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## GENERAL PRACTITIONERS AND TUBERCULOSIS

General Practitioners are mainly involved in diagnosis and treatment. Almost all cases with symptoms visit them initially. Tuberculosis cases are no exception. Frequently, however, tuberculous and non-tuberculous cases are wrongly diagnosed resulting on one hand in delay in diagnosis and on the other misuse of drugs.

To discharge these functions adequately, the General Practitioner should have adequate knowledge on the subject and opportunities to use our Control Programme set-up, specially the clinics. The responsibility for the quality of his services should not, therefore, rest with himself alone, but the Universities and Medical Colleges, the Central and State Governments, and others involved in the anti-TB Programme central also must share it.

Under-graduate study, intended essentially for preparing the general practitioners, should provide adequate knowledge on the subject. The curriculum of this study should be need and function based. It should be remembered that one-third of all cases in general practice relate to *Chest Diseases*. Time of teaching allotted to this discipline in the total course may not be exactly proportionate to this, but it will be irrational if this fact and its implications are not taken into account.

Mere clinical teaching at the hospitals is utterly insufficient as the causation and evolution of disease is closely associated with social, economic and other conditions. The teaching must, in addition, be community oriented and should have urban and rural "practice fields" especially in areas where the practice of the *National Tuberculosis Control Programme*, can be well-demonstrated. A competent teacher of this broad discipline should be able to draw a programme satisfying all its demands without over-burdening the under-graduate course. For guidance he may refer to the schedule of study prepared by the Tuberculosis Association of India for a uniform teaching and training programme in India.

Rapidly advancing science and technology and changing problems met in practice demand reorientation and enhancement of knowledge after graduation. The Tuberculosis Association of India and the Indian Medical Association should jointly organise symposia and other types of orientation courses for this purpose. The Government should grant leave and provide other facilities to make it a regular training programme. Rural practitioners, specially those who will run *G.P. Tuberculosis Clinics*, should have priority in attending these and other courses.

Holding State Tuberculosis Conferences in the District Centres and preferably in rural areas with participation of the local General Practitioners and eminent specialists should not only be of great educational value but may also pave the way for close co-operation between the anti-TB institutions and the General Practitioners. The Director, Tuberculosis Training & Demonstration Centre, the District Tuberculosis Officers and their colleagues must closely co-operate with the Tuberculosis Associations in these projects.

Teacher and Taught cannot be separated. Due to many disabilities in service conditions enough medical men are not coming to this speciality and good students are reluctant to join higher educational courses in this speciality. The Control Programme will be endangered if the staff strength falls faster than the fall in tuberculosis and dearth of good teachers will undermine undergraduate and post-graduate studies. These disabilities should be so removed that there should be no restrictions to the personnel of specialities for promotion even to the top posts of the Health Services.

National Tuberculosis Control Programme has no concrete programme to enlist the aid of the General Practitioners. In this connection the trend of "integration" should be foreseen. A time may soon come when the "Chest Clinics" will be functioning as guides to the "General Clinics" for proper diagnosis and management. The conduct of its operational part will rest with the general clinics. This trend may be extended to General Practitioners also, specially in suitable rural areas where a qualified and popular practitioner may be invited to hold a Tuberculosis Clinic. He should be supplied with proper record keeping schedules, facilities for X-ray and sputum examination if these can not be arranged at the clinic itself.

These physicians have a large number of unqualified practitioners who owe allegiance to them as most of them were compounders and assistants to the physicians. These men can be well indoctrinated by the General Practitioners and utilised to refer cases and to run these clinics without any fear of losing the cases. This method may be extended gradually to other practitioners even without such a clinic. Vast fields with tricky problems will have to be covered for this co-operative and collaborative effort between *General Clinics* and *G.P. Clinics*". Even so, it is worth a trial, initially in limited areas as *Pilot Project* as unlimited benefit may accrue from successful conduct of such a programme.

The chest clinics get cases referred to them by the General Practitioners. Such one-way traffic of activity has to be changed. Clinics should keep a register of the "General Practitioners" of the areas they serve, visit them at regular intervals, discuss problems and assure all possible help. At some large clinics there should be a *G.P. Cell* where they can be received for discussion etc. Frequent meetings for demonstration of cases and exchange of thoughts etc. should be arranged. Various other methods may be adopted by the clinics to keep close contact with the General Practitioners of the area.

Under current conditions a case referred to the clinic generally means loss of that case to the General Practitioner. This may be the most natural cause which prevents him from sending the reason to the clinics. A collaborative procedure may be developed in such manner that the diagnosis

and treatment will be decided by the clinics and the management of the cases including default actions, should be handed over to the General Practitioners. Drugs may also be distributed from his clinic provided proper records are kept and transmitted to the D.T.O. or local chest clinic. Other possible ways and means should also be explored according to local conditions.

The General Practitioner should remember that, besides the medical, he has social duties also. Control of tuberculosis should be one of these. Most General Practitioners care more for the welfare of their patients than the money. Failure to refer the cases to the clinics may well be due to lack of information about our Control Programme. Tuberculosis Association should disseminate such information by short and simple write-ups and making these available to the General Practitioners through the Indian Medical Association Journal and through the chest clinics. The General Practitioners should make serious attempts themselves to keep abreast of this knowledge. Some General Practitioners carry a very heavy load of patients. If the demand on time for motivation, follow-up etc. which are essential parts of management cannot be met by them, then they should not, in all fairness, undertake the treatment of tuberculosis.

B.C.G. Vaccination is not yet well accepted by a large section of the General Practitioners and the people. They should be convinced of its efficacy by personal contacts and other methods of education. Once convinced it should be their duty to help the campaign in every way.

That our National Tuberculosis Control Programme could not deliver the goods expected of it has to be sadly conceded. Why so and what is the remedy should now be our most important concern. For this the question of the General Practitioners' involvement in the Programme should loom large. The Tuberculosis Association of India had considered this matter previously also. It should now endeavour to develop a strategy in consultation with the Indian Medical Association and jointly submit the note to the Health Directorate for implementation with their co-operation. Feasibility should decide whether the project should be implemented totally or partially through pilot studies.

