

# The Indian Journal of Tuberculosis

---

---

Vol. XXXIII

New Delhi, January 1986

No.

---

---

## ERADICATION OF TUBERCULOSIS

John Bunyan in his world famous classic Pilgrims Progress had described Tuberculosis as the captain of the men of death. And that it verily was, all over the world, till recently. While this sobriquet still holds good in developing countries, the disease has been brought under control in almost all the developed countries. Indeed, the latter are already thinking in terms of eradication of tuberculosis. Is eradication possible under existing conditions and if not, why not?

It is usually said that if small pox has been eradicated from the entire world, why not tuberculosis (another infectious disease like small pox) too? Analogy of small pox, however, does not apply to tuberculosis. Firstly, immunisation against small pox is 100% effective. Role of BCG, on the other hand, is still controversial. In any case, its effectivity is much less than 100%. Secondly, small pox cases are never silent whereas Tuberculosis presents an iceberg phenomenon and many of the cases, even though infectious, remain undetected. And last, but not the least, once a patient of small pox gets well, he does not relapse and poses no hazard to the community thereafter. Not so in tuberculosis. Whether it is spontaneous healing of a subclinical primary lesion or arrest of clinical disease as a result of effective chemotherapy, all bacilli are often not fully eradicated. Some persist as dormant bacilli in the tissues in many cases and can reactivate later under unfavourable host conditions and cause disease again, even in the absence of fresh exogenous, reinfection.

Story of tuberculosis decline is rather fascinating. The disease started declining in the western world even before the bacillus was discovered and preventive measures could not even be contemplated, leave aside implemented. With the discovery of the bacillus and implementation of preventive measures, the decline, naturally, was hastened and the then high priests of epidemiology were rash enough to predict that it was but a matter of time before tuberculosis would be eradicated. That Utopia is still elusive, inspite of availability even of potent chemotherapy.

The curve of tuberculosis decline is exponential and it is well-known that an exponential curve can never touch zero side of infinity. Apart from mathematical consideration, there is a biological aspect also concerning the dormant bacillus. It is yet not known how and why a few bacilli become dormant when others are annihilated either by immunobiological defence mechanism of the host and/or drugs. And then, what triggers off their reactivation later, to initiate another episode of disease is equally unknown.

The position thus is that every community has, in its midst, a number

of persons, small or large, depending upon whether the community is a low prevalence or high prevalence one, who harbour dormant bacilli which are capable of causing disease by endogenous reactivation. This has been corroborated by a number of small epidemics in recent years in the countries where tuberculosis, on the whole, has been brought under control. Fortunately, these epidemics remain localised and are quickly brought under control because of the available diagnostic and treatment facilities. Therefore, it would not be wrong to say that as long as there is but one person in the whole world with dormant bacilli, he can initiate, theoretically, another epidemic and thus defeat total eradication of the disease. Even if fresh infections cease altogether, it will take a long time for elimination of those already infected (i.e. potential sources of fresh disease) by other causes of death. The stage of complete cessation of fresh infections has yet not been achieved anywhere in the world.

If we can develop the competence to prevent bacilli becoming dormant or prevent altogether their reactivation, it may be possible to solve the problem. Another alternative is that a new drug becomes available which, unlike all drugs available today, can completely annihilate dormant bacilli. Or, perhaps, some feat of genetic engineering may, in times to come, so change the bacillus that its eradication may become possible.

In the present state of our knowledge, eradication does not seem to be possible in the near future. All that we can do is to find all sources of infection as easily, completely and expeditiously as possible and to render them safe by effective chemotherapy. This will bring about consistent and significant reduction in the problem of tuberculosis. One can also hope that one day a solution to the problem of dormant bacillus will be found and this hope will sustain the endeavours towards the ultimate solution.

### **NOTICE**

The Tuberculosis Association of India is proposing to subsidise a few research projects on Tuberculosis. Preference will be given to studies which concern operational problems, are of short duration (say, not more than two years duration) and of relevance to the National Tuberculosis Programme. Applications for grants under this scheme may be sent on prescribed proforma obtainable from:

The Honorary Technical Adviser,  
**Tuberculosis Association of India,**  
3, Red Cross Road,  
New Delhi-110001.

## PERSPECTIVES AND PROSPECTS IN TUBERCULOSIS CONTROL\*

C.W.L. JEANES\*\*

### King Edward VII

*"Tuberculosis is a preventable disease. Why is it not prevented?"*

### Dr. Annik Rouillon

*"In the field of tuberculosis, the situation is a contradiction and a subject of concern".*

Tuberculosis today presents us with a paradox and a dilemma. In developed countries the disease is regressing at a rate of 10-15% per year, so that by the year 2000 it will reach the arbitrary limit set for eradication, i.e. less than 1 sputum, positive case per 1 million population. In contrast, in most developing countries the situation has not changed in 20 years. The rates of incidence and prevalence have remained the same, and therefore because the population of these countries has increased, the *absolute* number of cases of tuberculosis in the world is higher than ever.

Yet, we have the tools for diagnosis and for very effective treatment, and in India you have led the world in demonstrating how these should be used. With modern chemotherapy regimens nearly 100% sputum conversion can be achieved, and the cure of tuberculosis is no longer an impossible dream.

Yet reports have been presented, at this meeting indicating the many problems in the tuberculosis situation in India, viz.

- (a) Only between 10% and 25% of active tuberculosis cases are diagnosed and treated in a year.
- (b) This leaves a very considerable infect or pool in the community.
- (c) Of those who are diagnosed and treated, there is a high defaulter rate.
- (d) Incomplete or inadequate chemotherapy has led to the development of resistant strains of bacilli, which are a great hazard to the community.
- (e) The lack of resources, human, physical and financial, to deal adequately with this situation.

To examine this, one must consider three major factors:—

1. Governments.
2. Health professions.
3. The people and the community.

Firstly, governments have the overall responsibility to mobilise the budget for health services but governments have to be swayed by political will that health is a priority and should receive a fair share of the national budget. Most governments in the world accepted the principles for health development set out in the Declaration of Alma Ata, with the objective of achieving Health for All by the year 2000.

To achieve this, comprehensive health services have to be organised and aimed at *all* the people, and not just the 20% who live in urban areas. At the basic level, primary health care must include appropriately trained workers from the basic medical auxiliary/health assistant upto fully trained nurses with public health or other qualifications and doctors.

Tuberculosis services have historically been developed in many countries as a separate programme, but there now seems to be a good indication that tuberculosis services, especially at the local level, should be integrated into general health services. This, by utilising a much greater body of health workers, would increase case-finding through a much wider sputum, testing coverage and would also provide a better network for supervision of home chemotherapy.

Whether tuberculosis services should remain as a separate specialised programme, or be integrated into the general health programme

of the country is a decision which has to be taken politically, but this decision can be accelerated and its correctness assured, by appropriate pressure from the health professions and from the community.

At the international political level, the World Health Organisation provides great support for national tuberculosis policy and programmes through the work of the expert committees, whose documents and technical reports provide clear guidelines for national activities.

The resolution proposed by India at the 1983 World Health Assembly and which was adopted by the Assembly, has strengthened WHO's hand in its tuberculosis activities.

Secondly, the health professions have a great responsibility to set their priorities. Doctors are, in general, trained to do their utmost for their individual patients, striving for 100% success. However, in countries with limited resources, this cannot be justified. Priorities must be set to cover the needs of all people, especially the 80% who live in rural areas.

Doctors and trained nurses have to accept their responsibilities for team leadership providing direction and supervision to auxiliary health workers, so that health care can be provided with quality over a much wider segment of the population.

The health professions have to face up to the situation where in many developing countries of the world, as few as 25% of the sputum positive cases in a country are diagnosed and treated in a year. This leaves the tragedy of the undiagnosed cases to provide a great infective pool within the community. However, it must be very strongly stressed that the health professions have a strong responsibility to organise programmes against tuberculosis which encompass as nearly 100% of the population as

possible, and to ensure that all sputum positive cases receive an adequate course of chemotherapy and are not permitted to default. An inadequate programme of treatment and supervision provides the great risk of producing chronic sputum positive cases, often with resistant strains and these cases are actually much more dangerous to the community than if they had never been treated.

Thirdly, the people and the community must have an understanding and appreciation of their needs in health and they must have the knowledge and will to press for comprehensive health services.

In India, the Tuberculosis Association of India and the State Associations have fulfilled this function extremely well, influencing the community and governments and mobilising resources, not only financial, but also promoting community action and exerting pressures on public and political decisions regarding health. The Association has led in this field, but has much more work and challenge ahead.

Considering the magnitude of India's tuberculosis problem, the very large number of undiagnosed cases, the high defaulter rate in those who start treatment, the large infective pool in the community, and the scarcity of resources to deal with this situation, the three partners in this battle against tuberculosis, governments, the health professions, and the voluntary associations representing the community have a very great task ahead of them.

We have a more than adequate knowledge of the disease, the methods of diagnosis, especially, sputum examination have been simplified, and the drugs for treatment can give almost 100% certainty of cure if given adequately.

The challenge is to use all these tools so that the battle will eventually be won!

## SPECTRUM OF CHEST ROENTGENOGRAPHIC OBSERVATIONS IN CHRONIC AIRFLOW OBSTRUCTION

D.D.S. KULPATI\*, S. NAYAR\*\*, AND O.P. BHARDWAJ\*\*\*

Summary: A prospective study of 30 patients with chronic airflow obstruction (CAO) and 20 healthy controls was carried out for observing different pulmonary radiological changes according to severity of CAO. The analysis of radiological findings revealed that the range of diaphragmatic excursion was 2.8 to 6.8 cm (mean 3.6 cm) in normal healthy adults while a value of less than 2 cm always indicated the presence of airflow obstruction. Airflow obstruction was always present (specificity 100%) when the right dome of the diaphragm was at the level of the anterior end of the 7th rib, but the sensitivity of this index was low (36.6%). An increase in radiolucency with evidence of air trapping was consistently evident in severe CAO, but no significant relation was observed with severity of CAO. Diaphragmatic index of less than 1.5cm, retro-sternal space of more than 2.5cm and sternoidphragmatic angle of more than 90° were valuable radiological indices for the presence and severity of chronic airflow obstruction. The prominence of pulmonary artery segment and cardiothoracic ratio did not show any definite pattern in the present study. On bronchography, patients with increasing severity of CAO showed abrupt termination of bronchi with incomplete filling of tertiary and fine bronchi, leafless-tree appearance, patchy alveolarisation, mucus gland dilatation, crowding of bronchi in non-emphysematous areas, displacement and splaying of bronchi in the emphysematous areas.

### Introduction

Clinicians, physiologists and radiologists have developed several approaches to the antemortem diagnosis of chronic bronchitis and emphysema and, by implication, air flow obstruction. However, there is no unanimity on the frequency and variety of roentgenographic abnormalities associated with the severity of the chronic airflow obstruction (CAO). Roentgenographic findings (Knot and Christie, 1951; Simon, 1964) and pulmonary function impairment in CAO (Sukumal Chandra and Williams, 1965; Burrows and Earle, 1969) are well described but isolated reports are available regarding radiological observations in relation to magnitude of chronic airflow obstruction (Reid and Millard, 1964). The present study was undertaken to analyse the roentgenographic observations in chronic obstructive pulmonary disease according to the severity of CAO.

### Material and Methods

The present study was conducted on 30 patients of chronic obstructive pulmonary disease (COPD) and 20 normal healthy, age and sex matched adults. The work-up of the patients on a preplanned protocol included a detailed history, thorough physical examination, routine haematological investigations and urinalysis. The criteria for the inclusion of

the patients in the study were: history and physical findings suggestive of chronic bronchitis and emphysema (Kulpati, 1977) and impaired pulmonary function tests i.e. forced expiratory volume in one second (FEV<sub>1</sub>) less than 80 percent of FVC (forced vital capacity) and an improvement in FEV<sub>1</sub> of less than 10 percent, after 800 meg (2 puffs) of isoproterenol by inhalation. Severity of CAO was graded as the ratio of FEV<sub>1</sub> to FVC (FEV<sub>1</sub>/FVC%): Grade I—Healthy controls, no airflow obstruction. Grade II—Mild CAO, 61 to 80%, Grade III—Moderate CAO, 41 to 60%, Grade IV—Severe CAO 40%. The radiological examination included PA view of the chest in deep inspiration and expiration, right lateral view, fluoroscopic examination and bronchography. For each patient, the following observations were made: (i) Diaphragmatic excursion during breathing, (ii) The level of the right dome of the diaphragm in midclavicular line in relation to the anterior ends of the ribs, as the position of the left dome depends upon the presence of air in the fundus of the stomach and splenic flexure of the colon, (iii) The curvature of the diaphragm, as measured by the greatest vertical distance between the diaphragmatic dome and a line joining the costophrenic and cardiophrenic angles and was termed diaphragmatic index, (iv) The transverse diameter of the heart and the cardiothoracic ratio was calculated by dividing the diameter of the heart with the diameter of the chest, (v) Pulmonary artery

---

Department of Medicine and Department of Radiology, Maulana Azad Medical College and associated L.N.J. P.M. and G.B. Pant Hospitals, New Delhi.

\*Professor and Head, Respiratory Unit, Department of Medicine. \*\*Ex-resident. \*\*\*Ex-professor and Head, Department of Radiology.

segment was enlarged if the maximum curvature projected more than 0.5 cm from a line joining the points where the shadow of pulmonary segment met the aorta above and the left heart below, (vi) Each of the right and left main pulmonary artery trunks were measured in PA view of the chest. The maximum diameter of the main trunk before its bifurcation was also measured, (vii) A subjective assessment of radiolucency was made in the PA view of the chest. Any evidence of irregular or localised increase in radiolucency was noted. Any area of airtrapping in expiratory flow was also recorded, (viii) on the lateral view of the chest, contour of the diaphragm, sternodiaphragmatic angle and retrosternal space was measured. This space was measured 3 cm below the sternomanubrial junction as the horizontal distance from the posterior aspect of the sternum to the anterior end of the aorta. Bronchography was performed on one side only as chronic obstructive pulmonary disease is a diffuse process. The bronchogram was analysed for any evidence of peripheral pooling lumen of bronchi, mucus gland dilatation, patchy alveolisation, leafless tree appearance, abrupt termination of bronchi, any displacement, crowding or splaying of bronchi.

## Results

According to pulmonary function studies 10 patients each belonged to grade II, III and IV severity of CAO. Twenty healthy subjects, had no CAO and belonged to grade I. The range of diaphragmatic excursion in normal subjects was 2.8 to 6.8 cm (mean 3.6 cm). However, it was less than 3 cm in 15%, 50% and 90% of grades I, II and III subjects and in all the patients in grade IV (Table 1). It can be inferred from these observations that the range of excursion became progressively less with the

increase in the severity of airflow obstruction. In our study, excursion of 2 cm or less was always indicative of CAO. The level of the right dome of the diaphragm was above the level of anterior end of the seventh rib in all the healthy subjects (Table 2). The level increased with increase in severity of CAO in grades II, III and IV respectively. However, in 11 (36.6%) out of 30 patients of CAO, the diaphragmatic position was above the level of 7th rib and thus the sensitivity of this test was also low.

The value of diaphragmatic index decreased as the severity of CAO increased. It was more than 1.5 cm in grade I subjects and was either 1.5 cm or less in 93.3% of CAO patients (Table 3). In grade IV, it was 1 cm or less than it in 90 percent of patients. The subjective finding of irregular radiolucency of lung fields, localised to one or more zones increased in frequency with increasing severity of CAO but no definite correlation with severity of CAO was observed. The transverse diameter of the heart decreased in patients with CAO, but did not show any definite pattern. Cardiothoracic ratio decreased with increasing severity of CAO but did not show significant correlation with severity of disease.

The pulmonary artery was not properly visualised in 4 cases on the right side, and 10 cases on the left side. The size of the pulmonary artery was less than 1.4 cm in Group I and more than 1.4 cm in 1, 2 and 5 patients in Grade II, III and IV of CAO respectively.

The sternodiaphragmatic angle was less than 90° in all subjects of grade I but was more than 90° in 10%, 60% and 100% patients of grade II, III and IV respectively. The retrosternal space of more than 2.5 cm was observed

TABLE 1 Showing the Movement of the Domes of the Diaphragm

Grade	Diaphragmatic excursion in centimetres						
	0-1.0	1.1-2.0	2.1-3.0	3.1-4.0	4.1-5.0	5.1-6.0	6.1-7.0
I	—	—	3	8	3	2	4
II	—	1	4	1	1	1	1
III	2	3	4	1	—	—	—
IV	5	5					

TABLE 2

*Showing the position of the diaphragm*

Grade	Diaphragmatic level in relation to the anterior end of rib					
	5½	6	6½	7	7½	8
I	2	12	6	—	—	—
II	—	4	2	4	—	—
III	—	2	3	4	1	—
IV	—	—	—	—	—	4

TABLE 3

*The Diaphragmatic Index (cm) and Retrosternal space measurements in Healthy Adults and Patients with CAO*

Grade	0-0.5	0.6-1.0	1.1-1.5	1.6-2.0	2.1-2.5	2.6-3.0	3.1-3.5	3.6-4.0	4.1-4.5
Diaphragmatic index									
I	—	—	—	10	6	4	—	—	—
II	1	2	6	1	—	—	—	—	—
III	2	5	2	1	—	—	—	—	—
IV	3	6	1	—	—	—	—	—	—
Retrosternal space									
I	—	2	1	14	3	—	—	—	—
II	—	—	—	3	2	—	—	—	—
III	—	—	—	3	2	3	1	—	—
IV	—	—	—	—	—	2	2	4	2

in 15% in grade I and in 50%, 40% and 100% in grade TF, III and IV in that order (Table 3).

The various bronchographic abnormalities in COPD patients are shown in table 4. Incomplete peripheral filling, abrupt termination of bronchioles occurred together more often and gave an appearance of leafless tree pattern. Peripheral pools appeared as collections of contrast material, 2 to 6mm in diameter.

Mucus gland dilatations were observed as small extensions of contrast medium along the lumen of the main bronchus, usually on the inferior surface.

