver damage without any predilection. This points to the possibility that the liver damage is produced primarily by the tubercular process, the drugs act only secondarily.

Regarding etiopathogenesis of hepatic involvement in extrapulmonary tuberculosis multiple mechanisms may be operating. It may be due to the direct involvement by the bacillus which is rather rare. It may be secondary to primary infection somewhere in the body usually in the lungs or gastrointestinal tract or by haematogenous spread. It may be due to anti tuberculous drugs that are given or as a result of antigen-antibody reaction resulting with immunological involvement of the liver.

Summary

Twelve established cases of extrapulmonary tuberculosis were studied for evidence of liver damage. Out of these 3 were of abdominal tuberculosis, 7 bone and joint tuberculosis and 2 genitourinary tuberculosis. Vanden Bergh, Thymol turbidity, Serum bilirubin, Serum alkaline phosphatase, Pseudocholinesterase, SCOT, SGPT, Total protein and Serum albumin were done in them. Varying degrees of biochemical evidence of liver damage was found. Liver biopsy was done in two cases. It was suggested that abdominal tuberculosis will have worse effect on liver than other types of extrapulmonary tuberculosis.

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REFERENCES

1. Arora, Akbar Ali, M.M., Souza. D., Pawar, K.N. (1956). *J.I.M.A.*, 17, S.No. 2317.
2. Gambhir, M.S., Goyal, S.K., Rawat, M.L. (1972) *J. Assn. Phys. India*, 20:843.
3. Garibaldi, R.A., Drusin, R.A., Ferebee, S.H., Gregg, M.B. (1972) *Amer. Rev. Resp. Dis.*, 106:357.
4. Meade, G.M. (1972) *Clinical Paediatrics*, 11 : 498.
5. Mehrotra, M. and Agarwal, A.N. (1968) *J. Assn. Phys. Ind.*, 16 : 497.
6. Mendel, B., Mundell, D.M. and Rudney, (1943) *Chol Biochem. J.*, 37:473.
7. Mukherjee, B., Gulati, P.O., Vyas, P.B. (1968) *J. Assn. Phy. Ind.*, 16 : 451.
8. Osser, B.L. (1965) *Hawk's Physiological Chemistry*. 14th ed., McGraw Hill, London.
9. Prasad, M., Tyagi, S.P., Ahmed, K.N., Bahadur, P. and Tajuddin, M. (1973) *Ind. J. of Chest Dis.*, 15:38.
10. Sen, S. (1967) *J.I.M.A.*, 48 : 285.
11. Singh, D., Bapna, S.D. and Khandelkar, J.D. (1969). *J. Assn. Phys. India*, 17: 511.
12. Sherlock, S. (1968) *B.M.J.*, 1 : 227.
13. Wootton, I.D.P. (1964) *Microanalysis in Medical Biochemistry* 4th ed., J.A. Churchill Ltd., London.
14. Faber. I. (1943) *Acta Med Scand.* 114:59.

CASE REPORTS

ASSOCIATION OF PULMONARY TUBERCULOSIS AND LUNG CANCER

(Report of 3 cases from Kashmir Valley with a Review of Aetiological concepts)

A. NAFAE., S.P. MISRA., S.N. DHAR AND S.N.A. SHAH.
(From Govt. Medical College, Srinagar.)

Introduction

The presence of lung cancer is rarely suspected in a patient with active pulmonary tuberculosis. Symptomatology and physical findings may be ascribed to tuberculosis alone where the two conditions co-exist. Extension of radiographic abnormalities during treatment may be attributed to bacterial resistance. Even when carcinoma is suspected, through some unusual abnormality on chest skiagram or bizarre course of the illness, a diagnosis of co-existent neoplasm may be delayed especially where the sputum remains positive for tubercle bacilli. During the course of our observations on 25 male cases of bronchogenic carcinoma in the Chest Diseases (C.D.) and the S.M.H.S. Hospitals, Srinagar between September 1970 and June 1972, we encountered 3 cases wherein the association of tuberculosis with malignancy was demonstrable; these are being described in detail.

Case 1: H.A.N., 65 years., male, farmer, admitted to C.D. Hospital on 1.2.1971 had productive cough for 4 years with periodic exacerbations. During last three months he had breathlessness and blood stained sputum occasionally. Two weeks before admission generalised pains and aches had set in and cough became troublesome. History revealed that 7 years back he was treated for Pulmonary T.B on X-ray and sputum evidence. He initially received SM, INH and PAS; 4 months later SM was discontinued. He made remarkable recovery and was discharged after 6 months from Hospital (Fig. 1). On completion of 3 years regular chemotherapy his case was filed. He continued to have mild productive cough with occasional exacerbations, attributed to his smoking habits (smoked "Hukkah" and cigarettes for past 40 years).

On present admission he was dyspnoeic, had moderate pallor and clubbing but no lymphadenopathy, nor oedema. Temp. 98.8° F, Pulse 90/mt, B.P. 150/90 mm. Dullness, diminished breath sounds, medium sized crepts and rhonchi over upper 1/2 of Rt. chest detected. Lt. side revealed normal breath sounds. X-ray of chest on 2.2.71 (Fig. 2) showed dense opacity in Rt. upper zone with tracheal pull. Some productive infiltrates and calcifications in upper half of Rt. middle zone and fibrosis in Lower zone was seen. Left hilar and para-hilar regions

showed calcified shadows. There was compensatory emphysema in left lower zone.

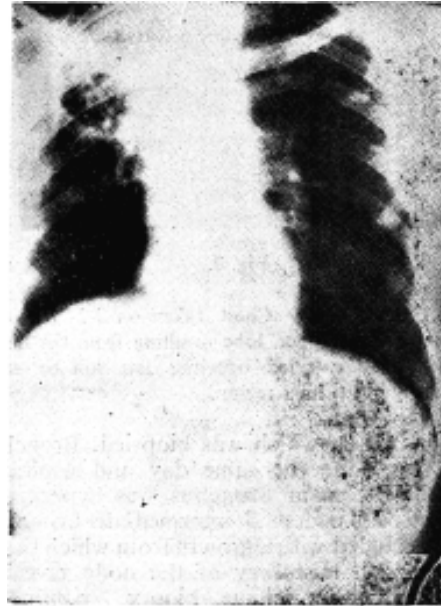


Fig. 1.

H.A.N. (Case 1) : X ray Chest on 22-10-67 taken just before termination of full course of Chemotherapy showing residual fibrosis and small calcified foci in Rt. tipper zone. Stray hard opacities are seen in Lt. lung.