# MILIARY TUBERCULOSIS SIMULATING ACUTE MYELOID LEUKAEMIA — REVIEW OF LITERATURE AND REPORT OF A CASE

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## Introduction

Tuberculosis has been associated with a variety of haematological abnormalities. Hypoplasia of the bone marrow (Evans et al, 1952), myelofibrosis (Andre et al, 1961) and polycythemia (Guild, 1950) have been reported in association with disseminated tuberculosis. In a substantial proportion of the reported cases, the underlying tuberculous process was diagnosed only at autopsy. Leukaemoid reaction closely simulating blastic leukaemia and in some cases impossible to differentiate from true leukaemia have been reported in patients suffering from disseminated tuberculosis. Such a mode of presentation, though distinctly rare, is important to recognise as the treatment of these two diseases is entirely different; anti leukaemic treatment given to a patient with disseminated tuberculosis associated with a leukaemoid blood picture will have disastrous consequences. Such cases are worthy of record from the points of view of therapy as well as diagnosis. Here is reported a case of disseminated tuberculosis presenting with a blood picture closely simulating acute myeloid leukaemia and treated as such. The diagnosis was evident only at autopsy.

## Case Report

The patient was a 20 year old aircraftsman with 4 months' service in the Indian Air Force. He reported to the hospital on 27-9-1973 with complaints of weakness, easy fatigability and headache of one month duration.

The salient clinical features were striking pallor and a non-tender smooth enlargement of the liver. Spleen was not palpable. Lymphadenopathy and bleeding tendencies were absent. Presence or absence of sternal bone tenderness is not documented. Preliminary blood examination showed haemoglobin level of 4 g% and a leucocyte count of 22,500/cmm; 80 to 90% of the leucocytes in the peripheral smear were immature and showed morphological features of myeloblasts; they were peroxidase negative. A few normoblasts were also seen. The bone marrow picture was interpreted as confirming the haematological diagnosis of acute myeloid leukaemia.

He was treated with prednisolone brand of corticosteroid (10 mg/4th hourly), methotrexate

(2.5 mg b.d) and ampicillin. After giving a total dose of 40 mg of methotrexate, the peripheral leucocyte count came down to 16,000/cmm. Methotrexate was stopped with effect from 16.10.73. The haemoglobin level was maintained round about 7 to 8 g% by repeated blood transfusions. But the leucocytes and platelets continued to fall steadily. The peripheral leucocyte count reached its lowest level of 2,100 /cmm on 28.10.73, a month after admission. The uric acid level in blood showed no raise at any time during life. He became febrile on 27.10.73 and continued to run an irregular pyrexia with temperatures ranging between 100°F and 104°F.

He became toxæmic; abdominal distension and loose stools set in. At this stage the total leucocyte count showed a spontaneous rise to 8,400/cmm. Since 7.11.1973, purpuric spots began to appear in crops all over the body. There was no haematological improvement. He was maintained on corticosteroids and blood transfusions. Meanwhile leucopenia returned in full force (count, 2,200/cmm) and there was severe thrombocytopenia (27,000/cmm). On 15.11.73, "Purinethal" brand of 6-mercapto purine was substituted for cortisone. Since a single urine culture report showed *E. coli*, "Furadantin" brand of nitro furanto in was added to the therapeutic regimen. Fundus oculi at this stage showed haemorrhages. It is not stated whether leukaemic deposits or tubercles were seen in addition to the haemorrhage recorded. His general condition began to deteriorate steadily and on 18.11.73 mild icterus was noticed. Though the liver function tests and blood ammonia levels were normal, he was treated as a case of hepatic precoma. He died of sudden cardio-respiratory arrest on 22.11.73 (88 days after the onset of illness).

## Salient Autopsy Findings

The body was that of a young male of average build. The conjunctivæ were mildly icteric. There were purpuric spots over abdomen, both shoulders and both sides of the neck. Both pleural cavities showed moderate sized effusions. Both lungs were oedematous and showed multiple miliary tubercles with surrounding areas of haemorrhages. The para trachea glands were enlarged and showed necrotic tubercles. The peritoneum and the gastro-intestinal mucosæ showed petechial haemorrhages.

The liver was enlarged (1650 g), congested and the cut surface showed numerous small whitish tubercles visible to the naked eye. The lymph node at porta hepatis was enlarged (3 x 1.5 cm) and showed frank caseation.

The spleen weighed 300 g. The appearance of its cut surface was striking. The entire splenic pulp was riddled with numerous whitish soft necrotic tubercles closely set against a congested background. The mesenteric lymph nodes and especially those around the pancreas were enlarged and caseous. The left kidney showed a solitary tubercle. The adrenals were unremarkable. The meninges were free. The sternal and vertebral marrow were hyperemic and did not show the characteristic soft whitish fleshy appearance of acute myeloid leukaemia.

#### Microscopic Findings

Microscopic examination confirmed the naked eye impression of disseminated miliary tuberculosis. Mediastinal lymph nodes, mesenteric lymph nodes, left kidney, liver, spleen, lungs, and bone marrow showed numerous discrete necrotic granular eosinophilic staining foci. The appearance in the liver, spleen and bone marrow was striking.

The liver (Fig. 1) showed numerous necrotic miliary granular foci in the portal tracts. These foci showed poor mesenchymal cellular response around them. They showed nuclear debris scattered as basophilic staining precipitates against a background of eosinophilic staining granular mass. The necrotic foci varied in size. Some were big enough to encroach upon and destroy the hepatic plates. There were no leukaemic infiltrates in the liver.

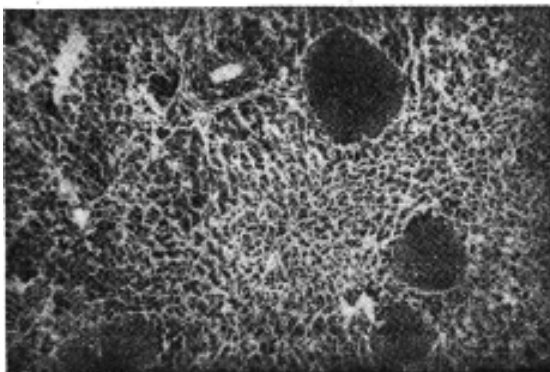


Fig. 1

Liver showing numerous miliary necrotic acellular tubercles in the portal tract.