#### Discussion

The normal range of diaphragmatic excursion was 3 to 10 cm (Simon, 1964) and 2.5 to 4.5 cm (Milne and Bass, 1969) in other studies

TABLE 4 Showing

*bronchography- findings*

Bronchographic abnormality	II	III	IV
Incomplete peripheral filling	6	6	10
Contracted bronchi	1	4	6
Leafless tree appearance -		6	10
Abrupt termination of bronchi		8	10
Beaded bronchi		6	7
Patchy alveolisation		7	8
Peripheral pooling	1	5	9
Mucous gland dilatation		9	7
Increased secretions	3	4	6
Crowding of bronchi	—	3	5
Displacement of bronchi		2	8
Dilatation of bronchi	—	—	2

which compared well with the range of 2.8 to 6.8 cm observed in our study. In COPD patients, the movement was less than 3 cm (Simon, 1964) and 0.3 to 2.0 cm (Milne and Bass, 1969) in other studies. However, in the present study, the restriction was below 3 cm in all the patients in grade IV only, while it was variable in less severe grades of AFO (Table 1). The diaphragm may be considered low if, in the mid-clavicular line, the right dome lies below the anterior end of the 6th rib.

Lennon and Simon (1965) found that in 5% of normal subjects the right hemidiaphragmatic dome may be at the level of the seventh rib. However, in none of our healthy subjects with normal airway function, the level of the right diaphragmatic dome was at this level. Because earlier workers did not obtain pulmonary function indices, it is probable that some of their controls had some airflow obstruction.

A low position of the diaphragm alone is not significant, as long as the diaphragm maintains its superior curve (Simon et al., 1973). In our study the frequency of low level increased with increasing severity of CAO (Simon, 1973).

The flatness of the diaphragm can be detected by eye, but diaphragmatic index provides a

more accurate measurement of the curvature of the diaphragm. Gamsu and Nadal (1973) have shown that diaphragmatic index was less than 1.5 c.m. in emphysema. In one of the grade I subjects the diaphragmatic index was less than 1.5 c.m. and was less than this value in 90%, 70% and 100% patients of grade I, IFF and IV CAO respectively. It appears to be a fairly accurate sign for early detection of CAO as this was the only sign present in 90 percent of grade I and in all patients with grade IV CAO.

The size of retrosternal space had a significant correlation with the degree of airflow obstruction. In one study, it was useful as an absolute indicator of airway obstruction only when larger than 4.4. cm (Burki and Krumpel man, 1980) ; a smaller retrosternal space may or may not be associated with obstruction. In our study, retrosternal space larger than 2.5 cm was indicative of CAO but smaller size than this did not exclude CAO either. Our results do support the observation that a retrosternal space of >2.5. cm is indicative of airflow obstruction (Nicklaus et al, 1966). But less than this value was observed in 33.3 percent of grade II and III CAO and thus the sensitivity of the test was low. Sternodiaphragmatic angle of more than 90° was regarded as a reliable radiologies!

sign for the diagnosis of CAO (Gamsu and Nadal, 1973; Nicklaus et al., 1966). In our study none of the control subjects without airflow obstruction had this angle more than 90° and this was an absolute indicator of CAO. The transverse diameter of the heart of less than 11.5 cm and hyperlucency had a significant but low correlation with the severity of CAO in our study although Burki and Krumpelmann (1980) observed that the transverse diameter of the heart is strongly indicative of airway obstruction with excellent specificity.

The abrupt termination of bronchioles in squared, rounded or tapered extremities was described by Simon and Galbraith (1953). This appearance was noted in 80% of the cases in Grade II and 100% of the cases in Grade IV group. Reed (1955) was of the opinion that these represented blind ends of bronchioles surrounded by collapsed lung. The appearance of incomplete peripheral filling and abrupt termination of bronchioles gave rise to leafless tree appearance (Freimanis and Molnar, 1960). This appearance was observed in 60% and 100% of the cases in Grades II and IV respectively.

Peripheral pools in emphysema have been reported by Reid (1955); Simon and Galbraith (1953) and Duinker and Huizinga (1962). Duinker and Huizinga (1962) were of the opinion that number of peripheral pools in a bronchogram was related to the severity of disease.

Patchy alveolarisation occurred in association with peripheral pools. This was observed in 7 cases in Grade II and 8 cases in Grade IV. This appearance of irregular filling is due to different rates of air flow or obstruction in the smaller branches of bronchial tree (Simon, 1959; Freimanis and Molnar, 1960) and is suggested of evidence of emphysema (Duinker and Huizinga, 1962).

Bronchi were contracted in 20%, 30% and 60% of cases in Grades II, III and IV respectively. Crowding of the bronchi was noted in non-emphysematous areas. Displacement of bronchi was observed around the emphysematous areas.

Bronchography has its own limitation? and prevalence of airway obstruction in any given population (Burki and Krumpelmann, 1980) may modify the predictive value of roentgenographic indices yet the present study shows that the roentgenographic level of the right hemidiaphragm when at or below the level of the anterior end of the seventh rib, indicates airway obstruction. Diaphragmatic index of less than 1.5 c.m., retrosternal space or more than 2.5 cm and sternodiaphragmatic angle

of more than 90° were important radiological indices. Though the sensitivities of these indices were low, they are very valuable as simple parameters for the detection of chronic airflow obstruction.

### Acknowledgement

We are thankful to Dr. K.B. Sharma, Dean, Maulana Azad Medical College, New Delhi for permission to publish these data.

### REFERENCES

- Burki, N.K. and Krumpelmann, J.L.: Correlation of pulmonary function with the chest roentgenogram in chronic airway obstruction. *Am. Rev. Respir. Dis.*; 1980; 121 : 217-223.
- Burrows, B. and Earle, R.H.: Course and prognosis of chronic obstructive lung disease—A prospective study of 203 patients- *N. Eng. J. Med.* 1969; 280: 397-402.
- Djinker, N.W. and Huizinga, E.: The "Flowers" in bronchography. *Thorax.* 1967; 17: 175-178.
- Freimanis, A.K., and Molnar, W.: Chronic bronchitis and emphysema at bronchography. *Radiology* ; 1960; 74 : 194-205.
- Garmy, G. and Nidel, J.A.: The roentgenologic manifestation of emphysema and chronic bronchitis. *Med. Clin. N. America*; 1970, 3 : 719-35.
- Knott, J.M.S. and Christie, R.V.: Radiological diagnosis of emphysema. *Lancet*; 1951, 1 : 881-83.
- Kulpati, D.D.: Prevalence of alpha-1-antitrypsin deficiency in COPD and some other respiratory illnesses. *Jr. Asso. Phys. Ind.*; 1977, 7: 443-49.
- Milne, E.N.C. and Bass, H.: The roentgenologic diagnosis of early chronic obstructive pulmonary disease. *J. Canad. Ass. Radiol.*; 1969, 20: 3-15.
- Nicklaus, T.M., Stowell, D.W., Christiansen, W.R., Renzetti, A.D. Jr.: The accuracy of roentgenographic diagnosis of chronic pulmonary emphysema. *Am. Rev. Respir. Dis.*; 1966, 93: 889-99.
- Reed, L., Millard, F.J.: Correlation between radiological diagnosis and structural lung changes in emphysema. *Clin. Radiol.*; 1964, 15: 307-11.
- Reid, L.M.: Correlation of certain bronchographic abnormalities seen in chronic bronchitis with the pathological changes. *Thorax.*; 1955, 10: 199-204.
- Simon, G., Galbraith, H.J.B.: Radiology of chronic bronchitis.; 1953; 2: 850-52.

- Simon, G.: Chronic bronchitis and emphysema—A symposium. *Brit. J. Radiol.*; 1959, 32: 292-94.
- Simon, G.: Radiology and emphysema. *Clin. Radiol.*; 1964 **15**: 293-306
- Simon, G., Pride, N.B., Jones, N.L., Raimondi, A.C.: Relationship between abnormalities in the chest radiograph and changes in pulmonary function in chronic bronchitis in emphysema. *Thorax*; 1973, 28: 15-23.
- Sukumal Chandra, Y. and Williams, M.H.: Serial studies of pulmonary function in patients with chronic obstructive pulmonary disease. *Am. J. Med.*; 1965, **39**: 941-48.
-

## CLUBBING IN PULMONARY TUBERCULOSIS

B.K. KHANNA AND K.S. KHARE

**Summary :** A study of left index finger cast of 30 normal, non-smoking, right-handed subjects revealed 185° as the upper limit of hyponychial angle. 78 non-smoking, hospitalised patients of pulmonary tuberculosis, who did not have any other pathology to account for clubbing, were studied likewise and revealed clubbing in 64 (82%) cases. The percentage and degree of clubbing did not show any correlation with age and sex of the patient, duration of illness, extent of involvement of lungs and number and size of cavities.

Pulmonary tuberculosis is considered to be an important cause of clubbing. The prevalence, as reported by various workers, has varied from less than 1% (Wierman et al 1954) to 90% (Neiffeld and Wallband 1952). The clinical criteria, adopted for clubbing, have been extremely variable (Pyke 1954). Moreover, most of the studies on clubbing in pulmonary tuberculosis have been based on clinical observations. To eliminate the subjective factor, Mellins and Fishman (1966) recommended the use of alginate impression material for production of accurate casts of digits. This method, besides its accuracy and the advantage of providing an objective reference material, also offers unique advantage of follow up and, therefore, has been used by many workers, viz. Regan et al (1967), Sly et al (1973) and Bentley et al (1976).

The present study was conducted on patients suffering from pulmonary tuberculosis to study the prevalence of clubbing and its correlation with various parameters relating to tuberculosis.

### Materials & Methods

1. *Normal Subjects:* 30 normal right-handed subjects, including doctors, nurses and laboratory technicians of both sexes, who were non-smokers and who did not suffer from any disease likely to have caused clubbing (respiratory, cardiac, hepatic, renal and miscellaneous diseases), were studied to measure the normal hyponychial angle.

2. *Pulmonary Tuberculosis Group:* 78 proved and randomly selected (by random number) cases of pulmonary tuberculosis, who were non-smokers, right handed and who had no pulmonary, cardiac, hepatic, renal or other causes to account for clubbing, were investigated to find out the prevalence of clubbing in pulmonary tuberculosis. There were 6 cases belonging to the age group of 10 to 19 years; 2

29, 30 to 39 years age group; 9 belonged to 40 to 49 years age group and 13 patients were more than 50 years of age; 51 patients were male and the remaining 27 female. An effort was made to correlate the percentage and degree of clubbing with age and sex of the patients, duration of illness, nature and extent of lesion including cavitation.

Cast of left index finger of each case was prepared by the method recommended by Mellins and Fishman (1966). The index finger was chosen on the basis of study conducted by Regan et al (1967). Furthermore, since all of our cases were right handed, the choice went to left index finger which is less likely to chaff or have broken nail.

Hyponychial angle was measured in all the cases by shadow-graph, Bentley et al (1976) (Fig. 1).

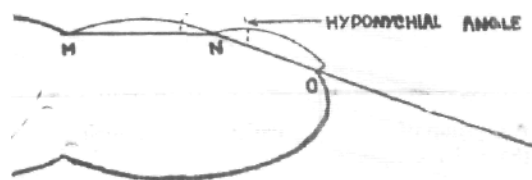


Fig. 1

Construction of hyponychial angle

M=Distal digital crease. N=Datum point (Cuticle).

O=Hyponychium (Thickened stratum corneum of epidermis lying under free edge of nail).

MNO=Hyponychial angle.

### Results

*Hyponychial Angle in Normal Persons :* The mean value in 30 normal persons was found to be  $176.83 \pm 3.71$ . A precise upper limit of normal was set at a value equal to the normal mean plus 2 standard deviations ( $176.83 + 2(3.71) = 184.25^\circ$  or  $185^\circ$ ) at 95% confidence limit.

*-Grading of Clubbing :* The clubbing was considered to be grade I if the hyponychial angle was 186° to 190°, grade II if between 191° to 195°, grade III if between 196° to 200° and grade IV if the angle exceeds 201° (Fig. 2).

**Clubbing in Pulmonary Tuberculosis**

*Overall prevalence of clubbing :* 64 cases (82%) out of a total of 68 had clubbing, put of these, 13 cases (20%) had grade I clubbing; 18 cases (28%) grade II, 12 cases (19%) grade III and 21 cases (33%) grade IV. (Table 1).

No significant association could be established between age and occurrence of clubbing.

Out of 78 patients, 51 (65.38%) were male and 27 (34.62%) were female. There was no significant difference in clubbing found in males and females as out of 51 males 42 (82.35%) had clubbing and out of 27 females 22(81.48%) had clubbing. (Table 2).

The occurrence of clubbing was significantly more in patients with more than 6 months duration of illness (Table 3).

Table 4 shows the proportion of patients with clubbing according to extent of pulmonary disease. It was found that patients with more extensive disease were likely to have clubbing more often than those with less extensive disease ( $X^2=6.8$  for 1 d.f.  $P<0.01$ ). The same table

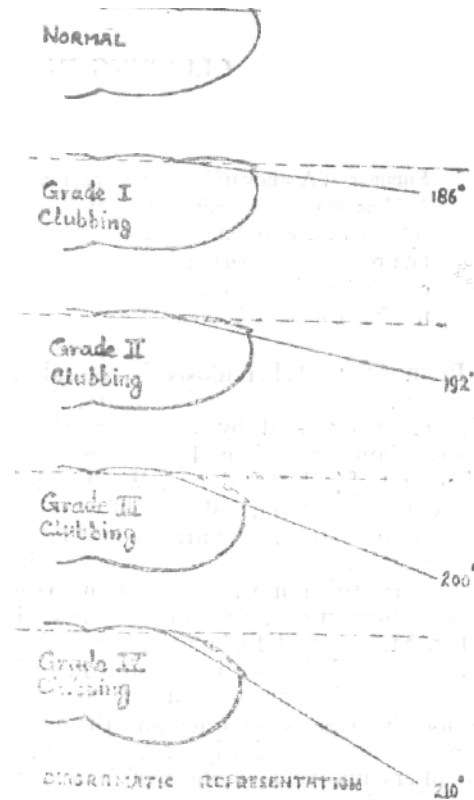


Fig. 2

**Diagrammatic Representation of Progression of Clubbing**

TABLE 1

*Clubbing in Relation to the Age of the Patients*

Age group of the patients	Patients with clubbing			Patients without clubbing		Total	
	No.	%		No.	%	No.	%
10—19 Years	6	100.00	} 85.1	0	0.0	6	7.69
20—29 Years	17	80.95		4	19.05	21	26.92
30-39 Years	23	79.31	} 1.3	6	2.69	29	37.18
40—49- Years	9	100.00		0	0	9	
50 Years and above	9	69.23					
<b>Total</b>	<b>64</b>	<b>82.05</b>		<b>14</b>	<b>17.95</b>	<b>78</b>	<b>100.67</b>

$X^2=0.3$ ; d.f. = 1;  $P>0.10$

TABLE 2

*Clubbing in Relation to the Sex of the Patients*

Sex of patients	Patients with clubbing		Patients without clubbing		Total	
	No.	%	No.	%	No.	%
Male	42	82.35	9	17.65	51	100.00
Female	22	81.48	18.52	27	100.00	
Total	64	82.05	14	17.95	78	100.00

 $\chi^2=0.01$ ; d.f.=1;  $P>0.10$ 

TABLE 3

*Relationship of Clubbing With the duration of illness*

Duration of illness	Patients with clubbing		Patients without clubbing		Total	
	No.	%	No.	%	No.	%
Upto 6 months	13	65.0	7	35.0	20	100.00
More than 6 months	51	87.0	12.1		58	100.00
Total	64	82.0	14	18.0	78	100.0

 $\chi^2= 5.2$ , d.f.=1;  $P>0.05$ 

also shows the distribution of patients according to gradation of clubbing. Numbers in various cells are too small for a proper test of significance but there appears to be no suggestion that gradation of clubbing is related to extent of pulmonary tuberculosis.

The relation between cavitory status and clubbing is shown in Table 5. In all 3 i.e. 50.0% of the 6 acavitory cases had clubbing as against 61 i.e. 84.7% of the 72 cavitory cases)

There is a suggestion that clubbing was encountered more frequently in cavitory cases but due to small numbers a proper statistical test of significance is not possible (Table 6).

Nor is there any indication from the table that more extensive cavitation is associated with clubbing.

The material was also analysed in respect of the size of cavities but it did not have any significant correlation with clubbing.

Another interesting observation was that during 12 weeks of hospitalization of the patients, 5 out of 64 patients with clubbing died as against 2 out of 14 without clubbing, though the difference was not statistically significant. It may, however, be pointed out that the period of observation was very short.

TABLE 4

*Clubbing In relation to Extent of Disease*

No. of zones involved	Patients with Clubbing				Total No.    %		Patients without clubbing		Total	
	Grade I	Grade II	Grade III	Grade IV			No.	%	No.	%
Upto 2 zones	2	1	—	3	6	66.7	3	33.3	9	
2-4 zones	7	12	7	9	35	79.6	9	20.4	44	
More than 4 zones	4	5	5	9	23	92.0	2	8.0	25	
Total	13	18	12	21	64	82.0	14	18.0	78	

TABLE 5

*Clubbing in relation to Cavitation*

	Patients with Clubbing	Patients without Clubbing	Total No.
Cavity Absent	3	3	6
Cavity Present	61	11	72
Total	64	14	78

TABLE 6

*Grade of Clubbing in relation to Extent of Cavitation*

	Patients with Clubbing					Total No.    %		Patients without Clubbing		Total	
	Grade I	Grade II	Grade III	Grade IV	No.			%	No.	%	
Single cavity		4	3	5	19	79.2	5	20.8	24	100.0	
2 or 3 cavities	3	8	7	7	25	86.2	4	13.8	29	100.0	
4 or more cavities	3	4	2	8	17	89.5	2	10.5	19	100.0	
Total	13	16	12	20	61	84.7	11	15.3	72	100.0	

## Discussion

Hyponychial angle, as a criterion of clubbing, was chosen by us because it has been found to be independent of age, sex, height and weight of the patient; its measurement is easy; it incorporates measurement of two different parameters e.g. profile angle and curvature of nails and has not been found to demonstrate any overlapping between those of normal persons and those with clubbed fingers (Regan et al 1967 and Bentley et al 1976). A nonml upper limit of  $185^\circ$  fixed by us is almost similar to that recorded by Regan et al (1967) and Bentley (1976) ( $180.1^{\pm 4.2}$ ).

In most of the studies relating to pulmonary tuberculosis, clubbing has been determined on the basis of clinical observation alone, in not more than 20—25% of the cases (Poppe 1947 and Mcfarlane et al 1979). Our observation, on the other hand, being objective and hence more accurate, has included early cases of clubbing, which, otherwise, would have been missed (on clinical examination). It may be significant to point out that in this series, grade IV clubbing, which is clinically apparent, was observed in 33% cases. On the other hand, Neufeld and Wallbank (1952), by objective measurement of curvature of the nails recorded clubbing in 90% cases out of 407 cases of pulmonary tuberculosis. Thus, it might appear that when objective criteria of clubbing are applied, it is observed in much higher percentage of cases than when the decisions are based on the clinical observations alone, which, no doubt, carry a high degree of subjective error and, of course, is not available for future reference.