Investigations : TLC-5800/cmm; Polys 48%; Lymphos 10%; Eosinos 35%, Monos 7%; Hh 9.2 gm%; ESR 30 mm (Westergren); Urine normal. Two successive morning sputum samples reported negative for AFB. Gram stained smears showed gram positive cocci and pus cells.

He was put on Ampicillin, haematenics, vitamins and supportive measures, diagnosed as lung abscess. Three weeks later fluoroscopy revealed extension of lesion. Sputum cultures for fungi and mycobacteria were put up. In view of past history and radiological worsening he was switched on to SM, INH, PAS and Oxytetracycline. His condition gradually deteriorated. About a month later one almond sized, non-tender, very firm node was detected in Rt. supra-

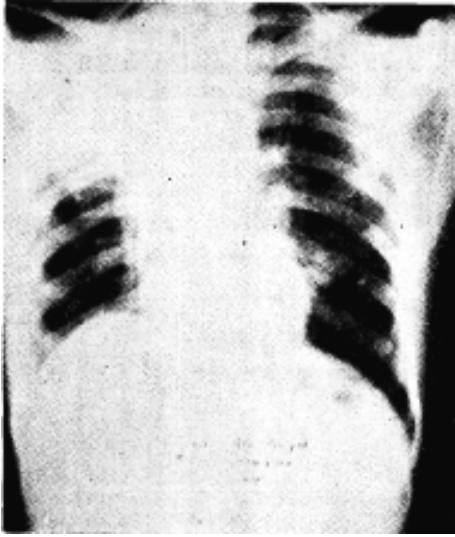


Fig. 2.

(Same Case): X-Ray Chest taken on 2-2-71 shows collapse of Rt. Upper lobe resulting from the neoplasm. Stray calcified opacities can still be seen, particularly in Lt. Mar region.

clavicular fossa, which was biopsied. Bronchoscopy was done the same day and aspirates collected. Rt. main bronchus was hyperaemic with mucosal oedema, intermediate bronchus almost occluded with a growth from which tissue was removed. Histology of the node revealed malignant nature. Tissue biopsy confirmed squamous cell carcinoma. Bronchial aspirates were negative, but sputum collected after "deep cough" on three successive mornings was twice positive for malignant cells. Subsequently, cultures for fungi and mycobacteria were reported negative.

Case 2 : G.R.B., 60 years, male, farmer, admitted to C.D. Hospital on 20.5.1971 complaining of productive cough 1½ years, blood-tinged sputum 4 months, loss of appetite weakness 3 months. Fifteen months earlier had been admitted to S.M.H.S. Hospital with cough, fever, night-sweats, weight-loss and anorexia, of 3 months' duration. Sputum was twice positive for AFB and X-ray chest revealed fibro-caseous lesion in Rt. upper zone. He was referred to District T.B. Centre; SM and INH started. Within 3 months, became afebrile, regained weight and appetite; felt normal except for morning cough. Subsequently he was put on INH and Thiacetazone. He collected his monthly drug quota regularly; remained well for 8 or 9 months, thereafter, began to feel run-down and losing appetite. During Jan. 1971 had blood-stained sputum after a bout of cough, for the

first time, and presented for check-up. One 'spot' and one 'collection' samples of sputum found negative for AFB. The episode was ascribed to bronchitis for which treatment was prescribed. (He had been smoking 'Hukkah' for 30 years). During last week of March 1971 again noticed blood streaked sputum for 4 or 5 days; it stopped by itself and was ignored. Anorexia and weakness increase. Two days before admission he had become breathless after a bout of cough accompanied by frank blood spitting.

On present admission he looked run-down, pale and dyspnoeic. Nails were clubbed. No lymphadenopathy; no oedema. Liver 1 cm. Temp 98.2° F, Pulse 102/mt, B.P. 160/110 mm. Rt. suprascapular, upper 1/3 interscapular and infraclavicular areas revealed harsh breath sounds with fine and few medium crepts. In addition there was dullness over middle 1/3 of Rt. interscapular region and medial half of III and IV anterior spaces. Faintly audible breath sounds and stray rhonchi were present over this area. X-ray chest on 21.5.1971 (Fig. 3) showed patchy infiltration with some fibrotic strands suggestive of regressing tuberculous lesion in Rt. upper zone. Rt. Hilar region showed dense opacity extending upto medial 2/5th of the middle zone, a few calcified spots were seen in left hilar region.

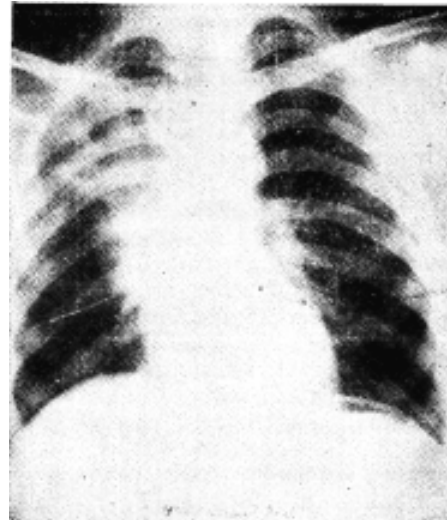


Fig. 3.

G.R.B. (case 2): X-ray chest on 21-5-71 showing resolving tuberculous infiltrates in Rt. Upper and upper middle zones. The neoplasm is seen as a dense opacity occupying Rt. hilar and para-hilar regions. Fissure of Azygos lobe can be made out clearly. The transverse line crossing, the lower zone is an artefact,

Investigations : TLC 7000/cmm; Polys 55 %, Lymphos 40 %, Monos 5 %; Hb. 10.4gm%; ESR 45 mm/hr (Westergren); Urine normal. Sputum collected on three successive mornings failed to reveal AFB or malignant cells. Cultures for mycobacteria were set up.

As patient was already on INH and Thiacetazone, SM and PAS were added. INH dosage was increased and pyridoxin, tranquilisers, aminophylline (I.V.) given as supportive measures. Despite lowering of B.P., dyspnoeic attacks persisted. Cultures for mycobacteria showed equivocal growth at 8 weeks. On 10.8.1971 bronchoscopy revealed a small smooth mass protruding into middle lobe bronchus; marked hyperaemia and patchy mucosal oedema extending upto posterior basal bronchus opening. Secretions collected were found positive on Papanicolaou staining. Biopsy from the growth confirmed squamous cell carcinoma on histology. Bronchoscopy, done in S.M.H.S. Hospital in Feb. 1970, had shown only, mild hyperaemia of Rt. main bronchus.