The spleen showed a picture similar to that seen in the liver. The whole of the splenic pulp was riddled with necrotic granular foci (Fig. 2). The primary lymphoid follicles were atrophic. Reticulum cells proliferation and plasmacytoid transformation of the lymphocytes in the surviving Malphigian Corpuscles were seen. The splenic sinuses were dilated and there was no evidence of leukaemia in the spleen.



Fig. 2

Spleen showing multiple necrotic miliary foci around a depleted Malphigian corpuscle.

The bone marrow (9th dorsal vertebral body) showed a well preserved cancellous bony trabeculae in the meshes of which were seen hypoplastic marrow elements and fat. Scattered against such a background were seen discrete eosinophilic necrotic granular foci dusted with basophilic nuclear debris (Fig. 3). There was no evidence of leukaemia.

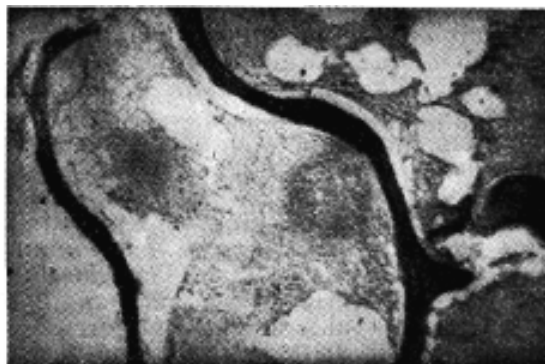


Fig. 3

Bone marrow showing necrotic tubercles.

The left kidney showed a solitary miliary tubercle. Both kidneys showed no evidence of leukaemic infiltration. Lungs showed focal oedema, generalised congestion and scattered

miliary tubercles. The myocardium showed no evidence of leukaemic infiltration. The lymph nodes from the mediastinum and the mesentery showed widespread foci of necrosis and haemorrhages and the necrotic areas were similar to those seen in other viscera. The brain showed only oedema and there was no evidence of leukaemic infiltration or meningitis. Ziehl-Neilsen's stain showed numerous acid fast organisms in all the involved organs.

### Discussion

Coley and Ewing (1911) were the first to show in their autopsy studies the association between leukaemoid reaction and disseminated tuberculosis. Mills and Townsend (1937) diagnosed this condition ante mortem. Twomey and Byrd (1965) give a full review of 38 cases of tuberculosis with leukaemoid reaction reported in the literature (1911-1965) and added 3 cases of their own. They have included only those cases which fulfilled two conditions : (1) Tubercle bacilli had to be demonstrated in the lesions. (2) There should be excessive leucocytosis or abnormal shift towards immaturity in the peripheral blood or in the bone marrow. "A diagnosis of leukaemia was considered to be excluded if a lasting haematological recovery occurred or if visceral infiltrations with leucocytes could not be demonstrated at autopsy" (Twomey and Byrd, 1965).

### Clinical Aspects

The clinical features of disseminated tuberculosis with leukaemoid reaction vary widely in the reported cases; the patients were usually middle aged. The ages range from 22 to 76 years. 47% of cases present with ill defined malaise and weakness as in the case under report. Only 10 % of cases show respiratory symptoms even though the lungs may be the seat of miliary tubercles. In the patient under report, gastrointestinal symptoms of distension and diarrhoea manifested towards the later stages of the disease when the toxæmia was advanced. A mild icterus was noticed towards the end. Hepatosplenomegaly is a frequently observed clinical feature. 88% of cases reviewed by Towmey and Byrd (1965) showed either hepatomegaly or splenomegaly or both. In this patient a smooth non-tender enlargement of the liver was a prominent clinical feature. Spleen was not felt. Lymph node enlargement is seen only in 16% of cases showing myelogenous type of leukaemoid reaction. Those with lymphoid type of reaction show frequent lymph node enlargement (Gardner and Mettier, 1949). In none of the reported cases was sternal tenderness elicited. It is unfortunate that in the case under report there is no reference

to the presence or absence of sternal tenderness during life. Absence of sternal tenderness may alert the clinician to the possibility that the leukaemic picture may be secondary to an infection.

### Haematological Aspects

Haematological picture accompanying disseminated tuberculosis may show diverse features. Haematological complications may fall under three broad groups, viz., (a) Leukaemoid reaction (b) Myelosclerosis with leucoerythroblastic reaction (c) Pancytopenia with normal marrow cellularity or hypoplastic marrow without fibrosis. These groups are net sharply differentiated from each other and intermediate forms may occur. The severity of anaemia may vary widely. But most of the reported cases show anaemia except in the case reported by Guild (1960) where polycythemia was a feature. In the case under report, the haemoglobin at the time of admission was low (4.0 gm %). It is this combination of severe anaemia and leukaemia-like peripheral picture that makes this condition so easily confused with acute leukaemia.

The total leucocyte count may vary from 368,000 to as low as 600 cells per cmm. In the 4 cases reported by Medd and Hayhoe (1955), the presenting haematological feature was that of a pancytopenia. In the majority of reported cases the leucocytic response is of the myelogenous type. A small proportion of cases may respond with a lymphocytosis of a degree sufficient to be confused with lymphatic leukaemia (Gardner and Mettier, 1949). Gibson (1946) reported monocytic leukaemoid reaction associated with tuberculosis and mediastinal teratoma.

The status of marrow response varied from hypercellularity to frank hypoplasia in the reported cases. The hypercellular state of the marrow may be a temporary phase and with efflux of time may pass into a state of hypoplasia (Crail et al, 1948). The hypercellular marrow showing predominantly blast cells is difficult to distinguish from true leukaemia as it happened in this case. In this situation special staining techniques like alkaline phosphatase scores may not be helpful. Presence of Auerbodies is believed to be characteristic of leukaemic blast cells. This assumption is open to doubt in view of their presence in cases of disseminated tuberculosis with leukaemoid reaction as reported by Twomey and Byrd (1965). The diagnostic value of Auer body is now questioned (Leavell and Twomey, 1964). In cases of doubt histological examination of marrow tissue for tubercles is mandatory. A reliable method is given by

Harowitz and Gorelich (1951). The nature of leucocytic response in cases of well established tuberculosis of diverse organs was investigated by Muller (1943). She found leukaemoid reaction extremely rare in blood and marrow. The cause of this abnormal haematological response to disseminated tuberculosis is obscure. An abnormal immunologic mechanism may play a part.