We could not obtain significant association between clubbing and age and sex of the patient, duration of illness, nature and extent of lesion including frequency of cavitation and mortality from tuberculosis during the period of hospitalisation (12 weeks). Hyponychial angle has been found to be independent of age and sex of the person (Bentley et al 1976). The history of duration of illness is highly subjective, though clubbing in a case of acute lung abscess has been noted to develop within a span of 10 days (Degowin 1965). As far as pulmonary tuberculosis is concerned, a study based on 1000 cases in USA (Toman, 1979) had shown that "(a) sudden symptomatic onset is not less frequent in pulmonary tuberculosis than insidious onset is (b) The extent of the lesion does not bear a direct relation to the duration of disease (of all patients reaching the far advanced stage, the majority do so within the first half year) (c) cavitation is not a late occurrence; its frequency is nearly the same\* at all temporal stages of the disease".

The mechanism of development of clubbing is still unknown. It has been observed that digital clubbing rather than the full hypertrophic pulmonary osteoarthropathy, is commonly associated with hypoxaemic conditions. There is evidence which incriminates vagal afferent stimulus for hypertrophic pulmonary osteoarthropathy syndrome (Flavel 1956, Huckstep and Brodtkin 1958 and Levi et al 1982). However, the efferent limb remains obscure. The role of peripheral hypoxaemia, with or without arteriovenous shunting is also not clear (Levi et al 1982); so is the case regarding the role of prostaglandins in its causation (Leman et al 1978). Consequently, on the basis of this study, we are unable to offer any explanation for the development of clubbing in pulmonary tuberculosis.

## REFERENCES

- Bentley, D., Morre, A. and Shwachman, H: Finger clubbing: a quantitative survey by analysis of the shadowgraph; *Lancet*, 1976, 164.
- Degowin, E.L.: Bed-side diagnostic examination. The MacMillan Company, New York, 1965, p. 546.
- Flavel, G.: Reversal of pulmonary hypertrophic osteoarthropathy by vagotomy; *Lancet*, 1956, 1, 260.
- Huckstep, R.L. and Brodtkin, P.E. : Vagotomy in hypertrophic pulmonary osteoarthropathy associated with bronchial carcinoma; *Lancet*; 1958, 2, 243.
- Lavi, Y. Paladugin, R.R. & Benfield, J.R.: Hypertrophic pulmonary osteoarthropathy in experimental canine lung cancer. *Journal of Thoracic and Cardiovascular Surgery*, 1982, 84, 373.
- Lemin, R.J., Gates, A.X, Mathe, A.A., Warling, W.W., Hyman, A.L. & Kadowitz, P.D.: Relationship among digital clubbing; disease severity and serum prostaglandins  $F_{aa}$  and E concentration in cystic fibrosis patients. *American Review of Respiratory Diseases* 1978, 117, 639.
- Macfarlane, J.T., Ibrahim, M. & Tor-Agbidye, S.: The importance of finger clubbing in pulmonary tuberculosis; *Tubercle*, 1979, 60, 45.
- Mellins, R-B. & Fishman, A.P.: Digital casts for the study of clubbing of fingers. *Circulation*, 1966, 33, 143.
- Neufeld, O. & Wallbank, W.L.: Clubbed fingers, *Ohio Medical Journal*, 1952, 48, 834.
- Pyke, D.A.: Finger clubbing; validity as a physical sign, *Lancet*, 1954, 2, 352.
- Poppe, J.K.: The diagnostic significance of clubbed fingers, *Diseases of Chest*, 1947, 13, 658.

- Regan, G.M., Tagg, B. and Thomson, M.L.: Subjective assessment and objective measurement of finger clubbing, *Lancet*, 1967, 1, 530.
- S-y, R M, Ghazinshahi, S., Bumkul, B. Puapan, P., Gupta, S., Warren, R. and Waring, W.: Objective assessment of digital clubbing in Caucasian, Negro and Oriental subjects, *Chest*, 1973, 64, 687.
- Toman, K.: Tuberculosis case finding and chemotherapy: questions and answers. World Health Organisation, Geneva, 1979, p. 60, 61.
- Wcirman, W.H., Clagett, O.T., McDonald, J.R. : Articular manifestations in pulmonary diseases, *Journal of American Medical Association*, 1954, 1459-1463.

## SERUM AND PLEURAL FLUID CHANGES IN PATIENTS WITH EFFUSIONS

SHASHI SETH, HARBANS LAL, S.C. SETH AND A.S. SAINI

**Summary** : Patients with pleural effusion, suffering from either tuberculosis or malignancy, were investigated for blood and fluid glucose, bicarbonate, protein, calcium, alkaline phosphatase, AST and ALT levels. The levels of the serum constituents were not significantly different in the two groups except the mean serum alkaline phosphatase which was significantly higher in effusions with malignancy. Pleural fluid glucose and bicarbonate levels were significantly lower in patients with tubercular pleuritis. However, the levels of the other constituents were comparable in the two groups.

### Introduction

Pleural effusion is a common complication of many disease processes. Traditionally only the cell count, sugar and proteins, and sometimes lactic dehydrogenase levels of the pleural fluid are measured in an attempt to determine the etiology of the effusions. These measurements however, are of value primarily in the differentiation of transudates and exudates (Feldstein et al, 1963; Light et al, 1972; Light, 1977). Recently various workers have tried to determine the etiological factors in exudates by studying fluid glucose and pH levels (Funahashi et al, 1973; Potts et al, 1978; Good et al, 1980). The present investigation included the analysis of certain other constituents of the effusion and of serum, in order to find out their relationship in the two conditions and also to determine whether their estimation could be helpful in differential diagnosis.

### Material and Methods

Seventeen patients with effusion (14 males and 3 females) in the age group of 20-45 years, from the Department of Tuberculosis and Chest Diseases, Medical College Hospital, Rohtak, were studied. The patients were investigated routinely by hemogram, X-ray chest, urine examination and sputum for AFB. Out of the 17 patients studied, 11 (9 males and 2 females) were suffering from tuberculosis and the presence of tubercular pleuritis was confirmed by pleural fluid culture. The remaining 6 patients (5 males and 1 female) were suffering from malignancy (lung cancer). The diagnosis in each case was confirmed by lung biopsy.

Pleural fluid was tapped by thoracentesis, at random hours, during the day. At the time of thoracentesis blood samples were also drawn for the measurement of the various constituents. Pleural fluid and blood samples were collected anaerobically, under paraffin for the estimation of bicarbonate or with fluoride for the estimation

of glucose. For the estimation of total proteins, calcium, alkaline phosphatase (EC 3.1.3.1), aspartic aminotransferase (EC 2.6.1.1.) and alanine aminotransferase (EC 2.6.1.2), pleural fluid and blood samples were collected without any coagulant.

Pleural fluid and plasma bicarbonate levels were determined titrimetrically (Segal, 1955). Glucose contents of the blood and the pleural fluid were determined using O-toluidine method (Dubowski, 1962). All the samples of effusion fluid and serum were also analysed for (i) calcium by the method of Clark and Collip (1925); (ii) total proteins by biuret method (Gornall et al, 1949); (iii) alkaline phosphatase according to King and King (1954); and (iv) aspartic aminotransferase (AST) and alanine aminotransferase (ALT) using the method of

### Results

Blood glucose, plasma bicarbonate, serum total proteins, calcium, AST and ALT levels were comparable in the two group of patients with pleural effusions. However, mean serum alkaline phosphatase activity was significantly high in patients with malignancy ( $p < 0.05$ ; table 1). All the patients had fluid protein concentration more than 3.0 g/dl. Fluid glucose and bicarbonate concentrations were significantly lower in patients with tubercular pleuritis compared to those with malignancy ( $p < 0.05$ ). Like serum, the mean activity of alkaline phosphatase was high in effusion from patients with malignancy. However, the difference was not statistically significant ( $p > 0.05$ ). Fluid calcium, AST and ALT levels were comparable in the two groups (table 2).

### Discussion

Pleural effusions are classically divided into transudates and exudates. A transudate occurs when mechanical factors influencing the

TABLE 1

*Some blood constituents in patients with pleural effusions (values are mean  $\pm$  SE; number of subjects in parentheses)*

Parameters studied	Tuberculosis 01)	Malignancy (6)
Total proteins (g/dl)	6.30 $\pm$ 0.47	5.80 $\pm$ 0.16
Glucose (mg/dl)	94.3 $\pm$ 5.63	109.8 $\pm$ 4.62
Bicarbonate (meq/L)	25.9 $\pm$ 0.75	28.5 $\pm$ 0.62
Calcium (mg/dl)	9.50 $\pm$ 0.27	9.95 $\pm$ 0.42
Alkaline phosphatase (KAU)	7.50 $\pm$ 0.39	12.58 $\pm$ 1.78*
Alanine aminotransferase (IU)	8.86 $\pm$ 1.10	8.33 $\pm$ 1.09
Aspartic aminotransferase (IU)	7.33 $\pm$ 0.49	8.67 $\pm$ 1.65

\*Difference statistically significant when compared with the tuberculous group ( $p < 0.05$ ).

TABLE 2

*Some pleural fluid constituents in patients with effusions  
(values are mean  $\pm$  SE; number of subjects in parentheses)*

Parameters studied	Tuberculosis (11)	Malignancy (6)
Total proteins (g/dl)	4.27 $\pm$ 0.51	4.83 $\pm$ 0.37*
Glucose (mg/dl)	63.2 $\pm$ 7.43	101.8 $\pm$ 3.17
Bicarbonate (meq/L)	20.4 $\pm$ 1.87	28.3 $\pm$ 0.98*
Calcium (mg/dl)	8.43 $\pm$ 0.39	10.21 $\pm$ 0.60
Alanine aminotransferase (IU)	6.50 $\pm$ 0.93	6.80 $\pm$ 0.96
Aspartic aminotransferase (IU)	8.33 $\pm$ 0.63	9.00 $\pm$ 1.34

\*Difference statistically significant when compared with the tuberculous group ( $p < 0.05$ ).

formation or reabsorption of pleural fluid are altered. An exudate on the other hand results from inflammation as in tuberculosis or due to the involvement of the pleural space as in malignancy, pancreatic disease or pulmonary infarction. A pleural fluid protein level of 3.0 g/dl is frequently used to separate transudate from exudate (Light, 1977). In the present study all the patients investigated had fluid protein concentration more than 3.0 g/dl, suggesting that the patients had exudative pleural effusions.

Light et al (1973) reported that the mean pH of the tuberculous effusions was significantly lower than the mean pH of the malignant effusions and that when these two possibilities exist, a pH below 7.30 was suggestive of tuberculosis while a pH of more than 7.40 was suggestive of malignancy. For the same reason patients with tubercular pleurisies had low fluid bicarbonate levels. However, serum bicarbonate levels in the two groups were comparable (Light et al, 1973). The pH of the pleural fluid

is known to be influenced by (i) pH,  $PCO_2$  and  $HCO_3^-$  of the arterial blood from which the fluid presumably originates; (ii) the transfer of  $FT-CO_2$  and  $HCO_3^-$  between the pleural space and the surrounding tissue and blood; (iii) the metabolism and the local environment of the pleural fluid (Light et al, 1973); and (iv) the production of the lactate from the glucose by the mesothelial cell?, pleural tissues and the cellular elements (bacteria and leucocytes) of the pleural fluid (Taryle et al, 1979). Acidosis of low glucose pleural effusions has been demonstrated by various workers (Light et al, 1973; Potts et al, 1978; Good et al, 1980). As shown in table 2, fluid glucose and bicarbonate contents are significantly lower in patients with tubercular pleuritis. Since lactate is the major end product of glucose metabolism and contributes to pleural fluid acidosis, this in turn may be responsible for the low levels of glucose and bicarbonate in pleural fluid in patients with tuberculous effusions.

Serum and fluid protein, calcium, AST and ALT levels were not significantly different in the two group of patients (tables 1 and 2). Feldstein et al (1963) did not find any relationship between serum and fluid calcium, phosphorus and alkaline phosphatase levels in patients with pleural effusions. However, it was reported that alkaline phosphatase content of the effusion fluid was generally lower than that of the serum but increased as the fluid protein level rose (Feldstein et al, 1963). Even in the present study alkaline phosphatase content of the effusion fluid was lower as compared to their levels in serum, although the difference did not attain statistical significance.

#### REFERENCES

- Clark, E.P. and Collip, J.B.: A study of the Tisdall method for the determination of blood serum calcium with a suggested modification. *J. Biol. Chem.*, 1925, 63, 461.
- Croxtan, F.E., Cowden, D.J. and Klein, S.: *Applied General Statistics*. Prentice-Hall of India, New Delhi, 1971.
- Dubowski, K.M.: An O-toluidine method for body fluid glucose determination. *Clin. Chem.*, 1962, 8, 215.
- Feldstein, A.M., Samachson, J. and Spencer, H.: Levels of calcium, phosphorus, alkaline phosphatase and protein in effusion fluid and serum in man. *Am. J. Med.* 1963, 35, 530.
- Funahashi, A., Sarkar, T.K. and Kory, R.C.: Measurement of respiratory gases and pH of pleural fluid. *Am. Rev. Resp. Dis.* 1973, 108, 1266.
- Good, J.T., Jr. Taryle, D.A., Maulitz, R.M., Kaplan, R.L. and Sahn, S.A.: The diagnostic value of pleural fluid pH. *Chest*. 1980, 78, 55.
- Gornall, A.G., Bardawill, C.J. and David, M.M. : Determination of serum proteins by means of the biuret reaction. *J. Biol. Chem.* 1949, 177, 751.
- King, P.R.N. and King, E.J.: Estimation of plasma phosphatase by determination of hydrolysed phenol with aminoantipyrine. *J. Clin. Path.*, 1954, 7, 322.
- Light, R.W.: Pleural effusions. *Med. Clin. North. Am.* 1977, 61, 1339.
- Light, R.W., MacGregor, M.I., Luchsinger, P.C. and Ball, W.C. Jr.: Pleural effusions: The diagnostic separation of transudates and exudates. *Ann. Int. Med.* 1972, 77, 507.
- Light, R.W., MacGregor, M.F., Ball, W.C. Jr. and Luchsinger, P.C.: Diagnostic significance of pleural fluid pH and  $PCO_2$ . *Chest*, 1973, 64, 591.
- Potts, D.E., Willcox, M.A., Good, J.T. Jr., Taryle, D.A. and Sahn, S.A.: The acidosis of low glucose pleural effusions. *Am. Rev. Resp. Dis.*, 1978, 117, 665.
- Reitman, S. and Frankel, S.: A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminases. *Am. J. Clin. Path.* 1957, 28, 56.
- Segal, M.A.: A rapid electrotitrimetric method for determining carbon dioxide-combining power in plasma or serum. *Am. J. Clin. Path.* 1955, 25, 1212.
- Taryle, D.A., Good, J.T., Jr. and Sahn, S.A.: Metabolic activity in pleural fluid: Possible role in production of pleural fluid acidosis. *J. Lab. Clin. Med.* 1979, 93, 1041.

## PERIPHERAL LYMPH NODE TUBERCULOSIS—A COMPARISON OF VARIOUS METHODS OF MANAGEMENT

B.P. NANDA\*, N.C. PADHI\*\* AND M.C. DANDAPAT\*\*\*

Summary : Total surgical excision of tuberculous nodes followed by chemotherapy has no extra advantage over simple chemotherapy. Surgery involves additional hazards including those associated with anaesthesia. Surgery is also expensive and skilled personnel to undertake surgery may not be available in peripheral hospitals. Thus, surgery may be recommended only for ulcers sinuses with a view to obtain a cosmetically acceptable scar or as a mopping up measure after chemotherapy for large nodes, sinuses and abscesses.

### Introduction

Tuberculous lymphadenitis continues to be a major health problem in our country. It is one of the commonest manifestations of extra-pulmonary tuberculosis (Murty, 1976). It usually affects adolescent and young adult females (10-29 years). Among children it commonly affects infants and toddlers (0-5 years). The treatment of lymph node tuberculosis has not been studied as systematically as of pulmonary tuberculosis. Many forms of treatment are practised including surgical excision alone (Barrington Ward 1937, Mason Browne 1957, Wilmo 1957, lies & Emerson 1974), anti-tuberculous chemotherapy alone for varying durations (Hooper, 1972) and various combinations of surgery plus chemotherapy (lies & Emerson, 1974; Campbell, 1977). Report of efficacy of these different methods have usually been based on retrospective and uncontrolled data (Campbell, 1977). With a view to find out the best treatment which will suit our people the present study was undertaken.

### Materials and Methods

The study was carried out in the M.K.C.G. Medical College Hospital on patients attending the out-patient and inpatient departments between September 1983 to May 1985. Out of 115 cases with clinical presentation of chronic peripheral lymphnode enlargement 52 cases of clinically suspected tubercular lymphadenopathy were taken up for the present study. Routine laboratory investigations like D.C., T.L.C., E.S.R. and special investigations like Mantoux test, Chest X-ray and sputum for A.F.B. and blood for M.P. were performed. All these 52 patients were subjected to biopsy. Smears for A.F.B. were carried out from the cut section of lymphnodes in all cases.

A diagnosis of lymphnode tuberculosis was based on the following histopathological findings.

*Case eating type* : Consisting of a central caseation necrosis, surrounded by epithelioid cells, lymphocytes and giant cells of Langhans type. 32 cases showed caseating type pathology.

### Lymphadenoid type

In these cases there was no caseation necrosis. There was reticuloendothelial hyperplasia, sheets of epithelioid cells with irregular arrangements of Langhans type giant cell. 8 cases showed lymphadenoid type pathology.

Culture for tubercle bacilli from the cut section of one-half of the resected glands was done in 20 cases. These cases were selected at random.

From aforementioned investigations 40 cases were diagnosed to be tubercular and 12 cases nontubercular. The tubercular patients were divided into 2 groups for treatment purpose. Grouping was done at random irrespective of generalised symptoms, site and characteristics of the nodes. The groups were comparable in respect of age and sex.

*Group A* :—Twenty patients were subjected to total surgical excision of involved lymph nodes with chemotherapy.

*Group B* :—Twenty patients were treated with chemotherapy alone.

Chemotherapy was given for a total period of 9 months in the form of Rifampicin, INH and Ethambutol for 2 months followed by Rifampicin and INH for 7 months.

\*Post Graduate student

\*\*Associate Professor of Surgery

\*\*\*Professor and Head of the Department of Surgery From the Department of Surgery, M.K.C.G. Medical College, Berhampur, Ganjam, Orissa, Pin-760 004.