Case 3 : M.S., 45 years., male, farmer, admitted to S.M.H.S., Hospital on 27.5.1972 was having cough for 3 months, irregular fever, weakness, impaired appetite 2 months, heaviness left chest 20 days. Cough became associated with muco-purulent sputum with onset of fever. Past history revealed that when 30 years old he was diagnosed and treated as a case of pulmonary TB (Sputum +) in C.D. Hospital, initially with SM, PAS and INH; 3 months later, injections were discontinued. He had improved remarkably with treatment which continued for 2 1/2 years., when, after detailed assessment, the specialist I/c discontinued the drugs. Remained healthy over next 12 years but for morning cough and occasional episodes of bronchitis (had been a "Hukkah" smoker since age of 15 years).

On present admission he looked ill, emaciated, moderately pale; had no dyspnoea, no clubbing, no lymphadenopathy. Temp. 100.8° F, Pulse 108/mt, B.P. 120/80 mm. Examination revealed dullness over middle 1/3 of Lt. chest with diminished air entry; in peripheral area bronchial breathing, medium and coarse crepts heard, with rhonchi at places. Harsh breathing present all over Rt. side X-ray chest on 28.5.1972 (Fig. 4) revealed a dense area of consolidation in left 1st and 2nd anterior spaces right upto hilum, with nodular opacities extending upto 3rd rib anteriorly. Rt. lung showed some fibrosis and few hard nodular opacities. Rt. paratracheal and hilar regions did not appear normal.

Investigations : TLC 11000/cmm; Polys 50% Lymphos 30% Eosinos 20%; Hb 9.4gm%,

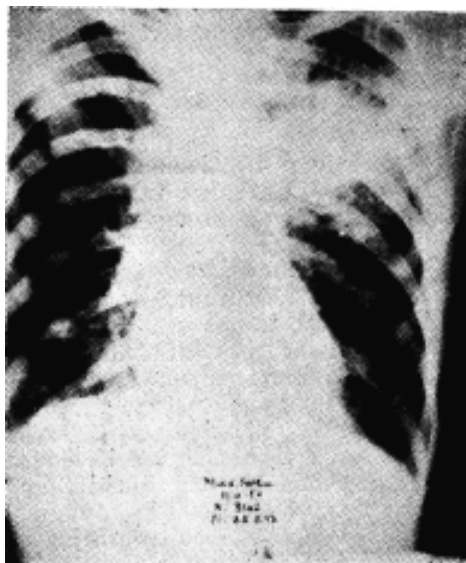


Fig. 3.

M.S. (Case-3): X-ray chest on 28-5-72 shows extension of the opacity on Lt-side and suspicious densification in Rt. paratracheal region.

ESR 42 mm/hr (Westergren); Urine normal. Two consecutive morning collections of sputum found negative for AFB and malignant cells. Cultures for fungi and mycobacteria were set up. He was put on crystalline penicillin 10 lacs 6 hourly, Streptomycin, vitamins and bronchodilators. Improved initially for 8-10 days, but began going down-hill thereafter. No growth appeared on Sabouraud's media upto 2 weeks. Left lateral X-ray on 11.6.1972 revealed a dense mass in apical and posterior segments confluent with dense hilar region. A cavity was partly visible through the lower limit of the density. Patient was transferred to C.D. Hospital where Penicillin was stopped, INH, PAS and Oxytetracycline were added. Bronchoscopy was done on 17.6.1972 Rt. bronchial tree showed slight congestion of mucosa. On Lt. side thick muco-purulent secretions, slightly blood-tinged, present; mucosa found congested, at places haemorrhagic spots noted. No growth visualised due to thick secretions. Secretions removed and bronchial biopsy taken. Histology of mucosal tissue revealed squamous cell carcinoma. Bronchial aspirates by Leishman's and by Papanicolaou staining found positive for malignant cells; surprisingly, Ziehl-Neelsen's staining revealed AFB. Left scalene node biopsy a week later proved unrewarding. The patient worsened with increasing dyspnoea. X-ray on 30.6.1972 showed some clearing at upper portion, but the density had now extended right upto the left hemidiaphragm. His relatives

took him home where he expired a few days later. Report of positive mycobacterial culture was later received.

Discussion

The frequency of association of lung cancer and pulmonary tuberculosis varies widely in different studies. Shah-Mirany et al (1966) observed that 56.8% of their 95 lung cancer patients had active or chronic inactive tuberculosis. Aspevik (1970) from Norway reported tuberculous manifestations in 38% of his 204 primary lung cancer cases. In contrast, Braude (1969) in Russia found pulmonary tuberculosis in 1.66% of his lung cancer cases and bronchial carcinoma in 1.8% of pulmonary tuberculosis patients. Le Roux (1968) reviewed 4,000 cases of bronchogenic carcinoma and found only 2% patients with tubercle bacilli in sputum. Mc-Querrie et al (1968) observed co-existing tuberculosis in 3.7% of lung cancer cases. In India, Nagrath et al (1970) found co-existent tuberculosis in 5.7%, and Guleria et al (1971) in 2.5%, of their lung cancer cases. We, in this Valley, observed the association of the two conditions in 3 of 25 proved lung cancer cases. However, true co-existence was demonstrable in only two (cases 2 and 3) i.e., in 8%. Steinitz's (1965) epidemiological studies in Israel revealed that the incidence of tuberculosis in bronchial carcinoma patients varied from 7% to 30% depending on the geographic area and the population group studied. Shah-Mirany et al's inclusion of active as well as chronic inactive cases of tuberculosis and their selection of cases out of the Sanatorium patients admitted primarily with pulmonary tuberculosis might account for such high incidence in their series. Moreover, we would prefer to make a clear distinction between the terms "co-existence" and "association" of the two diseases.

Two of our patients (Cases 1 and 2) belonged to the age-groups wherein lung cancer has been reported frequently. Case 3, who first suffered from pulmonary tuberculosis at the age of 30 years, developed the neoplasm when only 45 years old—rather an early period for malignancy. We can only speculate whether any or some of the probable aetiological factors *viz.*, smoking habits, secondary broncho-pulmonary inflammations, healed tuberculous scars, atmospheric pollution, X-ray radiation, or the possible tumorigenic activity of Isoniazid, could be incriminated in these cases.