### Pathology

The pathology of this condition shows a more or less uniform picture. The lesions are extensive and widely scattered in individual organs. The striking feature of these lesions is that they are granular eosinophilic masses in which are seen basophilic nuclear debris. Lack of mesenchymal cellular response around these lesions is a note-worthy feature, seen in this case as well as in those reported in the literature. Unless a Ziehl-Neelsen stain for acid fast bacilli is done, the tuberculous nature of these lesions may escape detection. Such foci have been described as "aregenerative tubercles" or acute miliary necroses" in the literature (Gougerot, 1912).

Occurrence of such bland lesions in patients rendered sensitive to the protein moiety of the tubercle bacilli were reported by Rich (1946) and Ball et al (1951). The pathogenesis of these lesions is obscure. Mammalian (human or bovine type) type of tubercle bacilli have been cultured from these lesions, (Rich, 1946). Necrosis can occur at any time in the life history of a tubercle. This is a function of the number of bacilli in the tissue and the state of tissue hypersensitivity. Even in a highly sensitised tissue, more than one or two bacilli are required to induce necrosis of the tissue. Where the number of bacilli is high, the necrosis is wide spread and the lesions abound in bacilli. In cellular tubercles, bacilli are scanty. As the fresh necrotic lesions age, the number of bacilli become less. Temporary depression of resistance accounts for the large number of tubercle bacilli seen in these lesions. Such a phenomenon is known to follow a massive bacterial inoculum in to the blood stream (Rich, 1946). In the case under report it is reasonable to postulate that one of the many caseous enlarged lymphnodes in the mediastinum and in the porta hepatis might have burst into a vein and initiated a tuberculous septicemia. Some believe that in addition to hypersensitivity mechanism direct toxic effect due to the bacilli themselves plays a part (Ball et al, 1953).

The lack of cellular response around the necrotic foci is attributed to a state of immunolo-

gical exhaustion following overwhelming infection (Arends, 1955). The cellular response in the lesions may improve with specific treatment and some may assume the appearance of a sarcoid (Medd and Hayhoe, 1955).

### Pathogenesis of Leukaemoid Reaction

The association of leukaemoid reaction with tuberculosis raises important questions. Is there a true leukaemoid reaction associated with tuberculosis? Can this be an association of two independent conditions, namely, true leukaemia and tuberculosis?

Some believe that what is seen is an association of true leukaemia and tuberculosis and the patient dies before visceral infiltration takes place (Milder et al, 1961). It is well known that infections modify the course of leukaemia and may even induce remission (Diamond and Tubly, 1951; Ulrich, 1940). The onset of tuberculous infection might induce a spontaneous remission and hence the lack of tissue evidence of leukaemia at autopsy.

There are, however, grounds to believe that there is a true leukaemoid reaction in tuberculosis. The evidence in favour is: (a) Reversion of the abnormal blood picture to normal under anti-tuberculous therapy (Mills and Townsend, 1937). (b) The tuberculous lesion antedates the leukaemoid reaction by several years in some cases, (c) Leukaemoid reaction has been elicited by injecting tuberculo-proteins into animals rendered previously sensitive to tuberculin (Stassney and Feldman, 1938). Injecting large doses of tuberculo-protein into sensitised animals produces depression of bone marrow and peripheral pancytopenia. This may explain the association of pancytopenia and miliary tuberculosis in the cases reported by Medd and Hayhoe (1955). Sabin (1932) showed that unsaponified higher alcohol derivatives of the waxes of tubercle bacilli induced striking hyperplasia of fibroblasts in tissue culture. This observation may be of significance in tuberculous myelofibrosis.

Friend and Thackray (1952) reported a few cases of hepatosplenic tuberculosis with unusual haematological manifestation and postulate a hypersplenic mechanism for pancytopenia. It should be noted that neither hypersplenism nor extensive involvement of bone-marrow by tuberculous necrosis can be invoked to explain all the haematological manifestations in the reported cases of disseminated tuberculosis.

The leukaemoid, pancytopenic and myelosclerotic manifestations of disseminated

tuberculosis may not only share a common casual agent but also an underlying mechanism, which is probably an abnormal immunological reaction.

In disseminated tuberculosis some product of the tubercle bacilli may act as a stimulant to the bone marrow, sensitised to the tuberculo-protein. Presence of large number of bacilli in the lesions, their peculiar necrotic granular nature and lack of mesenchymal cellular response are evidence for the operation of disordered immune mechanism.

In the case under report the tissues including the bone marrow showed no evidence of leukaemic infiltrates and the patient was treated with anti-leukaemic drugs (Methotrexate and 6-mecaptopurine) during life.

It is unlikely in this case that exhibition of antileukaemic drugs would have obliterated all evidence of leukaemia. The drugs used might have contributed to some extent to the lack of cellular response around the areas of tuberculous destruction (Aregenerative tubercles). However it is pointed that are generative tubercles were reported in patients who did not receive any such drugs.

#### Significance of the case under report

Ante mortem diagnosis is rendered easier if it is known that the patient has tuberculosis elsewhere in the body. It is difficult to diagnose this condition if the patient presents, as he did in this case, with severe anaemia, hepatomegaly, leucocytosis and leukaemoid peripheral blood picture. Cases presenting with fever, leucopenia and a palpable spleen may be mistaken for typhoid fever. Some cases of pancytopenia with myelosclerosis reported in the literature may well be cases of missed disseminated tuberculosis. Only 8 out of 47 patients reviewed by Twomey and Byrd (1965) were diagnosed antemortem. Most of these patients were diagnosed as suffering from leukaemia or other myeloproliferative disorder and treated with poor results. A correct diagnosis is vital to the patient. Since effective treatment for tuberculosis is available, "the clinical picture and means of diagnosis should be better known to the general physicians and haematologists into whose hands these cases usually fall" (Medd and Hayhoe, 1955).