PERIPHERAL LYMPH NODE TUBERCULOSIS

**Daily Dosage of the Drags:**

*Adults \**

Rifampicin — 450 mg for patients less than 50 Kg — 600 mg for patients more than 50 Kg  
*Children* : 15 mg/Kg body weight

Ethambutol

*Adults* : 800 mg for patients less than 50 Kg  
 1000—1200 mg for patients more than 50 Kg.

*Children* : 25 mg/Kg body weight

**I.N.H.**

*Adults* :— 300 nig daily for patien’s less than 50 Kg.  
 450 mg daily for patients more than 50 Kg. *Children* :—15 mg/Kg body weight

The patients were assessed at monthly intervals till the end of chemotherapy and then followed up further after the end of chemotherapy for 9 months.

**Results**

Age and sex distribution in each group is shown in Table 1.

Out of 40 cases, lymphnodes of cervical group were affected in 28 cases (70%), multiple sites in 5 cases (12.5%) and axillary group in 5 cases (12.5%) Inguinal nodes were affected in only 2 cases (5%). Matting and caseation were the usual mode of presentation and they were present in 62% and 25% cases respectively: Other cases presented with either discrete lymphadenopathy with other features of tuberculosis or with non healing ulcer or sinus.

Results of treatment are shown in Table 2. It will be seen that 12 patients (60%) of group A and 13 patients (65%) of group B finished their therapy successfully without any complication. Fresh nodes appeared during treatment in 2 and 4 patients in group A and B respectively; 10% cases in each group developed a discharging sinus during treatment. In group A the skin over the gland broke down giving an ulcer in 4 cases (20%). There was no break down in group B. In group A 2 patients were left with an unhealed ulcer and 3 patients (total 25%) had enlarged nodes at the end of chemotherapy. 4 patients of group B (20%) had enlarged nodes at the end of chemotherapy but none had residual sinus or ulcer.

Patients were followed upto 9 months. Out of 40 patients, 8 did not turn up for follow-up after the completion of chemothctapy. But all patients with residual nodes, discharging sinus or unhealed ulcer at the end of chemotherapy were followed up. Table 3 shows the final

TABLE 1

	Number of Cases	
	Group A	Group B
0-5 years	5	4
6-9 years	2	3
10-29 years	9	8
30-49 years	3	4
Above 50 years	1	1
Total	20	20
Males	10	9
Females	10	11

TABLE 2

*Results of Treatment*

	Group A		Group B*	
	No.	Percentage	No.	Percentage
Smooth progress	12	60.0	13	65.0
Fresh nodes appearing during treatment	1	10.0	4	20.0
Node enlargement during treatment	2	10.0	3	15.0
Discharge or sinus appearing during treatment	1	10.00	2	10.0
Breakdown during chemotherapy	4	20.0	0	—
Residual nodes or sinus and unhealed ulcer	5	25.0	4	20.0

TABLE 3

*Progress during follow-up of 32 cases*

	Group A	Group B
No. of patients	15	17
Residual nodes at the end of chemotherapy	-	
(a) Vanished	2	2
(b) Smaller in size	0	1
(c) Larger	1	1
Unhealed ulcer at the end of treatment		
(a) Ulcer healed	1	0
(b) Ulcer persisted	1	0
Transient new nodes	1	0
Smooth progress	12	16

status of these patients at the end of follow-up period.

### Discussion

In the present study majority of the patients were in the age group 10-29 years. This is in accordance with the findings of other workers (Wilnot et al 1957; Reddy 1962; Kent 1967 and

Pamra and Mathur 1974). The overall male/female ratio was 19:21. But among patients 10 years and above in age there was a female preponderance with female to male ratio being 8:5. Other workers e.g. Sen (1955), Sarkar (1971) and Pamra & Mathur (1974) also noted a female preponderance.

Most common site of involvement was

cervical group (70%). In other series involvement of cervical group has been 90%, 83.5% and 93% (Hooper, 1972, Murthy, 1976 and Summers, G.D., 1980).

Matting and caseation were the usual mode of presentation of the nodes and they were present in 62% and 25% cases respectively. Sarkar (1971) found matting in 56% and caseation in 50% cases. Pamra and Mathur, 1974, noticed matting and caseation in 73% and 27% cases respectively.

Direct smear from the cut section of the glands was positive for A.F.B. in 3 cases (7.5%). Pamra and Mathur (1974) reported a positive direct smear in 10% cases.

Out of 52 cases of clinically suspected tuberculosis, culture was done in 20 cases. Taking cases of tuberculous lymphadenitis alone (40 cases) culture was carried out in 17 cases and was found positive in 9 (53%) only. None of the cultures yielded growth of atypical or bovine bacillus,

Sarkar (1971), Murty (1976) and Campbell (1977) found positive culture in 64%, 71% and 62% cases respectively. The reason for such low positive culture may be due to the presence of bacteriostatic substances in the tuberculous glands which inhibit the growth of bacilli in vitro (Soltys, 1953) or as Campbell (1977) believes it could be that not all the enlarged nodes contain the bacilli, the enlargement being due to simple hypersensitivity response to tuberculoproteins. Mycobacterium tuberculosis was isolated in all the cases of positive gland culture. lies and Emerson (1974) found Mycobacterium tuberculosis in 13 of their 14 positive gbmd cultures. All 25 positive cultures of Newcombe (1971) and all positive cultures of Campbell (1977) were of M. tuberculosis. Similarly, Deitel, M. (1984) found M. tuberculosis in all his 23 gland cultures of cervical tuberculous lymphadenitis. This result is contrary to that of Griffith (1937) and Boyds (1944) where cervical tuberculous adenitis was caused by bovine bacillus.

As shown in table III during chemotherapy breakdown of the gland occurred in 4 out of 20 cases of group A<sup>1</sup> whereas in group B where only surgery or biopsy was undertaken there was no breakdown at all. No patient of group B was left with unhealed ulcer or sinus at the end of treatment. Similar findings were observed in the study of Campbell & Dyson (1977).

During follow up, out of 7 patients who had enlarged nodes at the end of chemotherapy 4 patients had complete regression of the nodes.

Three patients had persistent enlarged nodes during follow-up. In one patient in group A the nodes became larger and in group B the nodes increased in size in 1 patient but decreased in another one. Out of 2 patients of group A\* who had unhealed ulcer at the end of chemotherapy it healed completely in 1 patient but in the other case the discharging ulcer persisted. In one patient in group A new nodes appeared but subsided later. None of the patients developed abscess during follow-up.

#### REFERENCES

- Harrington Ward, L. Lancet; 1937, i, 980. Boyd, W.; Pathology of Internal Diseases; 1944.
- Campbell, I.A., Dyson, A.J.—Lymphnode tuberculosis - A comparison of various methods of treatment, Tubercle, 1977, D<sub>3</sub>c.; 58 (4) 171-9.
- Deitel, M., Saldanha, C.P., Borowy, Z.J., Ronald, A.F., Treatment of tuberculous masses in the neck, Can. J. Surgery, Jan., 1984, 27(1): 90-3.**
- Hooper, A.A. Tuberculous peripheral lymphadenitis, British Journal of Surgery, 1972, 59, 353.**
- lies, P.B., Emerson, P.A., Tuberculous lymphadenitis, British Med. Journal, 1974, i, 143-45.
- Kent, D.C. Tuberculous lymphadenitis; not a localised disease process, Amer. J. Med. Science, 1967, 254, 886.
- Madhusudan Murty, T.V. Tuberculous lymphadenitis in children. Indian Paediatrics, July, 1976 Vol. XIII, 7.
- Mason-Browne, J.J. Discussion on Tuberculous cervicu adenitis, Proc. Royal Soc. Med., 1957, 50, 1061.
- Pamra, S.P., Mathur, G.P. ; A co-operative study of tuberculous cervical adenitis, Indian Journal of Medical Research; 1974, 62 : 1641.
- Reddy, L.B., Munuswamy, M. & Reddy, D.R. Peripheral glandular tuberculosis, Current Medical Practice, 1962, 6, 195.
- Sen, S.K. Tuberculous lymphadenitis, Indian Journal of Tuberculosis, 1955, 2, 137.
- Sarkar, N.D., Taneja, O.P. and Ghosh-Ray, B. Management of peripheral tuberculous lymphadenitis, Proceedings of 26th T.B. and Chest Diseases Workers Conference, Bangalore 1971. 157.**
- Summers, G.D., McNicol, M.W., Tuberculosis of superficial lymph nodes, British Journal of Diseases of Chest 1980, Oct., 74(4): 369-73.
- Soltys, M.A., J. Comp. Path., 1953, 63, 2, As quoted by Wilmot et al. Lancet, 1957, ii, 1184.**
- Wilmot, T.J., James, E.F. & Reilly, L.V., Tuberculous cervical lymphadenitis. Lancet, 1957. ii, 1184.

## NIACIN TEST FOR MYCOBACTERIAL IDENTIFICATION : COMPARISON OF THREE METHODS

A.S. DAMLE\* AND D.V. KAUNDINYA\*\*

**Summary** : The niacin test was carried out on 200 strains of *M. tuberculosis* by 3 methods viz. modified Runyons, Medveczkys and Gutierrez-Vasquez. Medveczkys method was found to be the best and gave positive results in 100% strains. Modified Runyons method gave positive results in 80% and Gutierrez-Vasquez method in 64%.

### Introduction

For differentiation of *M. tuberculosis* from *M. bovis* and other mycobacteria, niacin test is one of the most important tests. Recently, susceptibility to TCH (Thiophen-2-Carboxylic acid hydrazide) has been described to be especially useful for differentiating *M. tuberculosis* from *M. bovis* (Runyon, Karlson & Kubica, 1974, Grange et al 1977). Niacin test, however, still remains the most important test in identification of mycobacteria.

In carrying out this test, we were facing some difficulty in interpreting the results of Runyons method (Runyon, Selin & Harris, 1959). We were getting green or blue-green colour instead of yellow as the end point of positive test. We modified the Runyons method slightly in our laboratory. By this modification clear-cut results were obtained. The original Runyons method was abandoned afterwards. Results of modified Runyons method were compared with two other methods viz. Medveczkys method (Medveczky, 1960) and Gutierrez-Vasquez method (Gutierrez-Vasquez, 1960).

### Material and Methods

The study was carried out at S.R.T. Rural Medical College and Hospital, Ambajogai between January 1982 and March 1983."

Two hundred strains of mycobacteria were isolated from cases of pulmonary tuberculosis. All the strains were identified on the basis of rate of growth, colony morphology, growth at 37°C, absence of pigment, nitrate reduction, semiquantitative catalase, 6S°C catalase and niacin tests.

The niacin test was performed by three methods described below. For all the tests L.J. slopes having 50 to 100 colonies, 3-4 weeks old were used. Slopes having confluent growth

places to extract niacin from the medium. H37 Rv served as positive control for all the tests. Uninoculated L.J. slopes served as negative control in all tests.

### Medveczkys method (Medveczky, 1960)

Proper L.J. slope as described above was chosen. 1 ml. sterile distilled water was added to it. The slope was kept in horizontal position to flood the complete medium for 15-30 minutes. The slope was autoclaved for 15 minutes at 121°C. After cooling, 0.25 ml. of this autoclaved distilled water (autoclaved extract) was taken in a small test tube. 0.25 ml of 3% w/v benzidine solution in ethanol was added to it. The tube was transferred to inoculation hood. 0.25 ml of 10% aqueous cyanogen bromide solution was added. Positive test was indicated by appearance of faint to dark pink colour. In negative test, solution remained colourless.

### Gutierrez-Vasquez method (Gutierrez-Vasquez, 1960)

The method was carried out exactly as above, replacing benzidine by 1.5% v/v O-toluidine in ethanol. Positive test was indicated by appearance of faint to dark pink colour. In negative test, solution remained colourless.

### Runyons method (Runyon et al, 1959)

This method was carried out on same lines as above, but as described originally by Runyon, autoclaving was not done. The chemical used was 4% v/v aniline in ethanol. Positive test was indicated by appearance of yellow colour. In negative test, solution remained colourless.

This test was modified (modified Runyons method) in our laboratory to include autoclaving.

Initially, 35 strains were tested by the original Runyons method. The modified test was subsequently applied to all the 200 strains

\*\*Lecturer

\*\*Professor

Department of Microbiology, SRTR Medical College, Ambajogai

including the 35 strains tested by original Runyons method. Original Runyons method was abandoned afterwards because of difficulty in interpreting the result?.

### Results and Discussion

All the 200 strains were identified as *M. tuberculosis*. Therefore, in this study, the niacin test procedures have been evaluated only for *M. tuberculosis* strains.

Results of Medveczkys method and that of Gutierrez-Vasquez were clear cut. All the 200 strains were positively Medveczkys method, only 128 (64%) strains gave positive results Gutierrez-Vasquez/s method.

Of the 35 strains initially tested by original Runyons method, 27 gave blue-green colour, 7 gave clear positive result and one was negative. All these 27 strains were tested by modified Runyons method. Twenty gave clear cut positive result and 7 gave clear cut negative result. The 7 strains positive by original Runyons method were positive by modified Runyons method as well. The one strain negative by original Runyons method remained negative by modified Runyons method also. Thus, the Modified Runyons method was positive in 160 (80%) strains only.

In the original Runyons method, frequent appearance of green or blue-green colour interfered with the interpretation of the test. The exact cause of appearance of green colour is not known. Malachite green from the L.J. slope may be the cause, it was observed that in other two methods, autoclaving made the L.J. slopes colourless. This led us to modify the Runyons method. Autoclaving of the slope before applying the test resulted in dramatic disappearance of the interfering green colour and the results became clear cut. Modified Runyons method was then applied for all the 200 strains abandoning the original method. This step also facilitated the comparison of three tests because of the uniformity in the technique.

Poor results obtained in our study from Gutierrez-Vasquez method are supported by

findings of **Gangadharam** and Droubi (1971). They clearly state that the test utilizing O-toluidine wa<sup>?</sup> found to be unreliable. However Venkatraman &Prabhakar (1977) reported that results of Medveczkys and Gutierrez-Vasquez methods were comparable. This is in contrast to our findings.

Lastly, we would like to point out that though Medveczkys method was found to be the best, the drawback with this test is the carcinogenic property of benzidine.

### REFERENCES

- Gangadharam, P.R.J., Droubi, A.J.: A comparison of four different methods for testing the production of niacin by mycobacteria. *Amer. Rev. Resp. Dis.*; 197], 104, 434.
- Grange, J.M., Aber, V.R., Allen, B.W., Mitchison, D.A., Mikhail, J.R., McSwigger, D.A. and Collins, C.H. : Comparison of strains of *M. tuberculosis* from British, Ugandan & Asian immigrant patients: A study of bacteriophage typing, susceptibility to hydrogen peroxide and sensitivity to thiophen 2 carboxylic acid hydrazide. *Tubercle*; 1977, 58, 207.
- Gutierrez-Vasquez, J.M.: Further studies in the spot test for the differentiation of tubercle bacilli of human origin from other mycobacteria. *Amer. Rev. Resp. Dis.*; 1960, 81, 412.
- Medveczky, E. : A micromethod for routine differentiation of human tubercle bacilli from other mycobacteria in primary culture. *Amer. Rev. Resp. Dis.*; 1960, 81, 757.
- Runyon, E.H., Selin, M.J. & Harris, H.W. : Distinguishing mycobacteria by the niacin test. A modified procedure. *Amer. Rev. Tuberc.*; 1959, 79, 663.
- Runyon, E.H., Karlson, A.G., Kubica, G P. : In Lennette E.H., Spaulding E.H. & Traunt J.P. (Editors) *Manual of Clinical Microbiology* ed. 2. Washington D.C. 1974. American Society for Microbiology. P. 150.
- Venkataraman, P. & Prabhakir, R. : Niacin production test in mycobacteria. Replacement of benzidine-cyanogen bromide reagent by O-toluidine-cyanogen bromide. *Ind. J. Tuberc.*; 1977, 24, 153.

## CASE REPORTS

### RIFAMPICIN INDUCED DISTURBANCES OF GASTRIC MOTILITY

P.R. GUPTA,\* K.C. AGARWAL,\*\* AND S.D. PUROHIT\*\*\*

**Summary :** A case of rifampicin induced post-meal dyspepsia and flatulence is reported. It was due to delayed gastric emptying during the drug therapy.

#### Introduction

Gastrointestinal adverse reactions to rifampicin include anorexia, nausea and mild abdominal pain, although vomiting and, rarely, diarrhoea may occur (Proust, 1971 and Aquinas, Allan, Horsfall et al 1972). These symptoms usually appear in 1st two weeks of the drug administration, shortly after ingestion of the drug and last for a few hours. They usually subside when the drug is administered with meals.

During daily therapy, most of these symptoms are a pan of hepatitis induced by the drug (Purohit, Gupta and Sharma et al, 1983) but direct gastric irritation may be responsible in others. A report mentioning rifampicin induced flatulence and dyspepsia after meals due to delay in gastric emptying has not been reported in the English literature to the best of our knowledge. Such a case is reported.

#### Case Report

A 25 years old Hindu male reported to the outpatient department of the Hospital for Chest and Tuberculosis, Jaipur. Investigation revealed him to be a smear positive case of pulmonary tuberculosis. The patient was put on isoniazid, ethambutol and rifampicin in the usual dosage. On these drugs the patient was progressing well until 10th day when he complained of flatulence and dyspepsia after meals. His serum alanine aminotransferase at this time was 11 units. The patient was advised to ingest the drug with meals but this did not relieve him of his abdominal trouble. However, the patient reported that whenever he omitted rifampicin capsules, he felt relieved.

While continuing rifampicin, the patient was investigated in detail. Haematological investigations, liver function tests and stool examinations revealed nothing abnormal. Results of fractional test meal were within normal limits. Gastroscopy using fiberoptic gastroscope did not reveal any pathology. Barium meal

revealed normal outline of stomach and duodenum. Follow through examination (6 hours) revealed passage of the barium upto sigmoid colon but a significant portion of it was still retained within the stomach (Fig. 1). On enquiry the patient admitted that after ingestion of barium, he was feeling similar abdominal trouble as after meals.