Our observations (1973) on 25 cases of bronchogenic carcinoma in Kashmir Valley, and those of Ibrahim (1954) in Pakistan, point to a close association between 'Hukkah' smoking and lung

cancer, though the implication of this form of smoking in the context of pulmonary carcinogenesis needs wider studies. According to Doll (1953) bronchitis was more closely related to squamous cancer than to other varieties; smoking was related equally to all types except adenocarcinoma (Spencer, 1968). All the 3 cases reported here had squamous cell carcinoma. Heavy smoking could be implicated in all these cases. In case 1, non-specific bronchial inflammations had persisted, but the duration of 4 years appears rather short to incriminate it. Both chronic bronchitis and lung cancer are also related to atmospheric pollution (Doll), but this Valley as yet has no significant industrialization; so this factor could not be considered operative in our cases. Healed scar could at best be implicated in Case 3 in view of the long interval of over 12 years.

Gofman and Tamplin (1970) think that by some mechanism other than cigarette smoking a record of extensive therapy of tuberculosis implies a high risk of primary lung cancer. They hypothesised that frequent fluoroscopic examinations of the chest, associated with past extensive use of collapse therapy, was the aetiological factor. This, however, could not explain occurrence of carcinoma in any of our cases who had received only conventional drug treatment.

The extensive use of Isoniazid in the treatment of tuberculosis coincided with the rapid decline in the popularity of pneumothorax and pneumoperitoneum therapies. Experimental studies by Biancifiiori and Ribacchi (1962), Biancifiiori and Severi (1966), Jones et al (1967), and by others, confirmed carcinogenic effects of INH in mice. A preliminary follow-up study by Hammond et al (1967) provided no evidence of excessive lung cancer in tuberculous patients treated with INH. Campbell and Guilfoyle (1970) also failed to find any possible implication of INH in production of lung cancer in tuberculous ex-servicemen. They, however, stated that since carcinogenic agents may take 10 to 20 years or more to induce tumours and since it was not possible to extrapolate to man those animal experiments which demonstrate tumor induction by INH in lungs and lymph glands, the ultimate evaluation of this drug must be made in man with larger retrospective studies than reported so far. If INH does have any carcinogenic effect in man it could at best be incriminated in only one of our patients (Case 3) who developed the neoplasm 15 years after his first contact with this drug.

An intimate association of lung cancer and pulmonary tuberculosis has been repudiated on immunological grounds. Von Rokitansky (1855) was the first to propose that cancer and

tuberculosis were incompatible. This antagonism theory has been corroborated by several animal experimental studies from time to time (Greentree, 1970) and by clinical observations of Villasor (1965), Mathe (1967), and others. Observations of Shah-Mirany et al (1966) led them to conclude that tuberculosis appears to impede the spread of cancer. Braude (1969) also observed that if lung cancer occurred in patients with pulmonary tuberculosis the tumor generally developed beyond the boundaries of the tuberculous lesion. This immunological concept does not exactly conform to our observations. Case 2 clearly demonstrates this point where the interval between tuberculosis and subsequent cancer was brief, unlikely to account for loss of the resistance supposedly induced by tuberculosis. However, we can concede to a probable loss of such immunity with the passage of time in case 3; and it appears that the onset of neoplasm led to reactivation by breakdown in body defence mechanism.

Conclusion

Whether tuberculous inflammation per se or the measures employed in its treatment have any aetiological role in inducing malignant changes in lung, or, whether active tuberculous process re-inforces the host's natural resistance to cancer, still remains debatable. The fact remains that the two conditions can and do co-exist. Lung cancer and tuberculosis should be expected to be seen associated more often in future in view of the increasing incidence of lung cancer, the longevity of persons with past history of tuberculosis, as well as the growing trend of new cases of tuberculosis shifting to the older age groups. In elderly tuberculous individuals, especially if the course of disease runs along unexpected lines, this association must be actively explored since surgical intervention in such cases has a chance of cure at least equal to, or perhaps better than, the usual lung cancer patient (Me Querrie et al, 1968).

Summary

In a series of 25 cases of bronchogenic carcinoma 3 cases revealed association of pulmonary tuberculosis with the neoplasm; in 2 of these the two conditions were found co-existing. The cases have been reported in detail and discussed in the light of various aetiological concepts. The importance of high suspicion index for this association in elderly tuberculous patients exhibiting bizarre course of illness has been stressed.

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REFERENCES

1. Aspevik, E. (1970) Co-existing carcinoma of the Lung and Tuberculosis, abstracted in *Excerpta Medica Chest Diseases, Thoracic Surgery and Tuberculosis*, 25.3; 197, 1972.
2. Biancifiore, C. and Severi, L. (1966), The Relation of Isoniazid and Allied Compounds to Carcinogenesis in Some Species of Small Laboratory Animals: A Review. *Brit. J. Cancer*, 20 : 528.
3. Bignall, J.R. (1958), *Monographs on Neoplastic Disease Vol. I. Carcinoma of the Lung*, Edited by J.R. Bignall, E & S Livingstone Ltd., Edinburgh and London.
4. Braude, V.I. (1969), Various Localization of Cancer Developed in Patients with Pulmonary Tuberculosis: abstracted in *Excerpta Medica Chest Diseases, Thoracic Surgery and Tuberculosis*, 23.4; 176, 1970.
5. Campbell, A.M. and Guilfoyle, P. (1970), Pulmonary Tuberculosis, Isoniazid and Cancer: abstracted in *Excerpta Medica Chest Diseases, Thoracic Surgery and Tuberculosis*, 25.1; 49, 1972.
6. Doll, R. (1953). Bronchial Carcinoma: Incidence and Aetiology, *Brit. Med. J.* 2: 521.
7. Doll, R. and Hill, AB. (1952), A Study of the Aetiology of Carcinoma of the Lung, *Brit. Med. J.* 2 :1271.
8. Gofman, J.W. and Tamplin, A.R. (1970), Fluoroscopic Radiation and Risk of Primary Lung Cancer Following Pneumothorax Therapy of Tuberculosis, *Nature (Lond)*, 221 j5255: 295.
9. Greentree, L.B. (1970), Cancer and Tuberculosis, *Amer. J. Obstet. Gynaec.*, 105/7 : 1098.
10. Guleria, J.S., Gopinath, N., Talwar, J.R., Bhargava, S., Pande, J.N., and Gupta, J.R. (1971). Bronchial Carcinoma; An Analysis of 120 cases, *J. Ass. Phys. Ind.* 19/31: 251.
11. Hammond, B.C., Selikoff, I.J., and Robitzek, E.H. (1967), Quoted by Greentree, L.B. in 'Cancer and Tuberculosis', *Amer. J. Obstet. Gynaec.* 106/7; 1098, 1970.
12. Ibrahim, M. (1954), Quoted by Nagrath, S.P., Hazara, D.K., Lahiri, B., Kishore, B. and Kumar, R. in Primary Carcinoma of the Lung: Clinico-pathological study of 35 cases, *Ind. J. Chest. Dis.* 12/182: 15, 1970.