Careful clinical examination and search for atypical features are important. Skiagram of chest for miliary shadows may or may not be rewarding. Bone marrow smears should be carefully assessed.

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Had the cytotoxic drugs been withheld in this patient, he would have shown with efflux of time evidence of metastatic tuberculosis in clinically sensitive locations like the meninges and that would have given a clue to the diagnosis and with it perhaps a hope of cure.

Bone marrow is frequently involved in children dying of miliary tuberculosis (Emey and Gibbs, 1954).; liver biopsy reveals miliary tubercles in such cases (Graddock and Meredith, 1949).

Bone marrow aspiration biopsy, staining the smears of the aspirate for acid fast bacilli, histological examination of the aspirated material (a sadly neglected procedure) liver biopsy, X-ray examination of the lungs for miliary shadows and careful fundoscopic examination for choroidal tubercle should be employed if we are to diagnose disseminated tuberculosis masquerading as a haemotological abnormality.

Clinical picture of tuberculosis is fast changing and in Western countries where tuberculosis is effectively controlled in the young it is not uncommon to read reports of cases of tuberculosis in the elderly presenting with unusual features and dying of undiagnosed tuberculous septicemia and leucopenia (Ball et al, 1951). This aspect is of particular importance to our country where tuberculosis is rampant and its protean manifestations can lead astray even the astutest of clinicians.

#### Summary

1. A young man of 20 years who had disseminated tuberculosis presented with clinical and haematological features of acute myeloid leukaemia.
2. A brief review of the literature pertaining to leukaemoid and other abnormal haematological reaction to disseminated tuberculosis is given.
3. The peculiar pathology and pathogenesis of this condition is discussed. The importance of bone marrow and liver biopsies in the diagnosis of this condition is emphasised.
4. The importance of recognising this association in our country, where tuberculosis still remains a major killer, is stressed.

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## ETHAMBUTOL IN RETREATMENT OF PULMONARY TUBERCULOSIS

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Management of drug resistant cases of pulmonary tuberculosis always poses difficult problems. 160 cases of pulmonary tuberculosis who failed to respond to primary drugs, were retreated with a combination of ethambutol and other reserve drugs. This paper is a report on the results obtained in these cases.

### Material and Methods

All the cases had a history of grossly irregular treatment, interruptedly, in inadequate dosages and combinations, with streptomycin, isoniazid, P.A.S. and thiacetazone for periods varying from two to four years before their inclusion in the present study. All of them failed to respond to the first-line anti-tuberculosis drugs. No sensitivity studies were done. None was previously treated with ethambutol, pyrazinamide and prothionamide.

All the cases were positive for A.F.B. on direct smear and had moderately advanced or far advanced disease (Table No. 1). 100 cases were male and 60 were female (Table No. 2). Cases were alternately allocated to the two groups having 80 cases in each (Table No. 3). Cases in

group 'A' were treated with ethambutol, prothionamide and pyrazinamide for six months followed by ethambutol and prothionamide, while cases in group 'B' were treated with ethambutol and prothionamide from the beginning. Ethambutol was given on empty stomach in a daily dose of 25mg/kg. body weight for the initial two months followed by 15mg/kg. body weight daily. Prothionamide 750mg. daily and pyrazinamide 2 gm. daily were given after breakfast. Patients of both the groups were more or less identical in every respect.

It was proposed to treat all cases for a minimum of one year. All patients were hospitalized for the initial three months. Progress was assessed clinically and by fortnightly sputum examinations and two monthly skiagrams. Sputum conversion was considered as three consecutive negative smears by concentration method of 24 hours collection specimens at weekly intervals.

Patients were questioned and examined regularly for any evidence of drug toxicity. Liver function tests were done in all cases periodically. Complete ophthalmic examination

TABLE I  
*Extent of Disease*

Extent of Disease	Group 'A'		Group 'B'	
	No. of cases	Percentage	No. of cases	Percentage
Moderately advanced	16	20	20	25
Far advanced	64	80	60	75
<i>No. &amp; size of cavities</i>				
Single	12	15	16	20
Multiple	68	85	64	80
<hr/>				
2—4 cms	24	30	28	35
More than 4 cm	56	70	52	65

TABLE 2

*Age and Sex Distribution*

Age in years	Group 'A'		Group 'B'		Total
	Male	Female	Male	Female	
15—24	10	12	8	10	40
25—34	24	12	26	16	78
35—44	8	4	8	4	24
45—54	6	—	4	2	12
55 or above	4	—	2	—	6
TOTAL	52	28	48	32	160

TABLE 3

*Allocation of Regimens*

Group	Number of patients	Drugs
A	80	1. Ethambutol 2. Prothionamide 3. Pyrazinamide
B	80	1. Ethambutol 2. Prothionamide

was done of all cases prior to the start of therapy and regularly every two months.

**Observation**

15 cases in group A and 13 cases in group B did not complete three months' treatment and were excluded from the study. The reasons for their exclusion are given in table 4.

Thus 65 cases in group A and 67 cases in group B have been analysed to assess the therapeutic efficacy of the drug regimens. At 6 months sputum conversion occurred in 59 cases in group A (90 %) and in 51 cases in group B (76.1 %). Cases in both groups maintained their progress at one year. 2 cases converted late (at 7 and 8 months) in group B. Thus at one year 59 of the 65 cases in group A (90 %) and 53 of the 67 cases (79.1%) in group B had a favourable response (Table No. 5). One case who died of massive haemoptysis after one week of therapy in group B has been counted among failures.

Cavity closure was observed in 28 cases (43 %) and in 22 cases (33.3%) in group A and B respectively (Table No. 6). Moderate to marked radiographic improvement occurred in 25 and 26 cases and open healing in 4 cases and 3 cases in groups 'A' and 'B' respectively. There was no case of radiological worsening. Slight improvement was seen even in some cases who failed bacteriologically.