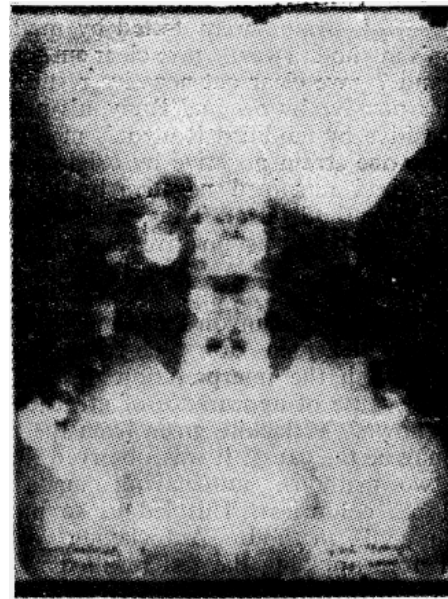


Fig. 1

Barium meal (Follow through: 6 hours) showing passage of barium upto sigmoid colon. A significant portion of the meal is still seen in the stomach.

All antitubercular drugs of the patient were withdrawn. After 3 days of this, the patient reported that his abdominal symptoms had disappeared. Barium meal studies at this time did not reveal retention of barium in the stomach (Fig. 2). Later, the patient tolerated isoniazid and ethambutol uneventfully.

#### Discussion

Onset of post-meal flatulence and dyspepsia

\*Ex Lecturer

Hospital for Tuberculosis & Chest Diseases, S.M.S. Medical College, Jaipur.

\*\*Sr. Registrar

\*\*\*Professor



Fig. 2

Barium meal of the same patient (Follow through : 6 hours) showing normal passage of barium in the large gut.

after starting the drug, disappearance after its withdrawal and uneventful acceptance of the other antituberculous drugs confirmed our belief that rifampicin was the offending drug in the present case. Rifampicin can induce gastrointestinal side effects by several mechanisms; of these drug induced hepatitis, and direct irritation of gastric mucosa are most widely accepted. Rarely, they may be a part of generalised immunological disorder induced by the drug when it is given intermittently. Liver function tests were within

normal limits, fractional test meal, gastroscopy and barium meal failed to reveal any organic pathology and the drug was administered in the usual daily dosage. Therefore, none of the above mechanisms was possibly responsible for the gastric disorder in the present case.

The normal gastric emptying time varies from 2-| hours to 6 hours (Keele and Neil, 1974). Follow through barium meal examination revealed undoubted evidence of gastric retention which coincided with the abdominal symptoms and these disappeared after withdrawal of the drug. This suggests that rifampicin delays gastric emptying. In an earlier case (Sharma, Gupta and Gupta et al 1980) we could not get an evidence of disturbed gastric motility, possibly because rifampicin was withdrawn prior to barium meal examination. The present case, on the contrary, continued to receive the drug while investigations were being carried out.

#### REFERENCES

- Aquinas, M., Allan, W.G.L., Horsfall, P.A.L. and others; *British Medical Journal*; 1972, 1, 765-71.
- Keele C.R. and Neil E. (Edi.) : *Mechanisms of the alimentary canal in Samson Wright's Applied Physiology*, 12th Edition, Oxford Medical Publications, London; 1974, 414.
- Proust, A.J. *The Australian Rifampicin trial*; *Medical Journal of Australia*, 1971, 2, 85-94.
- Purohit, S.D., Gupta, P.R.; Sharma, T.N.; Gupta D.N. and Chawla M.P.; *Rifampicin and hepatic toxicity*; *Ind. J. Tub.*, 1983, 30, 107.
- Sharma, G.S.; Gupta, P.R.; Gupta, P.R., Shankar A. and Sarkar S.K.; *Gastric Intolerance to rifampicin therapy*; *Ind. J. Tub.*; 1980, **XXVII**, 120-21.

## **STREPTOMYCIN INDUCED INTENSE HEADACHE P.K.**

GUPTA,\* M.L. GUPTA,\*\* P.K. BANSAL,\*\*\* AND A.K. RATHI\*\*\*\*

**Summary** : A case of pulmonary tuberculosis who developed intense headache following second dose of streptomycin is reported.

### **Introduction**

Common adverse reactions during streptomycin therapy are vestibular damage, hypersensitivity reactions and, rarely, nephrotoxicity.

Symptoms of vestibular damage during an acute stage include nausea, vomiting & vertigo. Moderately intense headache lasting one or two days may precede its onset. (McDermott, 1947). Difficulty in focusing eyes, positive Rombergs test and spontaneous nystagmus are the important signs.

The frequency & severity of vestibular damage is related to the dose and duration of administration of the drug. Bignall et al (1951) reported that with 1 gm daily dose, vestibular damage occurred after a mean duration of 45 days in the absence of predisposing factors. With the same dose given for less than 30 days, the damage was rarely seen (Manten, 1975). Early vertigo is extremely unusual after streptomycin therapy in 0.75 gm. daily doses.

We encountered a patient who developed intense headache, probably as a manifestation of acute vestibular toxicity following second dose of the drug (0.75 gm daily) which is unusual and merits reporting,

### **Case Report**

Forty years old sputum positive patient of pulmonary tuberculosis was admitted at Kamla Nehru Chest Hospital with respiratory complaints of 2 months duration. He was a non-smoker, vegetarian who never took alcohol. His vitals were within normal limits. His haemogram & urine analysis revealed no abnormality.

The patient was put on streptomycin 0.75 gm intramuscularly daily, with isoniazid 300 mg. and ethambutol 1 gm orally daily. Patient tolerated these drugs well on the 1st day. On the following day he complained of intense headache thirty minutes after streptomycin injection. The headache was frontal in location, was not associated with any other symptoms and subsided of its own within

three hours. Similar episode recurred after 3rd dose. On examination, Rombergs sign was negative, hot and cold calorie tests were within normal limits. His ophthalmic examination (including fundoscopy) did not reveal any abnormality. Biochemical investigation revealed blood urea 26 mg%, creatinine 0.7 mg % and fasting blood sugar 90 mg %. All the drugs were stopped.

There was no previous history of migraine, hypertension, glaucoma, psychogenic disorders, head injury etc. Headache was not associated with rise in blood pressure.

Streptomycin (0.75 gm. I.M.) was again given alone to the patient on 7th day which led to re-appearance of similar headache. On the following day, the patient was given 2 ml of normal saline, intramuscularly, which was uneventful. Streptomycin was withdrawn. Rest of the drugs were well tolerated by the patient.

### **Discussion**

Occurrence of headache within 30 minutes of administration of streptomycin, its recurrence on subsequent exposure to the drug but not the placebo, prove that it was the offending drug.

It has been well documented that early vestibular damage can occur in the presence of predisposing factors which include advanced age (Smith & Zirk, 1961) renal insufficiency (Line et al, 1970), high dose of the drug (Bignall et al, 1951), otitis media (Miszke, 1972) and concomitant intake of other ototoxic drugs (Manten, 1975). None of the reported predisposing factors were evident in our patient.

Although signs of acute vestibular damage were absent in the patient, the possibility of developing such a damage in due course, had the drug been continued further, cannot be ruled out. Acute vestibular damage with streptomycin after 3 gm total dose in the absence of predisposing factors has been reported by Glorig (1950). Tsuiki & Murai (1971) have suggested that an inherent susceptibility of the

---

\*Prof. & Head      \*\*Lecturer      \*\*\*Sr. Registrar      \*\*\*\*Registrar

From Department of Tuberculosis & Respiratory Diseases, Dr. S.N. Medical College, Jodhpur

Vestibular system to streptomycin could be responsible for the damage in such small doses of the drug. The other possibility is that the patient may not have developed vestibular damage even on continued administration of the drug. Isolated intense headache following streptomycin, therapy has not been so far reported in the literature to the best of our knowledge.

Whatever may be the mechanism, intense headache in our patient required withdrawal of streptomycin from the drug regimen.

## REFERENCES

- Bignall, J.R., Crofton, J & Thomas J.A.B. : Effect of streptomycin on vestibular function, *Br. Med. J.*, 1951, 1: 554.
- Daphne, H. Line., Graham, W. Poole and Pamela, M. Watenvorth. : Serum streptomycin levels & dizziness. *Tubercle*. 1970, **51**: 76.
- Glorig, A. : *J. Speech, Hearing Dis.* 1950, 15: 124.
- Mantel N: Antibiotic drugs, in *Meylers Side Effects of Drugs*. Dukes MNG(ed) *Excerpta Medica*, 1975, Vol. VIII Amsterdam, 627.
- Mc Dermott, W. Toxicity of streptomycin, *Am. J. Med.* 1947, 2: 491.
- Miszke (1972): quoted by Mantel N : Antibiotic drugs, in *Meylers Side Effects of Drugs*. Dukes MNG(ed) *Excerpta Medica*, 1975, Vol. VIII Amsterdam 627.
- Smith, J.M., & Zirk, M.M. : Toxic & allergic reactions during the treatment of tuberculosis. *Tubercle*, 1961, 42:287.
- Tsuiki, T & Murai, S (1971) quoted by Mantel N : Antibiotic drugs, in *Meylers Side Effects of Drugs*. Dukes MNG(ed) *Excerpta Medica*, 1975, Vol. VIII Amsterdam, 627.

## THE TUBERCULOSIS ASSOCIATION OF INDIA

### 40th National Conference on Tuberculosis and Chest Diseases held at Shillong (Meghalaya) from 16th to 18th November, 1985

#### A SHORT REVIEW

S.P. PAMRA\*

The 40th National Conference on Tuberculosis and Chest Diseases was held in the Auditorium of the State Central Library, Shillong (Meghalaya) from 16th to 18th November, 1985 under the joint auspices of the Tuberculosis Association of India and the TB Association of Meghalaya in collaboration with the National College of Chest Physicians. The Conference was attended by about 400 delegates, including about 10<sup>^</sup> from Meghalaya. Dr. C.W.I. Jeanes, Chief of the Health and Population Section, Canadian International Development Agency and Dr. James Bellran, Medical Attache, Canadian High Commission, New Delhi attended the Conference as special guests. Prof. Grzybowski of Canada was also scheduled to attend the Conference, but had to drop out because of unforeseen difficulties.

The Conference was inaugurated by the Honble Smt. Mohsina Kidwai, Union Minister for Health and Family Welfare and the inaugural function was presided over by the Honble Capt W.A. Sangma, Chief Minister of Meghalaya and Patron of the Organising Committee of the Conference.

The inaugural function opened with a song, the theme of which was stand up united. The song was rendered by representatives from the seven sisters (seven administrative units constituting the North Eastern Region of the country) in their colourful dresses. The Honble Shri S.K. Marak, Minister of Health and Family Welfare, Meghalaya, and President of the Tuberculosis Association of Meghalaya welcomed the distinguished guests and the delegates in a short address. He referred to the fact that the National Conference was being held in this part of the country for the first time and had therefore generated lot of enthusiasm for anti-TB work not only in Meghalaya but in the entire region. He referred briefly to the steps which the Government of Meghalaya was taking to take diagnostic and treatment facilities as near to the patients homes as possible with the help of two District Tuberculosis Centres and 300 tuberculosis beds. The main diffi-

culty that the State faced was the peculiar population pattern and he, therefore, made a plea for extending the District Tuberculosis Programme to three other districts and also setting up a Tuberculosis Training-Demonstration Centre in Shillong.

Capt. Sangma in his presidential address reiterated Meghalaya Governments commitment to achieve Health for All by the turn of the century through an effective and comprehensive Primary Health Care programme. He paid a tribute to the activities of the Tuberculosis Association of India and its affiliates in the States who had been spearheading the campaign against tuberculosis over the years and had established a complete rapport with the governmental agencies in the fight against tuberculosis. He also referred to the necessity for overall social and economic development of the people if tuberculosis was to be controlled quickly.

Smt. Mohsina Kidwai, Union Minister for Health and Family Welfare, while inaugurating the conference thanked the Government of Meghalaya and the Organising Committee for inviting her to this function and paid a rich compliment to them for hosting the conference so magnificently. She mentioned that with the inclusion of tuberculosis in the revised 20-Point Programme of the Government of India, there has recently been an upsurge in the activities against the disease all over the country. It was hoped that this upsurge, which was long overdue, coupled with the governmental efforts to improve the quality of life in general in the country, under the National Health Policy, will lead to an early control of the disease. She also referred to the stepping up of family planning activities and launching of an intensive programme of protective immunisation of children against all infectious diseases on the birthday of the late Prime Minister, both of which will help the Tuberculosis control programme also. She hoped that the deliberations of the Conference will help the administration in revamping the strategy to combat this scourge

---

\*Hony. Technical Adviser, Tuberculosis Association of India,

which is not only a medical but also a social malady,

Dr. D.B. Bisht, Director-General of Health Services, Government of India and Chairman, Tuberculosis Association of India reviewed briefly the developments under the National Tuberculosis Programme during the year and the role being played by the Tuberculosis Association of India in supplementing the government's efforts. He reiterated the pledge of the government as well as the Tuberculosis Association of India in stepping up anti-TB activities speedily in an attempt to achieve the target laid down under the National Control Programme for this year. He referred to the deliberations of the Technical Committee of the Tuberculosis Association of India and its recommendations from time to time which were of great help to the government in charting out policies and programmes for tuberculosis control. He noted with satisfaction that the Association had recently expanded considerably its health education activities not only through films, charts etc. but also through mass media, e.g. radio, television and the popular press. Organisation of refresher courses in district headquarter towns was another important activity. It was a matter of great satisfaction that the President of India who is the Patron of the Tuberculosis Association of India was taking a keen interest in the activities of the Association, more particularly the TB Seal Campaign. Regarding governmental activities, he mentioned that whereas approximately 6 lakhs of active tuberculous cases were being detected annually some years ago, this number reached 12 lakhs in 1984-85. During the same period, 15 lakh patients were under treatment. Consequently, the initial outlay of just Rs. 700 lakhs provided as central share for the Tuberculosis Programme for the 6th Five Year Plan, had to be increased to over 2000 lakhs. This has ensured the provision of free anti-TB drugs to all patients. No doubt, the gap between achievements and expectations was still considerable, but it was a matter of some satisfaction that our Tuberculosis Programme had perhaps no parallel in the world in respect of its size, organisation, infrastructure, etc. He also thanked the international organisations, particularly the Swedish International Development Agency and the WHO for their continued assistance to our programme. He also made a brief reference to the National Tuberculosis Institute, Bangalore which was celebrating its Silver Jubilee this year. As an integral part of the celebrations, it has been decided to hold intensive health education drive along with reorientation courses for general practitioners and para-medical staff in 50 districts of the country. With the expansion of the training programmes of the institute and enhancement of the stipend paid to the

trainees, he hoped that no district centre will remain without adequately trained staff.

He hoped that with the continued and concerted joint efforts by the Government of India, the State Governments, the Tuberculosis Association of India and its State affiliates, we will continue to make steady progress in reducing the gap between achievements and expectations and attain the target of Health for All by 2000 A.D..

Dr. D. Umapathy Rao, President of the 40th National Conference, in a brief address highlighted a few important aspects of the tuberculosis programme. He was of the view that the large dropouts from treatment at present, especially in the peripheral areas, could be reduced by introduction of short-course chemotherapy. The short-course chemotherapy trial being carried out by the ICMR in 18 districts of the country at present would bring out regimens which will be suitable and acceptable to our people. He also made a plea for more effective involvement of the general practitioners in the National Tuberculosis Programme with a view to augment the facilities available at the peripheral areas and requested the government to reconsider issue of drugs to general practitioners for free distribution to their patients. Adequate and regular supply of anti-TB drugs and x-ray films was absolutely essential for an effective Tuberculosis Programme. He also advocated setting up a monitoring and surveillance agency for assessment of the activities under the National Programme. He also made a plea to the Government of India to accept tuberculosis programme as a 100% centrally sponsored scheme for the 7th, 8th and 9th Five Year Plans, so that financial constraints of the States may not hamper the implementation of the programme.

The Union Minister for Health and Family Welfare gave away the various awards to the recipients and also released the souvenir brought out by the Organising Committee to mark the occasion. Shri D.D. Lapang, the Minister of Home and Finance, Meghalaya, moved a vote of thanks for the distinguished guests and delegates and the inaugural function came to an end with the playing of the national anthem.

The scientific programme started with two prestigious orations. Prof. V. Ramalingaswami, Director-General, ICMR, who could not deliver the Ranbaxy-Robert Koch Oration for 1984 at the 39th National Conference again could not come to Shillong to deliver his oration on Resisters and Persisters in Microbial Diseases because of last minute unforeseen

developments. Dr. S.P. Tripathy, Senior "Deputy Director-General, ICMR. read the oration in his absence. The 1985 Ranbaxy-Rober Koch Oration was delivered by Dr. A.S. Paintal on Significance of Dry Cough, Breathlessness and Muscle Weakness. Both these orations covered a large field, were very informative and educative and their excellence was highly acclaimed by the delegates. The programme also included the Wander-TAT Oration by Dr. S.B. Trivedi on Surgery in Respiratory Diseases. Dr. Trivedi traced the history of surgical treatment in tuberculosis and non-tuberculous chest diseases leading to its present role in the management of these diseases.

In a short thought-provoking address, Dr. Jeanes referred to the three major factors, viz. political will, the responsibility of the health profession and involvement of the community which were essential for tuberculosis control.

Modalities of Case-holding was the subject of the panel discussion, which was moderated by Dr. P.A. Deshmukh in the absence of Dr. S.P. Gupta, TB Adviser to the Government of India, who could not attend the conference because of urgent work in Delhi. Miss M.A. Seetfia, Dr. S.C. Khasgiwala and Dr. Ranga Rao were the panelists. Although two members of the panel could not attend the conference, the subject was very well and very systematically and comprehensively covered.

The Programme Committee of the Conference had selected 40 papers for formal presentation and 7 papers for poster presentation. Of these, only 39, including 5 poster presentation, were presented. Two papers from ValSabbhai Patel Chest Institute and the TCMR dealt with the Bhopal Gas disaster. Both the papers were very comprehensive and full of important observations on the respiratory system among the victims of the tragedy.

The maximum number of papers this year were on the subject of short-course chemotherapy under field conditions. The papers were followed by a long and lively discussion in which many delegates took a keen interest. The other main subjects discussed in the conference were non-pulmonary tuberculosis, pulmonary suppurations, problems of drug default, role of sputum examination in case-finding, hyper-sensitivity testing and treatment of bronchial asthma. The paper on A study of Chronopharmacokinetics of Pyrazinamide in Tuberculosis Patients which had won the Chanchal Singh Memorial Award of the Tuberculosis Association of India was also presented during the conference. The usual question and answer session was well attended and the

calibre of questions was of a high order and covered practically all aspects of tuberculosis work.

It is a matter of great satisfaction that the quality of the scientific papers at the conference continues to improve rapidly year by year. The presentations were very lucid, concise and kept to the time-limit. The quality of slides and charts was very satisfactory. Practically every session was followed by a lively discussion which was always to the point.