13. Jones, L.D., Fairchild, D.G., and Morse, W.C. (1971). The induction of Pulmonary Neoplasm in Mice by Isonicotinic Acid Hydrazide, *Amer. Rev. Resp. Dis.* 103/5 : 612.
14. LeRoux, B.T. (1968), Bronchial Carcinoma, *Thorax*, 23:136
15. Meckenzie, I. (1965), Breast Cancer Following Multiple Fluoroscopies, *Brit. J. Cancer*, 19 : 1.
16. Me Quarrie, D.G., Nicoloff, D.M; Van Nostrand, D., Rao, K., and Humphrey, E.W. (1968), Tuber- culosis and Carcinoma of the Lung, *Dis. of Chest* 54/5: 427.
17. Mathe, G. (1969), Quoted by Greentree, L.B. in 'Cancer and Tuberculosis', *Amer. J. Obstet. Gynaec.* 106/7: 1098, 1970.
18. Nafae, A., Misra, S.P., Dhar, S.N. and Shah, S.N.A (1973). Bronchogenic Carcinoma in Kashmir Valley, *Ind. J. Chest Dis.* 15/4; 285, 1973.
19. Nagrath, S.P., Hazara, O.K., Lahiri, B., Kishore, B., and Kumar, R. (1970). Primary Carcinoma of Lung: Clinico-pathological Study of 35 cases, *Ind. J. Tub., Vol. III, No. 2. J. chest Dis.* 12/182:15
20. Pearl, Raymond (1929): Quoted by Greentree, L.B. *Amer. J. Obstet. Gynaec.* 106/7 :1098,1970
- 21 . Shah-Mirany, J., Reimann, A.F., and Adams, W.E. (1966). Co-existing Brochogenic Carcinoma and Tuberculosis, *Dis. of Chest*, 50/3 : 258.
22. Spencer, H. (1968), Carcinoma of the Lung, in Pathology of the Lung, Pergamon Press Ltd., Headington Hill Hall, Oxford 4 and 5 Fitzroy Square, London, W. 1.
23. Steinitz, R. (1965). Pulmonary Tuberculosis and Carcinoma of the Lung: A survey from Two Population-based Disease Registers, *Amer. Rev. Resp. Dis* 92 : 758.
24. Villasor, R.P., (1965), Quoted by Greentree, L.B., 'Cancer and Tuberculosis', *Amer. J. Obstet. Gynaec.* 106/7 : 1098, 1970.

NEWS AND NOTES

INTERNATIONAL CONFERENCE IN DELHI

The Tuberculosis Association of India organised in Delhi along with its 29th National Conference on Tuberculosis and Chest Diseases, the IXth TB Conference of the Eastern Region of the International Union Against Tuberculosis from November 3 to 8, 1974. The Conference was held in the Mavalankar Hall, Constitution Club, New Delhi. Shri Fakhruddin Ali Ahmed, President of India and Patron-in-Chief of the Conference, inaugurated the Conference on November 4. The inaugural session was addressed by Dr. Karan Singh, Union Health Minister and Patron of the Conference. The President awarded the "TAI GOLD MEDAL" to Dr. M.D. Deshmukh and 'WANDER-TAI ORATION' prize to Dr. K.V. Krishnaswami of Madras.

The meetings of the Executive Committee and the Council of the Eastern Region were held in the Committee Room of the Association on 3rd November, 1974. In the unavoidable absence of Dr. M.S. Chadha, the President of the Region, Sri B.M. Cariappa, senior member of its Executive Committee, chaired the Executive Committee meeting and Sri S. Ranganathan, President, Tuberculosis Association of India, presided over the Council meeting.

Shri B. M. Cariappa was elected as the Vice-President of the Region.

It was decided to accept the invitation of the Korean National TB Association, Seoul, for hosting the 10th Conference of the Region in 1976.

XXXTH NATIONAL CONFERENCE

The Thirtieth National Conference on Tuberculosis and Chest Diseases will be held in Hyderabad (Andhra Pradesh) sometime in November/December, 1975. Details regarding the dates will be announced later. Subjects tentatively selected for the Conference are: (1) Follow-up of sputum negative X-ray positive cases of pulmonary TB (2) Short-term chemotherapy (3) Initial drug resistance in non-treated cases (4) Air-Pollution in relation to Chest Diseases (5) Emphysema (6) Pyogenic infections of the lung (7) Amoebic infections of the lung and pleura (8) Atypical mycobacterial infections and (9) Chronic obstructive lung diseases.

SEAL SALE CAMPAIGN

The 25th Seal Sale Campaign which commenced on 2nd October, 1974 will terminate on 26th January, 1975.

CHANCHAL SINGH MEMORIAL AWARD -1975

The Tuberculosis Association of India will award a cash prize of Rs. 500/- to a TB worker, below 45 years of age, for an original article not exceeding 30 double-spaced foolscap typed pages (approximately 6,000 words) excluding charts and diagrams on a subject relating to tuberculosis. Papers may be sent, in quadruplicate, to reach the Tuberculosis Association of India Office on or before 31st August, 1975. The cash prize will be awarded to the author of the selected paper at the 30th National Conference to be held in Hyderabad.

ESSAY COMPETITION—1975

The Tuberculosis Association of India will award in 1975 a cash prize of Rs. 300/- to a final year medical student in India for an original essay on Tuberculosis, adjudged best by a special committee of this Association. The subject selected for the 1975 competition is 'National Tuberculosis Control Programme'. The award will be made at the inaugural session of the 30th National Conference on Tuberculosis and Chest Diseases.

The essay should be in English, typed in foolscap size, double-spaced and should not exceed 15 pages (approximately 3,000 words) excluding tables, diagrams, etc. if any. Four copies of the manuscript should reach the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001, not later than 31st August, 1975 and should be forwarded through the Dean or Principal of the College/University.