Ethambutol in the doses used in this study was singularly free from side effects. 14 of the 160 cases (8.7%), however, complained of blurring of vision. But evidence of optic neuritis was not found in any case. Impairment of colour (green) perception was found in one case who regained it after one month. Ethambutol was not withdrawn in any case.

Toxic manifestations to the companion drugs were, however, frequent (Table No. 7). Thus hepatotoxicity with clinical icterus (1 case) and

TABLE 4

*Showing Cases Excluded from the study*

Causes	Number of cases		Total
	Group 'A'	Group 'B'	
Drug toxicity	7	4	11
Drug defaulters	8	9	17
Total	15	13	28

TABLE 5

*Showing Rate of Sputum Conversion*

Period in months	Number of cases	
	Group 'A'	Group 'B'
1	—	—
2	32	23
3	16	11
4	5	10
5	5	4
6	1	3
7	—	1
8	—	1
9—12	—	—
Total	59(90%)	53(79.1%)

joint pain (8 cases) were attributed to pyrazinamide toxicity. Gastro-intestinal disturbances (anorexia, vomiting, loose stool and pain in abdomen), attributed to prothionamide and/or pyrazinamide were noted in 20% cases. Toxic symptoms were severe enough to cause withdrawal of pyrazinamide in 3 cases and prothionamide in 8 cases. The major and severe toxic symptoms were observed only during the first three months of treatment in both the groups.

Five women were pregnant when treatment was started. They delivered normal infants.

#### Discussion

The number of patients with negative sputum (as percentage of those remaining in the study at the time of assessment at one year) was 90 % in group 'A' and 79 % in group 'B'. Sputum conversion occurred earlier in group 'A'.

TABLE 6

*Radiographic Improvement*

Improvement	Group 'A'		Group 'B'	
	No. of cases	Percentage	No. of cases	Percentage
Cavity closure	28	43.0	22	33.3
Cavity & Opacity reduced	25	38.4	26	39.3
Opacity reduced	10	15.3	14	21.2
No change	2	3.0	4	6.0
Worsening	—	—	—	—

TABLE 7

*Toxicity and Side Effects*

Toxicity	Number of cases	
	Group 'A'	Group 'B'
<i>Major &amp; Severe:</i>		
1. Jaundice	1	
2. Gastro-intestinal	4	4
3. Joint pains	2	—
<i>Minor:</i>		
1. Gastro-intestinal	14	10
2. Joint pains	6	—
3. Vertigo	2	1
4. Itching	1	—
5. Visual disturbances	8	6

Zierski et al (196&), Citron (1969), Mezulin et al (1971) and Lees et al (1970) treated their cases with ethambutol and two companion drugs (ethionamide, pyrazinamide, cycloserine, viomycin, capreomycin or kanamycin) and observed sputum conversion in 88% to 100% at 6 months. Our results using three drugs (group A) are comparable to those reported by these workers

Again, the results of two-drug regimen (Group 'B') compare favourably with those reported by Bobrowitz et al (1965), Sunahara et al (1966), Donomae (1968), Gyselen et al (1968) and Meyer et al (1969). These workers treated their cases with ethambutol and one companion drug (ethionamide, pyrazinamide, cycloserine or capreomycin) and observed successful results in 75% to 86% at 6 months.

Cavity closure was observed in 43% and 33.3% in groups 'A' and 'B' respectively. These results are satisfactory considering that most of the cases had thick-walled cavities and fibrosclerotic lesions.

No toxic or side effects to ethambutol were observed with the dosage used in the present study. Field defects were not observed in any case. None of the patients had a definite evidence of retrobulbar neuritis. The drug was not withdrawn in any case. The experience of other workers is similar. Thus Bobrowitz (1965), Pyle (1969), Lees et al (1970), Hetrick (1970) and Pines (1971) found no case of eye toxicity, side-effects or intolerance to ethambutol in a daily dose of 15mg — 20mg/kg. body weight. Leibold (1966), Donomae et al (1966), Sunahara et al (1966), however, observed ocular toxicity in 2% of their cases.

Teratogenic effect of ethambutol has been reported (Hinshaw, 1969). However, in the present study no adverse effects were observed in five patients who were pregnant when included in this study. All delivered normal infants.

### Summary

160 adult cases of pulmonary tuberculosis excreting bacilli in their sputum who failed to respond to previous treatment were retreated with ethambutol plus prothionamide and pyrazinamide (group 'A') and with ethambutol plus prothionamide (group 'B'). Successful results were obtained in 90 % and 79 % respectively in the two groups at one year. However, the three-drugs regimen was associated with higher incidence of drug toxicity. Ethambutol was free from side effects. No case of retrobulbar neuritis was observed.

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# A STUDY OF SERUM GLUTAMIC-OXALACETIC TRANSAMINASE AND GLUTAMIC PYRUVIC TRANSAMINASE IN PULMONARY TUBERCULOSIS

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## Introduction

Liberation of transaminase activity in serum as a result of tissue injury has attracted the attention of research workers, throughout the world, to evaluate the diagnostic and prognostic significance of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) in various pathological states.

Although some workers have studied SGOT and SGPT activities in respiratory diseases, the significance of these in pulmonary tuberculosis remains unexplored. The present study was carried out in the Department of Medicine, G.R. Medical College, and J.A. Group of Hospitals, Gwalior, to evaluate SGOT and SGPT activity in pulmonary tuberculosis.

## Material and Methods

In the present study, 120 individuals, consisting of 60 healthy individuals (30 males and 30 females of different ages serving as control), and 60 cases of pulmonary tuberculosis (who were admitted in the Tuberculosis Ward of J.A. Group of Hospitals, Gwalior, were investigated.

The diagnosis of pulmonary tuberculosis was based on detailed history, clinical features, laboratory investigations and fluoroscopic examination. Only those patients whose sputum was positive for AFB were taken for the study. Patients with pulmonary tuberculosis suffering from diseases which are known to influence serum transaminase activity and/or any other concurrent

illness like diabetes mellitus, myocardial infarction, portal cirrhosis, hepatitis and hepatic abscess, hypertension, congestive heart failure, empyema, severe anaemia, proved secondary bacterial infection or with tuberculous involvement of bone, meninges and pericardium were not included for purposes of this study.