The organising committee had also arranged entertainment programmes on two evenings and the programmes were highly appreciated. The Chief Minister of Meghalaya and the State Health Minister hosted reception/dinner for the delegates. In spite of limited resources available in Meghalaya, the Organising Committee had made excellent arrangements not only for the scientific sessions, but also for accommodation and transport of the delegates and these contributed a lot to the ultimate success of the Conference.

The scientific programme was followed by the usual business and closing session. Dr. Umamathy Rao reviewed briefly the scientific programme and reiterated the high scientific standards of the papers that were presented. Dr. M.M. Singh, P.A. Deshmukh, D. Umamathy Rao and S.N. Tripathy were unanimously re-elected by the delegates as members of the Central Committee for the ensuing year. Dr K.C. Mohanty moved the vote of thanks on behalf of the delegates. Dr. Chintey in a highly emotional address thanked the delegates for taking the trouble to come to Shillong for the Conference, the donors and the members of the organising committee without whose unstinted efforts and cooperation the conference would not have been such a grand success.

An informal meeting of the Secretaries of State TB Associations was held in the evening of 17th November, 1985. A proposal was made to the Secretaries that it may be possible for the Association to obtain substantial funds from outside the country for expansion of its health education activities. They were also informed that 25% of the total assistance will have to be met by the State Associations. The Secretaries were generally in favour of the proposal and agreed to put it before their Executive Committees and let the Association have their decision by April next year. A suggestion was also made to the Secretaries that their contribution to the Research Fund of the Association may have to be increased to at least 2% of the seal sale collections with a view to enlarge the scope of research activities. The Secretaries agreed to put this matter also before

their Executive Committees and to convey their decision at the Conference of Secretaries of State TB Associations to be held in April next. It was also decided to step up the programme of refresher courses.

Meeting of the Standing Technical Committee was held on 18th November, 1985 after the closing of the Conference. It was decided that the next Conference will be held in Hydera-

bad. A few subjects were tentatively selected for special discussion at the conference. The progress of the research studies was reviewed. Dr. Umapathy Rao was requested to suggest points arising out of his presidential address requiring special action by the TB Association of India. It Was also decided to approach the Government for reduction in the sales tax levied on anti-TB drugs all over the country as it had been clone in Maharashtra.

---

## ANNUAL MEETINGS OF THE I.U.A.T. (30th September to 3rd October, 1985)

### A. Conference of Chief Executive Officers of Constituent Members.

The conference was held on 2nd October, 1985 from 9.00 A.M. to 12.15 P.M. Forty five countries were represented. *Mr. Willberg* of Norway, one of the three board members, acted as the Chairman for this Conference. The format of this Conference was changed this year. Instead of the Executive Officers presenting a brief account of the activities of their organisations followed by a general discussion the board members had chosen four broad subjects for discussion. Each subject was introduced by a few selected participants and their presentation was followed by a general discussion.

- (1) The impact of medico-social measures on the fight against tuberculosis.

The subject was introduced by *Dr. B. Fah* of Switzerland, *Prof. S. Sangsre* of Mali and *Dr. S.P. Pamra* of India. The consensus was that whereas the activities of the National Associations some years ago were almost entirely humanitarian in all countries of the world, today, the activities in developing countries are directed mainly towards implementation of national control programmes and to a lesser extent are humanitarian. In the developed countries where tuberculosis is no longer a major health problem, the National Associations are diversifying towards control of non-tuberculous, chest diseases, smoking and air-pollution etc.

- (2) Are our constituents ready to commit themselves to the anti-smoking ?

The subject was introduced by *Sir John Crofton* of U.K. and *Mr. James Swornley* of USA in respect of smoking and *Dr. P. Denrieux* of France in respect of air-pollution. *Sir John Crofton* highlighted the difficulties posed by the multinationals dealing with tobacco industry vis-a-vis anti-smoking campaign and the ways in which the constituent members could help in containing the smoking epidemic. All constituent members were committed to stepping up anti-smoking and anti-air-pollution campaign in their countries.

- (3) How can constituent members contribute to reach the target of WHO to create

a satisfactory health situation in the world by the year 2000 A.D. ?

The subject was introduced by *Mr. Willberg*. He referred briefly to the document embodying the joint work programme of the WHO and the IUAT adopted at the last World Health Assembly. It was pointed out that the document mentioned the role of voluntary organisations in general terms. It was for the individual associations to specify in concrete terms their role in this activity. The subject could then be discussed again in the Singapore meeting. Improvement in the delivery of primary health care should be their main concern with a view to achieve the social target of Health for all by 2000 A.D.

- (4) How to strengthen fund-raising ?  
How could the universal stamp and the Tuberculosis Day help ?

The subject was introduced by *Dr. M. Bleiker* of Netherlands, *Dr. Tidjani* of Togo and *Mr. James Swomley* of USA. The consensus was that the methods of fund-raising may differ from country to country, though most of the countries are conducting their own seal sale campaign. Some of them observe Tuberculosis Days also with the object of concerted fund-raising. Regarding the universal stamp, it was felt that some countries who did not have a TB seal of their own, may adopt this stamp. However, it was left open to individual countries whether to produce their own TB seals or to procure universal stamps from the IUAT.

In the end, *Dr. N.C. Sengupta*, President of the I.U.A.T. made a brief reference to the arrangements that were being made for the next International Conference to be held in Singapore in November, 1986. He extended a cordial invitation to all the constituent members to send strong delegations for the conference.

### B. Executive Committee and Council Meetings

The meeting of the Executive Committee was held on Wednesday, the 2nd October, 1985 from 2.30 P.M. to 5.30 P.M. and on Thursday, the 3rd October from 9.00 A.M. to 12 noon and the meeting of the Council on Thursday, the 3rd October at 2.00 P.M. The

following are the important decisions arrived at the Executive Committee and Council Meetings:

(1) A small advisory group be constituted to go in depth into the work-load of the Secretariat vis-a-vis the existing staff, review the present and future activities of the IUAT and advise the President about these matters and its impact on the finances of the Union.

(2) The Scientific Committees on Epidemiology and Case-finding be merged into one committee which may be designated as Committee on Tuberculosis Control<sup>1</sup>.

(3) The value of one unit of quota for the year 1986 would be 25, 700 FF which Represents a 6% increase over the 1985 quota of the constituent members contribution. It was also agreed that the quota be split into two halves, one of which will be considered as the constituent member's contribution towards the funds of the IUAT and the other half will be considered as subscription for the IUAT bulletin. The quota value for individual members will remain unchanged at 100 FF per year. It was also agreed that those countries whose contribution was in arrears for three years or more may be informed that if they do not pay up all arrears immediately, they could lose their membership rights.

(4) The Committee on Revision of Constitution submitted a brief interim report the main features of which were:—

- (a) The name of the IUAT be changed to International Union Against Tuberculosis and Lung Diseases.
- (b) Associations, government agencies, companies and foundations which apply for organisational membership with the endorsement of their constituent member may receive approval of such membership from the council and pay dues as established by the Council.
- (c) A new category of benefactor members be introduced for those persons who make a substantial monetary contribution to the funds of the IUAT.

The consensus was that these recommendations require a full consideration. The sub-committee agreed to reconsider and redraft their proposals and the revised proposals will be circulated to the constituent members at least three months before the Singapore Conference where a final decision will be taken.

## **(5) Honorary Awards**

The Committee for Honorary Awards recommended

(a) the IUAT may honour prominent personalities who may have made an outstanding contribution to the tuberculosis programme in their own countries as well as to the activities of the IUAT for at least 10 years by conferring on them Honorary Membership of the Union. The awards will be limited to a maximum of 5 at each International Conference and will be open to medical and non-medical workers. The proposals for these awards will arise from members of the Executive Committee of the IUAT and its Executive Director. The selection for awards will be made by a committee consisting of the President of the IUAT, the Chairman of the Executive Committee, the Executive Director of the IUAT and the Chairman and Vice-Chairman of the Scientific Committees.

### **(b) Medals**

Persons who had made outstanding contributions against tuberculosis in their own country and may have also been associated with the IUAT will be eligible for this medal, the number being restricted to a maximum of 5 at each International Conference. The proposals for these medals will be made by the constituent members of the Union and the selection will be made by the same committee as for honorary membership of the IUAT.

(c) The recommendation of the Committee in respect of awards to junior workers who may have published an outstanding research work during the period, between two successive international conferences was referred back to the committee with a view to working out its financial implications. The proposal will be discussed further at the Singapore Conference.

The last date for proposals for honorary members and medals will be intimated later and the awards will be made at the Singapore Conference.

(6) Dr. Shimao, having completed his two terms as Chairman of the Executive Committee, Dr. Bleiker of Netherlands was elected as the new Chairman. Dr. Shimao and Prof. Larbaoui having completed their terms as Executive Committee members were replaced by Prof. Chaulet and Dr. Aoki of Japan.

(7) A glowing tribute was paid to Dr. Shimao for his signal contribution to the affairs of the IUAT.

### C. Programme Committee for the Singapore Conference

The conference will be inaugurated on the 4th November, 1986 in the afternoon and will be preceded by committee meetings on the 2nd, 3rd and 4th of November, 1986. On each of the three days of the Scientific Conference, viz. 5th, 6th and 7th November there will be two plenary sessions of 1½ hours each before lunch. The subjects for the plenary sessions will be Tuberculosis chemotherapy, acute respiratory infections, new approaches in immunology, including BCG vaccination. National TB Control Programmes and smoking. In the afternoon, on all three days, there will be four simultaneous parallel sessions dealing with free communications. On the last day i.e. 7th November, there will be a closing plenary session where the subjects of tuberculosis and non-tuberculous respiratory diseases will be reviewed. It was also decided to introduce sun-rise seminars and poster sessions. The sun-rise seminars will be held in two or three rooms on two mornings i.e. 6th and 7th November where the selected subjects will be discussed informally during breakfast. Guest speakers for the various plenary sessions were nominated.

The Committee was informed that abstracts of more than 400 papers for presentation at the conference had already been received. Selection of papers will be completed by the end of November, 1985.

### D. Scientific Committee on Treatment

Prof. J.A. Pilheu and Dr. S.P. Pamra were elected as the new Chairman and Secretary, respectively, of the Treatment Committee,

Dr. L.S. Farer, Director, Centre for Disease Control, USA, presented a paper on Role of Ansamycin (LM 427) in three groups of patients viz. 587 of Mycobacterial Avian Complex disease (MAC) in AIDS patients, 104 MAC patients without AIDS and 38 previously treated cases with *M. Tuberculosis* resistant to the commonly used anti-TB drugs. The daily dose of Ansamycin was 150/300 mg/kg. Amongst AIDS patients, nearly 75% had disseminated disease with bacilli in bone marrow, liver or blood. The companion drugs were Clofazimine, Ethambutol, INH and Aminoglycosides. The commonest regimen was Ansamycin with Clofazimine, TNH and Ethambutol. There were 46% deaths in low dosage Ansamycin patients and 38% amongst high dosage patients. Intolerance was seen in 8% cases, hepato-toxicity being the most frequent cause of intolerance. Clinical improvement was noted in about 30% patients. The survival rate was 15 to 30% at 35 weeks.

In MAC patients without AIDS, the commonest companion drugs were INH, Ethambutol and an injectable drug usually Streptomycin. In all 27% died, 30% improved and the remaining were either unchanged or worse. Survival rate was 60-100% at 42 weeks. Sputum conversion was attained in 4% after 26 weeks treatment.

In drug resistant tuberculous cases, Streptomycin was usually replaced by Kanamycin or Capreomycin or Amikacin and the other companion drugs were INH, Ethambutol and Pyrazinamide (in half the cases). 13% died and 45% improved. Sputum conversion was 35% at 26 weeks.

The author concluded that the real value of Ansamycin remains to be determined. In the reported patients, Ansamycin did not appear to be particularly helpful. Controlled clinical trials amongst newly diagnosed previously untreated tuberculous cases were contemplated.

In a joint meeting of the Treatment, Case-finding and Epidemiology Committees, the important subject of optimum dose of INH for children was discussed at great length in view of the current practice of many physicians using a much higher dose in children as compared to adults. Dr. Pilheu reported a study in which 5 mg/kg of INH was administered to 36 children in the age group 3-16 years and 20 adults in the age group 25-50 years. There was no significant difference between the serum concentrations in children and adults at 90 minutes and 180 minutes after administration of the drug, both amongst rapid and slow inactivators of INH. Dr. Kantor deployed two doses of INH (5 mgm. and 10 mg/kg) in 16 adults, 18 children 7-14 years in age, and 16 children 0-6 years of age. Serum levels were measured 3 hours after administration of INH and the concentration did not differ significantly in the three groups of patients in any of the two doses respectively. Dr. Khalid reported another study of treatment and chemoprophylaxis using the same dose of TNH for adults and children and the results did not vary.

It was felt that the number treated in the above studies was small and, furthermore serum concentration was not the only criterion on which this issue could be decided. Clinical results and availability of INH in the tissues were also important. It was agreed that a cooperative study with a common protocol be carried out in many places, particularly in Asia, Africa and Latin America to decide this issue, provided adequate finances for the study were available.

Dr. Udani from India presented some epidemic logical data derived from autopsies and a select group of children attending the Paediatrics unit of a big hospital in Bombay. He showed that tuberculosis, especially TB meningitis, continued to be a serious problem among population with poor socio-economic status in developing countries. He presented data about the use of radio-immuno assay of antigen in the diagnosis of 136 children, 54 of whom were tuberculin negative. He also suggested regimens consisting of Rifampicin, INH and a third drug for treatment (with pyrazinamide added in miliary and meningeal tuberculosis) and INH and Rifampicin/Ethambutol for chemoprophylaxis in children

Dr. Styblo presented the results of interim analysis of the case-finding and case-holding programme in progress in Tanzania under the Mutual Assistance Programme. Diagnosis and treatment were being carried out entirely by the general health workers. About half the patients were hospitalised for the initial intensive phase of treatment for the first 2 months with SRHZ and the subsequent 6 months treatment with HT was entirely domiciliary.

Prof. Khomenko presented a paper on effects of short-course chemotherapy under experimental and clinical conditions. The drug regimen was 2 SRH/4 ERH. The results in

guinea pigs showed that the cavities did not close but were rendered sterile. However, when the material from the cavity wall was passed through a special filter and examined under the electron microscope, coccoid forms were seen which, when injected into previously uninfected guinea pigs, made them tuberculin positive. These guinea pigs also showed evidence of antibodies and typical granulomatous lesions were present in liver, lungs and spleen. 62 patients were then treated with the same regimen as guinea pigs. 60% of those whose sputum was converted, showed coccoid forms in the filtrate of sputum after 6 months treatment. Two questions were posed. Are these patients in whose sputum coccoid forms are seen, infectious? Can these coccoid forms lead to endogenous re-infection?

The Committet felt that its meeting need not and should not become a mini-conference. Emphasis should be on informal to and fro discussion rather than on formal presentation of papers. Those who wish to present papers at the future meetings should send an abstract of their papers to the Secretariat of the IUAT in Paris *at least* 2 months before the date of the meeting, so that the Secretariat can send copies of the abstracts to all the members of the Committee well ahead of the meeting. This will ensure a full, free and purposeful discussion.

---

## NEWS & NOTES

### 36TH TB SEAL CAMPAIGN

As already reported in the October 1985 issue of this Journal, the 36th TB Seal Campaign was inaugurated on 2nd October, 1985—Gandhi Jayanti Day—by Giani Zail Singh, President of India and Patron, Tuberculosis Association of India, at a special function held at Rashtrapati Bhawan, New Delhi. The Campaign was inaugurated in the States by high dignitaries such as Governors, Ministers and other distinguished personalities.

In Andhra Pradesh, the Campaign was inaugurated by Sri M. Padmanabhan, Minister for Excise, on 5th October, 1985 and the function was presided over by Shri S.V. Giri, IAS, Secretary to Government, Medical & Health Department, Andhra Pradesh, Shri Y. Ramakrishnudu, Minister for Co-operation, distributed the awards for the best collections on population basis. Shri Ashok Kumar Sen, Union Minister of Law and Justice, Government of India, inaugurated the Seal Campaign in West Bengal, on 2nd October, 1985. Dr. M.D. Shukla, Managing Director, General Electric Company, presided over the inaugural function and Mrs. Shukla was the Guest-in-Chief. In Goa, Daman & Diu, the Campaign was inaugurated by Shri Shaikh Hassan Haroon, Minister for Health and the function was presided over by Smt. Sulochana Katkar, M.L.A., and President, Goa Pradesh Congress Committee. In Karnataka, Shri A.N. Banerjee, the State Governor, inaugurated the Seal Campaign at Raj Bhawan on 2nd October, 1985. Dr. H. L. Thimme Gowda, Minister for Health and President of the Karnataka State TB Association presided over the function. In Madhya Pradesh, the Campaign was inaugurated by Prof. K. M. Chandy, the State Governor on 2nd October, 1985. In Meghalaya, the Campaign was inaugurated by the State Governor, Shri Bhishma Narayan Singh at a special function held at Raj Bhawan on 2nd October, 1985. Shri S.K. Marak, the Minister of Health and Family Welfare, presided over the function. In Maharashtra, Shri Kona Prabhakar Rao, the State Governor, inaugurated the Campaign at a special function held at Raj Bhawan on 5th October 1985. Dr. N.C. Puri, Chair man-Fund Raising, Maharashtra State Anti-TB Association, presided over the function. In Uttar Pradesh, the Campaign was inaugurated on 2nd October, 1985, by Dr. B.N. Sinha, Chairman of the Association and Prof. B.B. Sethi, Principal, K.G. Medical College, Lucknow, was the Chief Guest. Dr.

M.M.S. Siddhu, Honorary Secretary of the Association welcomed the guests.

### 41st NATIONAL CONFERENCE

The 41st National Conference on Tuberculosis and Chest Diseases will be held in the last week of October 1986 in Hyderabad (Andhra Pradesh). The tentative subjects proposed for discussion at this Conference are:

1. Current status and strategy for BCG vaccination.
2. Management of treatment failures and resistant cases.
3. Role of various multi-purpose health workers.
4. Bio-availability of drugs—pharmacokinetic studies.
5. Bronchial Asthma.
6. Air-pollution.
7. Results of pilot studies on short-course chemotherapy being carried out under the auspices of the Tuberculosis Research Centre, Madras.
8. Operational studies both in case-finding and case-holding.
9. Non-tuberculous chest diseases.
10. Role of various camps in National TB Programme.
11. Effects of smoking and lung cancer.
12. Gas inhalation and its effects.
13. Socio-economic aspects of tuberculosis.
14. Parasitic diseases.

There will also be a panel discussion on Problem of Tuberculosis amongst children.