SEMINARS/CONFERENCES

The District TB Association of Salem (Tamil Nadu) organised a Seminar on Tuberculosis on 29.12.1974 at the Indian Medical Association Hall, Salem. The Collector and President of the District TB Association, Salem, Shri A.M. Swaminathan, I.A.S., presided. Dr. T.B. Venugopal, Dist. Medical Officer and Vice-President of the District TB Association, Salem, delivered the welcome address and Dr. K. Jayaraman, President, Indian Medical

Association Tamil Nadu, inaugurated the **KASAULI SANATORIUM**, Seminar.

The Uttar Pradesh TB Association contemplates to organise a State TB Workers' Conference at Lucknow in February or March, 1975. The exact dates are being finalised.

The Karnataka State TB Association intends to hold a Seminar on Tuberculosis sometime in May next at Hassan.

The Goa, Diu & Daman TB Association proposes to conduct a Seminar on TB during May next in collaboration with the Lions Club of Panaji.

"BEAT TB"—INCENTIVE FOR STUDENTS

The Kerala TB Association has introduced an interesting scheme for educating school children about tuberculosis. They organised a Seminar for the benefit of school teachers in which teachers from several schools participated and subsequently under instructions from the Director of Public Instruction, Kerala the pamphlet "BEAT TB" was distributed to students of secondary schools in Trivandrum District. The Association will hold an examination to test the knowledge of the students about TB given in the-booklet and award a number of prizes.

OFFICIAL NEWS

The following promotions in the Headquarters establishment of the Tuberculosis Association of India have been approved:

Shri P.N. Raman,	
Administrative Officer	as Secretary
Shri N.R. Tikekar,	as Administrative
Superintendent	Officer
Shri V.K. Badlani,	as Account Officer
Accountant	
Shri N.P. Lakshmanan,	
Senior Asstt.	as Superintendent

Dr. S.S. Goyal, Dy. Director, New Delhi TB Centre, has been posted as Offg. Medical Superintendent of the Lady Linlithgow Sanatorium, Kasauli, with effect from 22.11.1974 *vice* Dr. S.K. Basu Chaudhury.

TAMIL NADU

Dr. S.S. Bolar, State TB Officer, Tamil Nadu has taken over charge as Honorary Secretary of the Tamil Nadu TB Association, *vice* Dr. S.K. Sudarsan Lal (Retd.).

PONDICHERRY

Dr. V. Sivarama Iyer has taken over charge from Dr. M.L.J. Many as the Honorary Secretary of the TB Association of Pondicherry.

RAJASTHAN

Dr. J.C. Bhagi, Assistant Director of Health Services (TB), Rajasthan, Jaipur, has taken over as Honorary Secretary of the Rajasthan State TB Association.

DR. P.K. SEN

Dr. P.K. Sen, Chairman, Bengal TB Association and member of the Central, Executive and Technical Committees of the Tuberculosis Association of India and the Chief Editor, Indian Journal of Tuberculosis, has been re-elected as the President of the South Club, Calcutta.

ASTHMA, BRONCHITIS FOUNDATION

Applications are invited for one Warner Chest Junior Fellowship from Medical graduates of less than 35 years of age. The problem for research should pertain to any aspect of asthma or any other chronic obstructive airway disease. The fellowship is tenable for one year and will not exceed Rs. 3,000/-.

The applications should reach by the end of February 1975. For details contact the President, Asthma, Bronchitis Foundation of India, C/o V.P. Chest Institute, University of Delhi, Delhi-110 007.

The Indian Journal of Tuberculosis

ABSTRACTS

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Abst. No. 1

Cost-benefit analysis of medi-care BCG vaccination.

S.-Endo & K. Aoki. Kekkaku; (1972) 47, 215.

The cost and benefit of BCG vaccination was analysed for the period 1958 to 1978 in Japan. The reduction of active cases of tuberculosis has been estimated by using epidemetric model finalized in 1970. It has been assumed that the BCG programme as at present will be continued. The protective power of BCG has been taken as 50%, which is likely to fall by 1 % per year during the study period. With these assumptions, it can be calculated that 270,000 cases of tuberculosis could be saved upto the end of 1978 as a result of BCG vaccination. During the entire 20 years period of the study, morbidity could have been reduced by 4.17 million person-years.

The cost of BCG vaccination and medi-care for one case has been calculated on the basis of annual expenditure incurred in the whole of Japan from 1958 to 1970 and estimated from 1971 to 1978, providing for 5% increase per year. Total cost of BCG vaccination has been estimated at 9.6 billion yens until 1978 and the saving in expenditure on medi-care for 270,000 active cases (prevented by BCG) totalled 3 25.9 billion yens. This latter figure did not include the indirect cost of medi-care and the loss of production on grounds of tuberculosis. The authors conclude that even if BCG vaccination costs ten times as high as the present estimate, vaccination would still be a very profitable investment.

S.P.P.

Efficacy of Bacillus Calmette-Guerin and Isoniazid Resistant Bacillus Calmette-Guerin with and without Isoniazid chemoprophylaxis from day of Vaccination.

H.M. Vandiviere, Morris D war ski, Irene G. Melvin, Keene A. Watson and June Begley. Amer Rev. Resp. Dis.; (1973) 108, 301.

Field trials in Haiti to determine the efficiency of conventional BCG and INH-resistant

BCG, with and without INH chemoprophylaxis from the day of vaccination for a 8 week period, were carried out in a population with a high incidence of tuberculosis. During the period of observation BCG vaccination reduced the new case rate to approximately 20% of the amount that occurred among tuberculin non-reactors without BCG. However there was no difference in the reduction of cases between conventional Montreal strain of BCG and INH-resistant BCG derived from the same strain with or without simultaneous INH chemoprophylaxis. Therefore, a potent strain of BCG and INH can be given concomitantly without decreasing the protection afforded by conventional BCG and vaccination with INH-resistant BCG is not justified.

This conclusion is contrary to the results obtained in a trial on guinea pigs (see abstract of Dworski, 1973). This may be due to the difference in the volume of the challenge dose in guinea pigs, its route and time of challenge, which factors can obviously not be equated with the study in human population. It could also be due to the fact that small number of resistant mutants present in the conventional BCG which would not be influenced by concomitant prophylaxis with INH but while continuing to multiply would confer immunity on the host. Another possibility may be that INH may not act very well on slow multiplying BCG strains (as against actively multiplying virulent strains) and, therefore, the results obtained with sensitive and INH-resistant strains would tend to be the same.