SGOT was estimated by photolorimetric method of Mohun and Cook (1957) and SGPT was estimated by Photolorimetric method of Cabud and Wroblewski (1956). Estimation of SGOT and SGPT was done in patients with pulmonary tuberculosis at the time of hospitalisation (before starting antitubercular chemotherapy).

Pulmonary tuberculosis patients were divided into three groups depending upon the severity of the disease (Scheme of classification advocated by the National Tuberculosis Association of America).

## Observations

The values of SGOT and SGPT obtained in 60 normal, healthy individuals are shown in Table 2.

## Discussion

The values of SGOT and SGPT in 60 normal healthy individuals (control group) in the present series were : SGO-T ranging from 12.0 to 26.0 units per 100 ml. with a mean value of 19.5 units per 100 ml. and standard deviation of  $\pm 4.5$ ; SGPT ranging from 12.0 to 26.0 units per 100 ml. with a mean value of 19.75

TABLE 1

*Showing the different groups of Pulmonary Tuberculosis*

S. No.	Group I	Disease	Number of cases
1.	I	Minimal Disease	13
2.	II	Moderately advanced disease	27
3.	III	Far advanced disease	20

TABLE 2

*Showing the statistical analysis of the values of SGOT and SGPT in 20 normal healthy individuals (control)*

S.No.	Statistical Measures	SGOT in Units per ml.	SGPT in units per ml.
1.	Mean	19.50	19.75
2.	S.D.	± 4.5	±3.6
3.	Range	12.0 to 26.0	10.0 to 26.0

Fig. 1

Fig. 2

TABLE 3

*Showing statistical analysis of the values of SGOT & SGPT in 60 cases of pulmonary tuberculosis In different groups*

Statistical	SGOT in Units per 100 ml.				SGP-T in Units per 100 ml.			
	Control	Gr. I	Gr. II	Gr. III	Control	Gr. I	Gr. II	Gr. III
Mean	19.5	18.1	18.3	21.6	19.75	22.3	24.6	24.2
S.D.	± 4.5	±5.0	± 5.0	± 5.5	±3.6	±3.5	± 4.8	± 6.7
Range to	12.0 to 26.0	11.5 to 28.0	8.5 to 35.0	11.5 to 36.5	12.0 to 26.0	18.0 to 31.5	13.5 to 36.5	13.5 to 36.5
Value of 'P'		0.12	0.45	0.97		1.13	0.59	0.19
'P' Result		>0.05	>0.05	>0.05		>0.05	>0.05	>0.05
		Not significant						

TABLE 4

*Showing statistical analysis of the values of SGOT & SGPT in 13 cases of minimal pulmonary tuberculosis (Group I)*

Statistical	SGOT in Units per 100 ml.		SGPT in Units per 100 ml.	
	Unilateral	Bilateral	Unilateral	Bilateral
Mean	19.1	16.5	23.4	20.4
S.D.	±4.30	±6.6	±3.99	± 2.93
Range	15.0 to 28.0	11.5 to 28.0	18.0 to 31.5	18.0 to 24.0
Value of 't'	0.69		1.4	
'P'	>0.05		>0.05	
Result	Not significant		Not significant	

TABLE 5

*Showing the Statistical analysis of the value of SGOT and SGPT in 27 cases of moderately advanced pulmonary tuberculosis (Group II)*

Statistical	SGOT in Units per 100 ml.		SGPT in Units per 100 ml.	
	Unilateral	Bilateral	Unilateral	Bilateral
Mean	14.9	19.2	23.9	24.8
S.D.	±3.79	± 6.16	±2.27	± 7.86
Range	11.52 to 20.0	8.50 to 35.0	13.5 to 24.0	13.5 to 36.5
Value of t'	1.47		0.45	
'p'	>0.05		>0.05	
Result	Not significant		Not significant	

units per 100 ml. and standard deviation of ±3.6.

The age, sex, occupation did not seem to influence the values of SGOT and SGPT. These values of SGOT and SGPT are in agreement with those of Mohun and Cook (1957) and Wroblewski and LaDue (1956) respectively, and those reported in literature by Kochar et al (1970).

The values of SGOT and SGPT in cases of

pulmonary tuberculosis observed in the present series did not differ significantly from normal control values. Extent and duration of pulmonary tuberculosis, age and sex of the patient did not seem to influence SGOT and SGPT activity of these patients.

Hearing (1959) reported his observations on SGOT and SGPT activity in 250 cases of pulmonary tuberculosis and failed to find any alteration in transaminase activity in his cases. Similar observations reported by Chinsky

TABLE 6

Showing the statistical analysis of the values of SGOT and SGPT in 20 cases of far advanced pulmonary tuberculosis (Group III).

Statistical measures	SGOT in Units per 100 ml.		SGPT in Units per 100ml	
	Unilateral	Bilateral	Unilateral	Bilateral
Mean	22.7	20.9	23.1	25.1
S.D.	± 4.05	± 6.99	±6.09	±7.48
Range	15.0 to 28.0	11.5 to 38.0	13.5 to 31.5	13.5 to 36.6
Value of 't'	0.69		0.66	
'P'	>0.05		>0.05	
Result	Not significant		Not significant	

and Sherry (1957), Conard (1957) in pulmonary tuberculosis are also in agreement with those of present workers.

This insignificant change in blood-transaminase activity in pulmonary tuberculosis may possibly be due to insignificant release of these enzymes during damage or disease of lung parenchyma. This in turn could be due to relatively low content of these enzymes in pulmonary cells in comparison to tissues of liver, heart and skeletal muscles, which form large store houses of SGOT and SGPT and in diseases of which increased transaminase activity serves as a very sensitive index of cellular damage.

Lung morphologically consists of huge numbers of alveoli containing air with thin walls penetrated by elastic fibres and blood capillaries which are basically meant for oxygenation of blood. Further a disease of lung produces patchy and heterogeneous destruction, leading to caseation, cavitation and fibrosis which simultaneously goes on disrupting the basic structure of spongy aggregation of alveoli, inter-alveolar septa and its capillary network. This to some extent hampers the absorption of these enzymes even if they are released in significant quantities. Further the caseated tissue is expectorated out. In addition the continuous caseation of the lung and presence of oxygen could oxidise and destroy these enzymes.