### REFRESHER COURSES

*Andhra Pradesh* : Under the joint auspices of the Tuberculosis Association of Andhra Pradesh and the District TB Associations of Karim Nagar, Krishna and Medak and in collaboration with the respective branches of

the Indian Medical Association, three refresher courses in tuberculosis for general practitioners were held at the Indian Medical Association Hall, Karimnagar, Machilipatnam and Siddipet On 22nd September and 8th and 29th December, 1985 respectively. These courses were attended by 50, 70 and 50 doctors respectively. The course at Karim Nagar was sponsored by M/s Alembic Chemicals Works Ltd., Baroda and the Siddipet (Medak) course was sponsored by the National Academy of Medical Sciences.

*Andaman & Nicobar Islands* : The Directorate of Health Services, Andaman and Nicobar Administration, under the auspices of the Tuberculosis Association of India, organised two refresher courses at Rangat and Port Blair on 15th October and 8th November, 1985 respectively. About 50 doctors attended these courses. These courses were sponsored by M/s Themis Chemicals Limited, Bombay.

*Bihar* : Under the auspices of the Tuberculosis Association of India, two refresher courses were held in Ranchi and Nasrganj on 5th October and 3rd November, 1985 respectively. The Ranchi course was organised by the Mahadevi Birla TB Sanatorium in collaboration with the local branch of the Indian Medical Association. The course was attended by 101 doctors and was sponsored by M/s Lupin Laboratories Private Limited, Bombay. The course at Nasrganj was organised by the local branch of the Indian Medical Association. The course was attended by 80 doctors and was sponsored by the National Academy of Medical Sciences.

*Maharashtra* : 12 courses were held in different districts during the months of September, October, November and December, 1985. These courses were attended by 50-150 doctors and held in collaboration with the local branches of the Indian Medical Association and under the auspices of the Maharashtra State Anti-TB Association. The course at Bhusawal was sponsored by the National Academy of Medical Sciences.

*Tamil Nadu* : Under the joint auspices of the Anti-TB Association of Tamil Nadu, Madras City TB Association and Institute of TB and Chest Diseases, a refresher course was held at the auditorium of the TB Research Centre Madras on 27th October, 1985. Dr. T.B. Venugopal, Director of Medical Services and Vice-Chairman of the Anti-TB Association of Tamil Nadu, presided. 49 medical officers from the government institutions of Madras city and the Madras Corporation and a few general practitioners attended the course.

With these courses, the total number of refresher courses so far held in various parts of the country under the Tuberculosis Association of India and its State affiliates has reached 111.

#### **CHANCHAL SINGH MEMORIAL AWARD—1986**

The Tuberculosis Association of India will award a cash prize of Rs. LOGO/- to a medical graduate below 45 years of age and working in tuberculosis, for an original article not exceeding 30 double-spaced foolscap typed pages (approximately 6000 words) excluding charts and diagrams on a subject relating to TB. Articles or papers already published or based on work of more than one author will not be considered for this award. Papers may be sent, in quadruplicate, to reach the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-1, before the 21st July, 1986.

#### **ESSAY COMPETITION, 1986**

The Tuberculosis Association of India awards every year a cash prize of Rs. 500/- to the best medical student in India for an original essay on Tuberculosis, adjudged best by a Special Committee of the Association. The subject selected for the 1986 competition is "Basis, technique, interpretation and scope of Tuberculin test". The essay should be written in English, typed in fool-scrap size, double spaced and should not exceed 15 pages (approximately 3000 words excluding tables, diagrams, etc.) Four copies of the manuscript should be forwarded through the Dean or Principal of College/University to reach the Secretary-General, TB Association of India, 3, Red Cross Road, New Delhi-110001, before 31st July, 1986.

#### **HEALTH VISITORS COURSE**

The 1986-87 TB Health Visitors Course will commence in July 1986. The course will be of nine months duration and will be held at the New Delhi TB Centre. The minimum qualification for admission to this course is Higher Secondary/Pre-University with Science or Hygiene and Physiology in Matriculation. Application forms for admission to this course can be had from the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001. The last date for receipt of applications is 30th April, 1986.

#### **13th ANDHRA PRADESH CONFERENCE**

The 13th Andhra Pradesh Tuberculosis and Chest Diseases Workers Conference under the

joint auspices of the TB Associations of Andhra Pradesh and East Godavari District was held at the Clinical Lecture Hall of the Government General Hospital, Kakinada, on 5th and 6th October, 1985. The Conference was inaugurated by Dr. M.S.S. Koteswara Rao, Minister for Medical & Health, and Shri S.V. Giri, Secretary to Government, Medical and Health Department, presided. Sri Y. Ramakrishnudu, Minister for Cooperation, distributed the Awards. Dr. C.R.R.M. Reddy, Director of Medical Education, released the Souvenir brought out on the occasion. Dr. D. "Narasimha Rao, former Director, State TB Centre, was the President of the Conference. Dr. D. Sundara Rao, Director of Health & Family Welfare, inaugurated the Scientific Session, which included three Orations, two Guest Lectures, a Panel discussion, a session on Para-medical personnel and four sessions of assorted papers on various aspects of tuberculosis. Over 150 delegates attended the Conference.

#### **22nd MAHARASHTRA CONFERENCE**

The XXIIInd Maharashtra State Tuberculosis and Chest Diseases Workers Conference will be held at Hotel President, Bombay, on 1st and 2nd March, 1986. For further details, kindly contact Dr. T.B. Master, Secretary-General, XXIF Maharashtra State TB & Chest Diseases Conference, Organised Home Treatment Clinic, Jerbai Wadia Road, Sewree, Bombay-400 015.

#### **14th GUJARAT CONFERENCE**

The 14th Gujarat State TB and Chest Diseases Workers Conference will be held at Gandhi Smruti Timaliyawad Nanpura, Surat on 1st and 2nd March, 1986. For further details, please contact Dr. H.R. Navalgund, Organising-Secretary, 14th Gujarat State TB Conference, District TB Centre, Surat, Gujarat.

#### **HEALTH CHECK-UP CAMP**

A general Health Check-up Camp was organised in collaboration with the TB Association of Ranga Reddy District and District Medical & Health Office staff duly sponsored by Rotary Club of Tandur, at Yalal under Primary Health Centre, Peddemal on 2nd and 3rd September, 1985. Out of 1,596 persons attended, 73 sputum specimens were examined, of which 4 were found positive and 69 cases were referred for x-ray. 411 persons were given BCG.

#### **MEMBERSHIP OF THE IUAT, PARIS**

The Tuberculosis Association of India is enrolling individual members on the Interna-

tional Union Against Tuberculosis, Paris, for the year 1986. By virtue of this membership, members will receive, free of cost, copies of the I.U.A.T. Bulletins, News-letters, W.H.O. Publications dealing with Tuberculosis and Chest Diseases, I.U.A.T. circulars, etc. The annual subscription per member is 400 French Francs equivalent to Rs. 660/-. Those who wish to emol themselves as members of the International Union Against Tuberculosis may kindly remit a sum of Rs. 660/- to the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001, by the 10th March, 1986.

#### **SILVER JUBILEE OF THE NATIONAL TB INSTITUTE**

The National Tuberculosis Institute, Bangalore, celebrated its Silver Jubilee on the 1st and 2nd November, 1985. An inter-disciplinary workshop on Tuberculosis and Primary health care<sup>1</sup> was organised on 1st November, 1985. It was attended by representatives of the Health Ministry, senior staff of the NTL, about 20 senior tuberculosis workers from the country and representatives from Sri Lanka, Nepal, Bangladesh and Bhutan. Status of the National Tuberculosis Programme today and operational problems including those of treatment and case-finding were discussed in detail in the workshop.

The silver jubilee meeting was held on 2nd November and was presided over by the Union Minister for Health and Family Welfare, Smt. Mohsina Kidwai. Dr. H. Mahler, Director-General of World Health Organisation, was the chief guest. Shri Rumakrishna Hedge, the Chief Minister of Karnataka, delivered the silver jubilee address. Dr. H.L. Thimme Gowda, Minister for Health and Family Welfare, Karnataka, welcomed the guests which included Dr. Y. Ko Ko, Regional Director of SEARO and Dr. D.B. Bisht among others. Dr. G.V.J. Baily, Director of the Institute, proposed the vote of thanks.

In her address, the Union Health Minister paid a rich tribute to the sagacity, vision and leadership of late Pt. Jawahar Lal Nehru who inaugurated this Institute on 16th September, 1960. It was encouraging, she said, that the National Tuberculosis Programme formulated by this Institute assisted by international personnel has been accepted as a workable and useful model by almost all countries of the world and by integrating tuberculosis with the general health services, it had given a new direction in the field of public health. The Institute had also trained thousands of health personnel of different categories from

our own country and abroad *in* the new methodology. With the inclusion of tuberculosis in the revised 20-Point Programme of the government, there had been considerable improvement in the implementation of the programme recently, though much more had still to be done. On the 19th November, 1985, the Government of India would be embarking on a programme of universal immunisation of infants against infectious diseases like diphtheria, whooping cough, tetanus, tuberculosis, measles and polio and it was hoped that by 1990 all infants would be covered by the programme.

She uttered a word of caution to those at the helm of affairs today. They must not rest on their cards which is a sign of decay and stagnation. Jubilees, naturally, were occasions to celebrate but they were also occasions for taking stock of the situation, to see how far it had been possible to fulfil the objectives; to identify the unfinished tasks and to continue working with dedication with a view to achieve the objective fully. New challenges had surely risen since 1960 and the Institute must forge ahead to meet these challenges. She thanked the WHO and the Government of Karnataka, especially the Chief Minister, for all support and help given to this Institute all these years, and hoped that this assistance will continue in future also.

Dr. Mahler made a very sentimental reference to his association with this Institute during its earlier years and with the tuberculosis programme in general in the country. He paid a rich tribute to the Late Rajkumari Amrit Kaur and the late Dr. Benjamin without whose dedication, farsightedness and pragmatism, this Institute would not have attained

its present stature. It was the determination, conviction and courage of late Dr. Benjamin which made this Institute deviate from the western model of tuberculosis control and evolve the revolutionary concept which was considered crazy by the then experts. The contributions of NTT today had fully vindicated the revolutionary approach. He said that the country and the NTI should be proud of its contributions to tuberculosis control and he was not saying this because he was an NTI chauvinist, but because his long association with tuberculosis activities all over the world had convinced him that this was the only practicable approach for the developing countries. He praised the NTI as well as the Madras Chemotherapy Centre for the new trials that they had blazed during the last 25 years. He also referred to the efforts of the Expert Committee under the chairmanship of Dr. K.N. Rao whose technical report of 1964 was now a gospel for tuberculosis control everywhere in the world. He hoped that the Institute will in future broaden its base for incorporating health system research, and employ new and better technology to improve the delivery of health care. He ended with a quotation from the Danish philosopher, Kaffegaurd, who had said "Life can only be understood backwards, but it must be lived forwards".

The Government of India has also decided to organise a programme of re-orientation of the medical and para-medical personnel and motivation of the community in general in 50 districts of the country with a view to boost up the activities under the National Tuberculosis Programme. A two-day intensive programme of health education and re-orientation, subsidised by the WHO, is being organized in the selected districts.

# The Indian Journal of Tuberculosis

## ABSTRACTS

Vol. XXXIII

January, 1986

### **Histological Characteristics of Tuberculous Cavity Treated with Rifampicin— 4 Comparative Study with Cases Treated with Primary Drugs**

*Issei Tanaka and Ketzuro Iwai: Report on Medical Research Problems of the Japan Anti-Tuberculosis Association: 1981: 30, 20.*

Histological features of tuberculous cavities of resected lungs treated with regimens of chemotherapy including rifampicin were compared with those of patients treated with primary drugs by the matched pair method. The following findings were noted as peculiar to lung specimens treated with rifampicin : (i) Caseous material tends to get dehydrated, (ii) there is migration of macrophages into the caseous lesion, followed by digestion of necrotic debris by the macrophages and (iii) invasion of capillaries into caseous lesion. These findings suggest that caseous material behaves like a foreign body due to very strong bactericidal activity of rifampicin and as a foreign body is ultimately degraded, ingested and organized.

### **Interstitial Lung Disease Assessment by Bronchoalveolar Lavage**

*William J. Martin II, et al, Mayo Clinic Proceedings: 1983, 58, 751.*

Bronchoalveolar lavage, a simple modification of routine bronchial washing, is a relatively new investigative technique that permits assessment of changes in the cellular traffic in the alveolar spaces. During a 16-month period, 120 patients underwent bronchoalveolar lavage at our institution. Control subjects (N = H) had a predominance of alveolar macrophages (94±1%) with a few lymphocytes (4±1%), whereas 35 patients with idiopathic pulmonary fibrosis had a substantial increase in the number of polymorphonuclear leukocytes (17±2%), and 32 patients with sarcoidosis had an appreciable increase in the number of lymphocytes (27±2%). Further subtyping of these lymphocytes in 13 patients with sarcoidosis revealed the cells to be predominantly from the T-helper subclass (helper/suppressor ratio of 5.3/1.0; normal 1.8/1.0). In contrast, three other patients with a lymphocytic alveolitis

(51 ±8% lymphocytes) had a pronounced predominance of T-suppressor lymphocytes (helper/suppressor ratio of 0.1/1.0) in the lavage fluid. Two of the three patients were thought to represent an unusual subset of patients with idiopathic pulmonary fibrosis, and the third patient had pulmonary involvement secondary to angioimmunoblastic lymphadenopathy. Thus, bronchoalveolar lavage may be a useful means by which to assess the influx of inflammatory or immune effector cells into the alveolar structures in patients with interstitial lung disease, and this procedure offers promise as a quantitative means by which to assess the disease activity and the response to therapeutic intervention in these patients.

### **The management of thirty immune-compromised patients with Tuberculosis**

*American Review of Respiratory Diseases : 1984, 129, 494.*

Thirty out of 870 bacteriologically confirmed cases of pulmonary tuberculosis treated between 1978 and 1981 were immune-compromised. The immuno-compromised patients comprised 11 cases of carcinoma (lung 4, larynx 5, GI tract 2), 7 of haematologic disease, 6 kidney transplants and 6 other miscellaneous diseases. One year after start of treatment, 11 patients died (only 2 of them due to tuberculosis). In the other 19 patients, the course of tuberculosis under standard chemotherapy was the same as in non-immuno-compromised patients. The authors conclude that the clinical response of immuno-compromised tuberculous patients was good and the treatment of the underlying disease should not be modified.

### **Ten-year evaluation of a trial of chemoprophylaxis Against Tuberculosis in Frobisher Bay., Canada.**

*E. Dorkcn, et al; Tubercle; 1984, 65, 93.*

A trial of chemoprophylaxis to prevent tuberculosis in Canadian Eskimos was carried out during 1971-1974. A completely supervised regimen of isoniazid and ethambutol thrice weekly for 18 months was administered. A

10-year evaluation of 370 treated persons and 217 control subjects demonstrates the sustained value of adequate chemoprophylaxis in reducing the risk of developing active tuberculosis in the 3 groups under study (1) those with a previous episode of active tuberculosis (2) positive tuberculin reactors with normal chest X-ray and (3) BCG vaccinated individuals with large tuberculin reactions. There were 3 cases of active disease in the treated group, a risk of 0.1% per annum, and 13 cases among the controls, a risk of 1.0% per annum.

**Changes in tuberculosis notification rates in ethnic groups in England between 1971 and 1978-79**

*Jan Sutherland, et al; Tubercle; 1984, 65, 83.*

Between special surveys in 1971 and 1978-79 the estimated annual tuberculosis notification rate for males in England fell from 30.5 per 1,00,000 to 22.6 per 1,00,000 (adecline of 3.8% per year). For xemales the rate fell from 18.4 per 1,00,000 to 15.8 per 1,00,000 (1.9% per year).

In each survey, the lowest rates were those for the white ethnic group born in the United Kingdom. The highest rates, some more than 50 times as great, occurred in immigrants from the Indian sub-continent (Indian or Pakistani/Bangladeshi). The rates for immigrants from the West Indies were 3 to 4 times as great as those for the white group.

The most rapid reductions in rate between the surveys, of about 10% per year, occurred in West Indian immigrants of both sexes and in Pakistani/Bangladeshi male immigrants. The rate for Pakistani/Bangladeshi females fell by 6.5% per year. For whites born in the U.K. the annual rate of decline was 5.1% in each sex. There was very little change for Indian immigrants of either sex.

Between the surveys, continued immigration of groups from the Indian sub-continent with high notification rates considerably slowed the declined in notification rate for the whole population.

The steep downward trend in notification rate for the white ethnic group may be expected to continue, but changes in the other ethnic groups are more difficult to assess because they are influenced by so many uncertain factors. In addition, the trends in the non-white ethnic groups born in the United Kingdom cannot yet be ascertained, but will become of increasing importance.

**Study of a fully supervised programme of chemotherapy for pulmonary tuberculosis given once weekly in the continuation phase in the rural areas of Hong Kong**

*Tubercle; 1984, 65, 5.*

In the rural areas of Hong Kong outpatient treatment is organised from general primary health-care clinics which are visited only once a week by chest clinic staff. A daily 18-month, self-administered regimen of isoniazid and sodium PAS supplemented by daily streptomycin injections for the first 3 months has been the standard regimen, the patients attending a clinic once a month to collect their oral drugs, even during the first 3 months.

In 1979 a new rural service programme of fully supervised chemotherapy was introduced for a trial period of 1 year. Patients were to be admitted to hospital initially for upto 2 months for daily treatment with streptomycin, isoniazid, rifampicin, pyrazin amide, and ethambutol, followed by once-weekly streptomycin, isoniazid, rifampicin, and ethambutol upto 12 months, fully supervised in the primary health-care clinics.

The therapeutic results achieved with this new regimen were excellent. Among SO! patients with one or more positive sputum smears or cultures and 24 with all their smears and cultures negative pre-treatment, who were assessable upto 30 months, there were no bacteriological failures during chemotherapy and only one bacteriological relapse after stopping. However, the regimen had a major operational defect in that 41% of the 263 patients treated during the year had to be prescribed standard chemotherapy, which was not fully supervised, instead of the study regimen, 37% because they refused an initial period of hospital admission. The therapeutic results were far less satisfactory with the standard regimes,

**Survey of patients presenting to the Government Chest Service in Hong Kong and the effects of Active Tuberculosis case-finding by publicity campaigns**

*Tubercle; 1984, 65, 173.*

A previous survey showed that many of the patients diagnosed in a government chest clinic as new cases of active pulmonary tuberculosis had already attended one or more private practitioners, and that this often resulted in a considerable delay before first attending the Government clinic. Furthermore, outside the government clinics the standards of investigation, diagnosis and treatment were found to be very variable and patients were, in genera

ill informed about the government chest clinics and the free service they offered.