S.P.P.

Efficacy of bacillus calmette-guerin and Isoniazid resistant bacillus calmetteguer in with and without Isoniazid chemoprophylaxis from day of vaccination.

Morris Dworski. Amer. Rev. Resp. Dis.; (1973) 108, 294.

This study was primarily designed to determine the atlergenicity and immunogenicity of the INH-resistant strain of BCG which was developed from the potent standard (susceptible)

strain of BCG in Montreal in guinea pigs with a view to compare the results obtained in a human trial in Haiti. The INH resistant mutants proved to be as allergenic and immunogenic as the parent strain. In guinea pigs vaccinated with a standard strain, simultaneous prophylaxis with INH for 8 weeks significantly decreased the size of induration of the post-vaccinal tuberculin reactions as well as immunity. In guinea pigs vaccinated with INH-resistant strains, concomitant chemoprophylaxis with INH for 8 weeks reduced the size of tuberculin reaction only slightly but did not lessen the degree of immunity.

S.P.P.

Tuberculosis in Eskimo Children

Josephine M. Wilson, J. Douglas Galbraith & Stefan Grzybowski. Amer. Rev. Resp. Dis.; (1973) 108, 559.

Eighty seven Eskimo children were diagnosed to be suffering from tuberculosis in a Canadian community during the period 1958 to 1969. Forty three of these children had earlier been vaccinated with BCG and 44 had not had BCG. There was no significant difference in the type and clinical course of disease in the two groups. Primary disease comprised 80% of the total sickness in both groups. There were 2 cases of miliary tuberculosis, one in each group and one case of skeletal tuberculosis in the vaccinated group. There was no case of meningitis.

There were no age and sex differences. More than one half of the cases in both the groups occurred in the first 5 years of life. Approximately two-third of the cases were discovered by routine radiographic surveys and the remaining one-third attended health facilities voluntarily because of symptoms. Two children had BCG vaccination within 8 weeks of the diagnosis of tuberculous disease. In the remaining children the mean time interval between vaccination and diagnosis of disease was 45 months for all and 56 months for those with tubercle bacilli in the sputum.

S.P.P.

Treatment with pyrazinamide given in increased doses twice a week in combination with other drugs

W. Pregowski, A. Stanczuk-Holub. Gruzlica, Chor.Pluc.; 1973,41, 795.

The paper presents the effectiveness and tolerance of 65 mg/kg pyrazinamide twice a week in combination with other anti-tuberculous drugs given every day to 104 patients. Eighty nine of these were patients who had been under

treatment previously for 2-22 years. Sixty patients were excreting drug resistant bacilli. In 65 % of the cases the disease was very extensive and cavitary. Sputum conversion was obtained in 93.3% of the fresh cases and 78% of the re-treatment cases. The rate of sputum conversion was 73.3 % in those excreting drug resistant bacilli. Cavities disappeared in 24.7%. Pyrazinamide had to be discontinued because of side effects in 9 patients (8.6%). Liver toxicity was noticed in 3.3 % of the cases. Among the patients showing liver toxicity 3 were being given ethambutol and PAS and one was having INH in addition to pyrazinamide. Seventy nine of the patients were followed for 26 to 37 months. Sputum reversion occurred in 23 of these 79.

S.P.P.

Rifampicin Hepatitis

P.J. Scheuer, S. Lal, J.A. Summerfield & S. Sherlock. Lancet; 1974, i, 421

Eleven patients in whom clinical or biochemical evidence of liver damage appeared during anti-tuberculous therapy were studied. All patients had received Rifampicin and INH and some had also been given PAS, streptomycin, ethambutol or prednisolone. Hepatitis was seen within a month of giving the treatment in 6 patients, 2 of whom had no evidence of hepatitis in pre-treatment liver biopsy. One patient receiving several drugs including PAS died of massive hepatic necrosis. The hepatitis in the others was usually mild and liver function and histological examination (following repeat biopsy) returned to normal in 5 patients without discontinuing Rifampicin.

Liver biopsy showed diffuse liver-cell damage with acidophilic bodies, but little inflammatory response. Resemblance to viral hepatitis was only partial. Clinically there was a tendency for hepatitis of early onset to be more severe. Early onset and histological appearances suggested that hepatitis was due to Rifampicin alone or in combination with INH, rather than to the latter alone because INH hepatitis usually appears several weeks after the beginning of the treatment in contrast to early onset of hepatitis in Rifampicin.

S.P.P.

Serum concentration and anti-tuberculosis activity of Thiacetazone :

G.A. Ellard, Jean M. Dickinson, Patricia T. Gammons and D.A. Mitchison. Tubercle (1974), 55, 41.

Peak thiacetazone serum concentration

proportional to dosage when single dose of 150 to 600 mgm thiacetazone were given.

The thiacstazone serum concentration of Chinese, Indian and Malay tuberculous patients from Singapore who were being treated with daily regimen containing 150 mg thiacstazone were similar and were unaffected by concomitant administration of a vitamin and anti-histamine supplement or by streptomycin. The urinary excretion of unchanged thiacetazone by tuberculous patients in Singapore and Kenya averaged about 20 per cent of the dose. Significant deacetylation of the drug was not detected.

Slide culture sensitivity test showed that strains from 12 Kenyan patients were considerably more sensitive to thiacetazone than strains from 107 Hong Kong patients. However a concentration of 0.4 ug/ml completely inhibited all of the Kenyan strains and partially inhibited 77 per cent of the Hong Kong strains.

From consideration of the results of clinical trials of regimens of isoniazid and thiacetazone, the minimal concentration of thiacetazone in the lesions necessary to prevent the emergence of isoniazid resistance appeared to be about 0.4 ug/ml in E. Africa and Hong Kong. It is suggested that the efficacy of thiacetazone containing regimen is dependant not only on the characteristics of tubercle bacilli (sensitivity and virulence) but also on the defence mechanism of the patient.

H.B.D.

Aspiration needle biopsy of thoracic lesions: An assessment of 227 biopsies.

R. Dick, B.E. Heard, K.F.W. Hinson, I.E. Ken and M.C. Pearson. Brit. J. Dis. Chest. (1974) 68, 86.

In 166 (73%) of 127 patients, histological diagnosis was made by aspiration needle biopsy. In 45 (20 %) no diagnosis was made on aspiration specimens but by other means. In the remaining 45 (7%) no diagnosis was made by any means.

Minor complications occurred in 51 biopsies (23%).

Needle aspiration is a safe technique.

H.B.D.

Intermittent chemotherapy of pulmonary tuberculosis using rifampicin and isoniazid for primary treatment the influence of various factors on the frequency of side effects :

H. Eule, Werner, K. Winsell and H. Wainsky. Tube (1974), 55, 81.

Of 112 patients, 40 had side effects. In 39

there was transient febrile reaction (flu reaction), the other had thrombocytopenia and purpura. The casual drug proved to be rifampicin in 33 and considered probable in further 2. In 6 of these 35, the reaction was also produced by isoniazid, in the remaining 5, the reaction was produced only by isoniazid. Of the 42 patients treated with 30 mgm/ Kg. rifampicin, 45 per cent had side effects, compared with 23 per cent of 70 treated with 15 mgm./Kg. a significant difference. Reactions were more frequent in males than females and in older than in young patients. No male patients younger than 36 years had side effects.

The increased incidence in females and older patients appears to be associated with the observed increased serum concentration of rifampicin in these patients.

H.B.D.

A Controlled Clinical Trial of daily and intermittent regimens of rifampicin plus ethambutol in the retreatment of patients with pulmonary tuberculosis in Hong Kong

A Hong/Kong, Treatment Service, Brompton Hospital! British Medical Research Council investigation. Tub. (1974), 55, 1.

A total of 575 Chinese adults with sputum positive pulmonary tuberculosis, with strains resistant to isoniazid, who had previously been treated with first line drugs, but not with drugs under study.

384 patients were allocated at random to

- a. rifampicin plus ethambutol daily (ER> 107 patients)
- b. rifampicin plus ethambutol twice a week (ERZ=89 patients).
- c. rifampicin plus ethambutol once a week (ERI=57 patients).
- d. rifampicin plus ethambutol daily for 2 months and then once a week (ER>ERI = 69 patients)
- e. ethionamide plus pyrazinamide plus cycloserine daily for 6 months and then ethionamide plus pyrazinamide daily (FtZc = 62 patients).

At 12 months, 89 per cent of 107 ER>, 80 per cent of 89 ERZ, 82 per cent of ERI, 91 per cent of 69 ER>ERI and 95 per cent of 62 Et Zc patients had favourable status.

Bacteriological failure on the rifampicin regimen was associated with the early emergence of rifampicin resistance of the 396 patients (91 ER>, 80 ERZ, 78 ERI, 85 ER> ERI, 62 EtZc) in the analysis of adverse reactions, 12 of 91 ERZ patients, but no other patient on the other rifampicin regimens, had reactions to ethambutol. Nine (10 per cent) of ER> patients had reaction to rifampicin, 111 (46 per cent) of the 243 patients on intermittent rifampicin had reaction to rifampicin, 34 (55 per cent) of the EtZc patients had adverse reaction.

Reactions to daily rifampicin with either cutaneous or transient increase in serum transaminase levels were without jaundice.

Six main types of adverse reactions to intermittent rifampicin occurred, cutaneous, abdominal, flue syndrome, respiratory, hepatic and purpura.

In 11 patients (5 per cent of 243 on intermittent rifampicin), drugs were stopped due to adverse reactions.

Adverse reactions to EtZc regimens (the commonest of which were cutaneous, hepatic, gastrointestinal, neuro-psychiatric reactions and arthralgia) led to termination of one drug in 11 and all 3 drugs in 4 of 34 patients with reactions, circulating rifampicin dependant antibodies, detected by the indirect antiglobulin method were found in 1 (2 per cent) of 47 ER> patients, in 30 per cent of 40 ERZ, 41 per cent of 44 ERI, and 32 per cent of 44 ER>ERI patients in none of EtZc patients. They were associated with flue syndrome (P=0.001).

Twice weekly rifampicin plus ethambutol with or without an initial phase is now a reserve regimen in Hong Kong.

H.B.D.

A study of adverse reactions to high dosage Intermittent Thiacetazone.

Wallace Fox-et-al. Tuber (1974), 55, 29.

In a blind study, the incidence of adverse reactions to individual doses of thiacetazone of 150 mgm, 225 mgm, 300 mgm, 375 mgm, 450 mgm, 525 mgm and 600 mgm have been compared with a placebo.

Adverse reactions were reported in 2.3 per cent of 2589 doses of thiacetazone and 1.6 per cent of 568 doses of placebo. The reactions were mild.

All the doses of thiacetazone were well tolerated.

H.B.D.

Ind. J Tub., Vol. XXII, No. 1

Right ventricular hypertrophy and its relationship to chronic bronchitis and Emphysema.

J. Millord and Lyrme Reid. Brit. J. Dis. Chest (1974) 68, 103.

Centriacinar emphysema is an uncommon finding and no relationship is found between centriacinar emphysema and right ventricular hypertrophy while severe panacinar emphysema, wide spread through the lungs does not preclude the development of severe right ventricular hypertrophy (over 100 g) as assessed here. It is striking that most of the patients with this condition had no ventricle hypertrophy and if the later was present, it was usually mild or moderate. A right ventricle over 100 g in weight was always associated with a packed all volume- of 55 % or more. Right ventricle upto 80 g were not associated with a packet all volume over 48%.

H.B.D.

Tuberculosis in 84 B.C.G. vaccinated young adults.

Birath, Groth, Peterson. Chest 65: 2 Feb. 74.

The pattern of pulmonary tuberculosis in B.C.G. vaccinated patients is indistinguishable from ordinary post primary tuberculosis in the un-vaccinated. B.C.G. vaccination has not changed the pattern of clinical disease.

It is of practical significance that case finding through skin testing for tuberculin conversion or marked increase in reaction site has been impossible in our vaccinated population.

H.B.D.

Aspiration Pneumonia

Richard A, Arms, David E. Denis and Thomas C. Tinstman. Chest, 65: 2 Feb. 74.

Factors responsible for aspiration pneumonia were studied in 88 cases. These were debilitation, impaired consciousness (including general anaesthesia), oesophageal and neurologic disorders, cardiac resuscitation and the presence of a nasogastric tube or tracheostomy.

For its management, administration of oxygen, endotracheal intubation and assisted ventilation, tracheostomy, administration of steroids, antibiotics, digoxin, diuretics and broncho dilators are indicated.

The mortality is about 35 per cent in patients not having operation and 28 persons in patients having operation.

H.B.D.