Active case-finding campaigns using television, radio, posters, and leaflets were, therefore, conducted in 1979 and 1981 and the effects of the campaigns monitored. The aim was to encourage people with a cough which had lasted for a month or more to attend a government chest clinic for free advice and, if necessary, treatment. In the event, during and immediately after the campaigns there were only minor increases in the numbers of new clinic attenders and of patients with cough, and there were no detectable increases in new cases of tuberculosis. The campaigns failed, in particular, to persuade middle-aged and elderly men with cough and sputum to attend a clinic, although there is evidence that in this group there is a high incidence of tuberculosis requiring treatment.

**Survey of the previous investigation and treatment by private practitioners of patients with pulmonary tuberculosis attending Government Chest Clinics in Hong Kong**

*Tubercle*; 1984, 65, 161.

A questionnaire was applied to 159 consecutive sputum positive and 187 sputum negative new patients of pulmonary tuberculosis reporting at the government chest clinics in Hong Kong. The great majority (86%) of the patients had originally attended a private practitioner because of symptoms. Only 18% had their sputum examined, although 76% had had a chest radiograph; 65% of the smear positive and 71% of the smear-negative patients had been told that they had, or might have, tuberculosis. For 40% there was an interval of more than a month between their first attendance at a private practitioner and at a government chest clinic. Only 11% of the patients were referred without delay to a Government chest clinic, and another 21% once tuberculosis had been diagnosed or suspected. Only 11% of the patients could name some or all the drugs used by them previously and a further 76% could identify the drugs when samples were shown to them. The findings suggest that there is considerable scope for active case-finding aimed at encouraging patients who are likely to have tuberculosis to attend government chest clinics.

**Lymphadenitis as a late complication of BCG Vaccination**

*P.A. Easton, et al; Tubercle*; 1974, 65, 205.

A case is reported of a 45-year old Canadian white woman with a painless swelling in her

right axilla. There were no other complaints and there was no known exposure to tuberculosis. Eighteen years, previously, she was given BCG vaccination by scarification method over both para-spinal muscles, (Tuberculin test was negative to 1 in 1000). Seven years earlier a mass 2 cms in size was excised from the left axilla. It was a non-caseating granuloma and was interpreted as sarcoid. No culture was put up and the tuberculin test at that time gave a reaction of 17 mms. At the time of reporting at the hospital, no evidence of any tuberculous lesion anywhere else in the body was found and the mass in the right axilla which was excised showed confluent epithelioid granulomas with numerous multinucleated giant cells and central eosinophilic necrosis. Culture was found positive for AFB.

**Supervised six-months treatment of newly diagnosed pulmonary Tuberculosis using Isoniazid, Rifampicin and Pyrazinamide with and without Streptomycin**

*D.E. Snider, et al; American Review of Respiratory Diseases*; 1983, 130, 1091.

Two hundred and thirteen patients with newly detected smearpositive pulmonary tuberculosis were randomly assigned to the following two 6-months treatment regimens viz. 2 RHZ/4 R<sub>n</sub>H<sub>2</sub> and 2 RHZS/4 R<sub>2</sub>H<sub>2</sub>. 116 out of 136 patients in the former regimen and 56 out of 78 patients in the latter regimen completed the stipulated duration of treatment. Adverse reactions requiring withdrawal of drugs for 7 days or longer were observed in 3.7% of the patients on the former regimen and 5.1% of the patients on the latter regimen. At the end of treatment, all patients in the latter regimen had negative smear and cultures. However, two of the patients on the former regimen developed INH resistance in the fourth month of treatment and remained positive at the end of treatment. During the 2 years follow-up, 4 patients (3.4%) on the former regimen and 1 (1.8%) on the latter regimen relapsed. The only significant difference between the two regimens was the higher drop out rate in the streptomycin containing regimen.

**The yield of active case-finding in persons with Inactive Pulmonary Tuberculosis of Fibrotic Lesions. A five-year study in Tuberculosis Clinics in Amsterdam, Rotterdam and Utrecht**

*D.C. Bekkers, et -al; Tubercle*; 1984, 65, 237

Nearly 15,000 persons with inactive pulmonary tuberculosis lesions attending four chest clinics in Netherlands were kept under observation for three years with a view to study

the breakdown rate amongst these. They were randomly allocated to either the check-up group or the discharge group. In the check-up group, the persons were examined bacteriologically and radiologically annually for three years while those in the discharge group were not followed routinely after the initial examination but were encouraged to attend the chest clinics if they developed any suggestive chest symptoms. Every person was examined at the end of three years. Nearly 90% in the check-up group attended regularly for annual examination and there were 28 reactivations (23 pulmonary and 5 non-respiratory) amongst them during 3 years. Twelve of these reactivations (1.2 per 1000 per year) were amongst those who had had chemotherapy previously and 15 (0.3 per 1000 per year) were amongst those who had fibrotic lesions but had had no treatment earlier. Sputum was positive in 2 by smear and 24 by culture. In the discharge group, 917 persons only attended for the final examination. Twelve reactivations were seen amongst them, 10 out of which had had previous chemotherapy. Only 2 patients had positive sputum smear and 10 were positive by culture. The authors conclude that routine annual check-up of arrested patients with inactive fibrotic lesions is not necessary.

#### **Osteitis of the Humerus Following BCG vaccination**

*Kamal M. Al-Arabi, et al; Tubercle; 1984, 65, 305.*

A 22-month-old boy in Saudi Arabia was given direct BCG vaccination when he was 15 days old. Nearly 21 months after BCG he developed a painful swelling around the left shoulder without any symptoms of toxæmia. X-ray revealed a destructive lesion of the left humeral metaphyseal area with elevation of the periosteum and new bone formation. ESR was 65 mm in one hour and blood cultures for both pyogenic organisms and tubercle bacillus were negative. Mantoux test with 10 TU gave a reaction of 15 mm after 48 hours. Histopathological examination of biopsy material showed granulation tissue with multinucleated giant cells, Necrotic bone spicules and areas of caseation were also present. **Anti-tuberculous** treatment was started. At the end of 6 months treatment, a lymphnode appeared in the axilla on the same side. The node was excised and histopathological examination showed epithelioid cell granuloma with multinucleated giant cells and areas of caseation necrosis. No tubercle bacilli could be seen in any of the sections. Radiological examination showed complete healing of the bony lesion after treatment for 9 months and the shoulder showed full range of movements.

#### **Survey of Deaths in Hong Kong attributed to Tuberculosis during a five-year period**

*Tubercle; 3985, 165, 253.*

For the 12-month period from September 1st 1975 to August 31st 1976, and for the years 1979 and 1980, records were obtained for patients certified on Part I of the death certificate as having died from tuberculosis in Hong Kong. In addition, records were obtained for patients in whom tuberculosis was a contributory cause of death (Part II certifications) in 1979 and in 1980. The records for each survey were reviewed by an independent assessor. In the assessor's opinion, the diagnosis of tuberculosis was adequately established in 93%, 92% and 92% of the patients in the 3 periods respectively, but among the Part I certifications tuberculosis had in fact been the cause in only 74%, 78% and 76%, active disease being the cause in 53%, 48% and 42%, and the late results of previous disease, inactive at the time of death, in 21%, 30% and 35%, respectively. Among the Part II certificates, 39% in 1979 and 45% in 1980 should have been Part I certifications, and only 32% and 24% respectively had been correctly certified in Part II.

If a) the patients certified in Part I had really died from tuberculosis, the death rates would have been 13.1 per 100,000 population in 1975/76, 9.7 in 1979, and 10.3 in 1980. According to the assessor's classification these should have been 9.7, 7.5 and 7.9 respectively, the rates from active disease declining from 6.9 in 1975/76, to 4.6 in 1979 and 4.3 in 1980. Among both Part I and Part II certifications there was a marked preponderance of males, and the death rates were particularly high in patients of both sexes aged 55 years or over.

#### **Rapid Diagnosis of Tuberculous Meningitis by latex particles agglutination**

*Elias Krambocitis et al, The Lancet, 1984, II, 1229*

A simple latex particle agglutination test for the rapid detection of Mycobacterium tuberculosis plasma membrane antigen in cerebrospinal fluid was evaluated in 18 children with tuberculous meningitis and 134 control children with other disorders. The antigen was detected in all 18 patients with tuberculous meningitis, although an initial sample from 1 patient did not contain detectable antigen before it was concentrated. 133 of 134 control samples gave negative results.

#### **Toxic Oil Syndrome; Report of the WHO Regional Office for Europe March 1984**

In May 1981, a previously unknown disease

syndrome broke out in Spain and adjacent province in Spain. The epidemic reached a peak by mid-June when over 600 daily hospital admissions were recorded due to the disease. The epidemic was proved to have been caused by ingestion of illegally sold denatured rapeseed oil. Many cases of the disease were severe and needed intensive care. By March 1983, a total of 340 deaths had occurred, the total number of cases recorded exceeding 20,000.

The disease had an acute and chronic phase. In the acute phase there was fever, myalgia, lymphadenopathy, noncardiogenic pulmonary oedema, eosinophilia and high IgE levels suggesting a type 01 eosinophilic pneumonia. As the acute phase resolved, lung function tests, which had initially shown volume loss with impaired diffusion capacity for carbon monoxide improved; in the majority of patients radiographs and lung functions tests returned to normal in three months. About 20% of the patients showed evidence of pulmonary hypertension, which resolved in all but 3%. Corticosteroid therapy may have assisted the resolution of long lesions.

Twenty consecutive autopsies were performed. During the acute phase the main pathological changes were found in the lungs. Intense pulmonary interstitial oedema with only scanty inflammatory mononuclear infiltrates was noted. Ultrastructural studies showed hydropic degeneration of pneumocytes types I and II with desquamation of type I cells. The cause of death in this stage was respiratory failure. Blood vessels of every type and size located in almost any organ were affected by a non-necrotizing vasculitis, mainly in the intima. In addition, interstitial inflammatory infiltrates and/or fibrosis were seen in most organs. When the pulmonary changes of the acute phase had cleared, thromboembolic complication became the cause of death in patients in the transitional phase of TOS. Patients in the chronic phase died from various infections, complications and respiratory failure. In this phase, peripheral nerves exhibited an inflammatory neuropathy with a lymphocytic perineuritis leading to perineural fibrosis and secondary axonal degeneration. Muscle tissue showed interstitial inflammatory myopathy, followed by a neurogenic muscular atrophy as the disease progressed. The scleroderma-like skin lesions showed fibrosclerosis and vasculitis of the small arteries. The salivary glands also showed vasculitis and some interstitial inflammation that progressed towards interstitial fibrosis and parenchyma atrophy. The liver showed both portal area lesions and infiltration, as well as lobular changes, such as hepatocyte degeneration and infiltration. Some cholestasis was

seen. Surprisingly, few changes were seen in brain and kidneys. Six placentae from these patients showed no significant changes. Thus, the most prominent feature was the ubiquitous vascular lesion common to all the cases examined.

### Early Lung Cancer Detection

*American Review of Respiratory Diseases*; 1984, 130, 565.

Approximately 10,000 men, all heavy smokers and 45 years of age or older, were kept under surveillance for five years in three institutions in USA to assess the effects of various screening programmes for lung cancer. In one institution, all men received dual screening with PA stereoscopic chest x-ray and sputum cytological test at the initial examination. At another institution, the procedure was dual screening with PA and lateral chest x-rays and sputum cytological tests and at the third institution, only x-ray screening was carried out. The following conclusions have been drawn on the basis of the three programmes:—

- (1) If screening for lung cancer is to be carried out it should be done within the framework of general health care; that is, in the private practitioners office, health-maintenance organisation, or a general medical clinic.
- (2) The chest roentgenogram is the most sensitive method of detecting lung cancer currently available. Approximately 40% of radiologically visible cancers in a screening programme are found in Stage I (AJCC), where the chances for long-term survival are excellent.
- (3) Sputum cytology is the most effective method of detecting early squamous cell carcinomas of the lung. The technique is highly specific, and the patients with radiologically occult cancer detected by this method can usually be treated with expectation of lung survival.
- (4) Our data do not yet indicate whether long survival in prevalence cases of lung cancer means a decreased mortality from the disease or simply reflects one or more of the artifacts of screening discussed above. Conclusions with regard to the impact of screening on mortality must await the outcome of long-term follow-up and incidence data now being collected in these controlled clinical trials.

### **Diagnosis of Pulmonary Disease in Acquired Immune Deficiency Syndrome (AIDS)**

*American Review of Respiratory Disease*, 1984 130, 659.

The effectiveness of fiberoptic bronchoscopy with the addition of broncho alveolar lavage (BAL) was evaluated in 72 patients with the acquired immune deficiency syndrome (AIDS) and parenchymal pulmonary disease. The diagnostic yield varied for different pathogens and was 94% (45/48 cases) for *Pneumocystis carinii*, 67% (14/21 cases) for cytomegalovirus, and 62% (8/13 cases) for *Mycobacterium avium* intracellulare. Of the 11 cases of documented Kaposi sarcoma in the lung parenchyma, none were diagnosed from bronchoscopy, although characteristic endobronchial lesions were seen in 6 cases. Overall, the yield of bronchoscopy for all pathogens was 65%. Both trans bronchial biopsy and BAL had high independent yields (88% and 85%, respectively) for diagnosing *P. carinii* pneumonia but combining the procedures gave the best yield. Cytomegalovirus was most often diagnosed from examination and culture of the BAL. Recovery of *Mycobacterium avium* intracellulare was highest with culture of both washings and lavage. Neither granuloma nor organisms were seen on examination of histologic specimens. Bronchoscopy with BAL was well tolerated with few complications even in 5 patients with thrombocytopenia and 10 patients requiring mechanical ventilation. Sixteen patients (22%) had an increase in temperature after the procedure without hypotension or sepsis and 1 patient (1.5%) had a moderate pulmonary hemorrhage after transbronchial biopsy. Fiberoptic bronchoscopy with BAL is a safe procedure with a high diagnostic yield in AIDS patient with lung disease.

### **A successful supervised outpatient Short-Course Tuberculosis Treatment Program in an open refugee camp on the Thai-Cambodian border**

*Steven H. Mites et al, American Review of Respiratory Disease*, 1984, 130, 827.

The operation of a tuberculosis treatment program in an open refugee camp of 45,000 refugees on the Thai-Cambodian border is described. Fifty-eight patients received 6 months of supervised daily, outpatient therapy with a protocol employing isoniazid, rifampicin, streptomycin, and Pyrazinamide. Patient compliance was high, with only 15 of 10,209 patient days being missed, despite a high incidence of minor side effects. Three patients died, 4 defaulted and 1 moved to another camp for treatment. The therapies of 4 patients were extended because

of the need for reduced doses of medication, the development of extrapulmonary disease, treatment failure and slow resolution of infiltrates on radiographs. There was 1 late relapse. The report demonstrates the feasibility of integrating short-course therapies with program designs to produce high compliance under difficult field conditions.

### **Predictors of drug-resistant *Mycobacterium tuberculosis***

*Moira L. Aitkin, et al, American Review of Respiratory Disease*, 1984, 130, 831,

From January 1, 1980, through December 31, 1982, cultures from 803 patients were positive for *M. tuberculosis*; 766 of these (95%) were tested for drug resistance. The incidence of resistance was 13 % (101/766). Of the 101 patients with drug-resistant organisms, 61 (60%) were Asian, supporting the need to routinely test Asian immigrants for drug-resistant disease. The ability of the other risk factors to separate the 40 non-Asians (10%) with drug-resistant disease from the group of 513 non-Asians with drug-sensitive organisms was poor. All risk factors were insensitive and had a high false positive rate. These results demonstrate that the presence of drug-resistant disease in non-Asians cannot accurately be predicted. This finding suggests that all cultures of *M. tuberculosis* should be tested for drug sensitivity and that in areas where the incidence of drug resistance is sufficiently high, initial treatment should be with 3 drugs until drug susceptibility is known.

### **Inhibition by Streptomycin of Tubercle Bacilli within cultured human macrophages**

*A.J. Crowle, et al, American Review of Respiratory Disease*, 1984, 130, 839.

The strategy for using streptomycin against tuberculosis assumes that it is not effective intracellularly. But according to animal cell experiments, this is probably incorrect. We retested this assumption with a new experimental model using cultured human macrophages infected with tubercle bacilli so that the results would be directly relevant to human disease. At 5 and 50 u.g/ml, streptomycin inhibited the bacilli strongly and killed some; at the lowest tested concentration of 0.5 pg-ml, it inhibited them weakly. It was acting intracellularly, because it could inhibit even when added 2 days after the macrophages had been infected and washed free of extracellular bacilli, and because in our experimental model the bacilli were shown to be unable to multiply extracellularly. However, as has been reported for animal macrophages, the antibiotic was quantitatively

more than 2 orders of magnitude less effective in human macrophages than in simple bacteriologic medium. Probably, this is because streptomycin is concentrated within lysosomes where low pH greatly inhibits it. The human macrophage-tubercle bacillus chemotherapeutic bioassay described here for the first time could be a superior patient consonant new method for testing antituberculous agents and treatment regimens. It retains important *in vivo* features, the complete host cell-parasite relationship for instance, without giving up the *in vitro* advantages of rapidity and objectivity.

**IgG Antibody to Purified Protein Derivative by Enzyme-Linked Immunosorbent Assay in the diagnosis of Pulmonary Tuberculosis**

*C.R. Zeiss, et al, American Review of Respiratory Disease, 1984, 130, 845.*

We studied the diagnostic utility of an enzyme-linked immunosorbent assay (ELTSA)

in hospitalized patients with suspected pulmonary tuberculosis (TB). A positive culture for *M. tuberculosis* identified active disease, and 3 negative cultures and smears defined the negative group. TgG antibody activity was determined by adding a 1:1,000 dilution of serum to plates coated with PPD antigen. Alkaline phosphatase labeled anti-IgG was added, color developed, and an optical density index (OD<sub>i</sub>) was determined. Twenty-one patients with *M. tuberculosis* TB had a mean ODI of 0.27, which was higher than 99 patients without TB, ODI 0.10 ( $p < 0.001$ ). An ODI of 0.15 or greater was established as a positive ELISA test. For patients with *M. tuberculosis* TB, the ELTSA had a sensitivity of 67 and a specificity of 79%. The first smear had a sensitivity of 57 and a specificity of 99%. With the first smear and the ELISA test results, a combined sensitivity of 86% was achieved. When both ELISA and the first smear were negative {101 cases}, active BT caused by *M. tuberculosis* was found in only three patients (3.0%).

---