These factors working singly or in combination can explain to some extent the behaviour of transaminase activity in the face of pulmonary damage by tuberculosis.

### Summary

The present study comprised of study of SGOT and SGPT activity in 60 normal healthy individuals and 60 patients of pulmonary tuberculosis with various grades of severity. There was no significant change in SGOT and SGPT activity in cases of pulmonary tuberculosis, irrespective of severity and transaminase activity was found to be within normal limits.

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## TOXICITY OF THIA CETAZONE (WHEN USED IN COMBINATION WITH ISONIAZID) A STUDY AMONG 1225 PATIENTS

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The combination of isoniazid (300 mg) plus thiacetazone (150 mg) daily was found to be effective and cheap regimen with a low level of side effects (East African/BMRC investigation, 1960, 1963). Since then combination of thiacetazone and Isoniazid in above doses is being increasingly used because of its low cost and efficacy, but contradictory views regarding frequency and pattern of the toxic manifestations to thiacetazone have been advanced by different workers (Sikand et al, 1963; Menon, 1965; Gothi et al, 1966; TCC Madras, 1967; Mathuswami, 1969; Khanna, 1969) from different centres and factors like geography, race, dietary habits, exposure to sunlight, exercise etc. have been attributed to the variation in the thiacetazone toxicity (Miller et al, 1966 and Aquinas, 1969).

It was, therefore, advisable that the toxic manifestations of thiacetazone should be studied in different countries at different centres (WHO, 1964; Menon, 1965; Fox, 1966; Miller, et al, 1966). Except one on a small number of patients (109) (Mathur and Razdan, 1968) no report on the subject of thiacetazone toxicity was available in the literature from this desert part of the country. It was, therefore, decided to study the various aspects of thiacetazone toxicity under local working conditions.

### Material and Methods

#### (A) Selection of patients

All the patients of pulmonary tuberculosis admitted in T.B. Hospital, Bikaner, during the period from 1st October, 1968 to 31st March, 1972 were eligible for this study provided (a) they were previously untreated, (b) they did not manifest any sign or symptoms suggestive of toxicity attributable to thiacetazone, (c) general condition of the patient allowed oral medication and (d) age was 15 years and above.

#### (E) Observation period

Since various workers (East African/BMRC investigations 1957, 1960, 1963, Miller et al, 1966 and TCC Madras, 1967) have reported that most of the toxic reactions attributable to thiacetazone appeared in first eight weeks. Therefore patients of the present study were observed for first eight weeks under direct supervision in

this hospital and later on as ambulatory patients to complete the total observation period of thirteen weeks.

#### (C) Pretreatment Investigations.

Before the start of treatment, routine investigations, viz. complete hemogram, urine-examination including urine urobilinogen were done.

#### (D) Assessment

At monthly intervals and whenever warranted by side effects same set of investigations was repeated as mentioned above.

#### (E) Chemotherapy

All the patients included in the study were treated with combination of 150 mg thiacetazone plus 300 mg of isoniazid. Those patients who were included in the study during the period from October, 1968 to September, 1971, were given an antihistaminic (buclizine HC 17.5 mg) in addition to the above combination., they constituted "Antihistaminic" group. The remaining patients did not get any antihistaminic and constituted the non-Antihistaminic group".

#### (F) Management of toxicity

If any patient reported any symptom or if author noted any sign attributable to thiacetazone toxicity, the drug (thiacetazone) was immediately stopped and patient was observed without giving any symptomatic treatment. After a week the drug was restarted if toxicity disappeared.

#### (G) (a) Grading of toxicities

(i) Moderate: which did not reappear on resumption of the drug after one week.

(ii) Severe: which did not completely disappear within a week after stopping of the drug or which reappeared on resumption of this drug. Stevens Johnson's Syndrome, exfoliative dermatitis and jaundice were taken as severe toxic manifestations, and the drug was not challenged again.

### Observations

Total number of patients included in the study

was 1225, of which 986 were registered during first three years (October 1968 to September, 1971) of the study period and remaining 239 were registered during next six months (October, 1971 to March 1972). Table 1 deals with their age and sex-wise distribution.

Of the total of 1225 patients 688 (56.1%) completed 13 weeks of observation period while 957 (78.9%) could be observed for eight weeks.

Of the total of 1225 patients, 355 (28.9%) complained of some type of toxicity attributable to thiacetazone, during the observation period (Table 2). Of them 228 (18.6%) and 127 (10.3%) patients manifested moderate and severe toxic reactions respectively. Table 2 further reveals that 20.5% of the patients manifested gastro-intestinal reactions, out of which 14.9% were moderate and 5.6% were severe in degree.

Corresponding figure for dermal reactions were 6.0%, 1.5 and 4.5% respectively. Among all moderate reactions commonest was pain abdomen (4.3%) while nausea/vomiting was the commonest (3.2%) among all severe toxic reactions. Incidence of S.J. (Stevens Johnson) syndrome was 1.7% and of exfoliative dermatitis was 0.2%. There was no evidence of any toxicity related to haemopoetic system in any case. None of the three patients who manifested giddiness of severe degree was getting streptomycin, as an additional drug. Therefore severe giddiness could not be attributed to streptomycin. Among those 26 patients who manifested giddiness of moderate degree, there were seven patients who

were getting streptomycin as an additional drug but in these cases giddiness completely disappeared on withdrawal of thiacetazone only making us presume that the giddiness among them was most probably due to thiacetazone and not due to streptomycin. Toxic reaction attributable to isoniazid was conspicuous by its complete absence.

Of cases of the gastro-intestinal toxicity 72.5% and 21.1% were noticed in first and second weeks respectively (Table V) while for dermal toxicities corresponding figures were 40.0% and 44.0% respectively. However, about 60% and 90% of toxicity of any type manifested itself in first four and first eight weeks of the treatment respectively (table 3)

Age and sex had not influenced the incidence of the toxic reactions (not tabulated).

Table 4 reveals that general incidence of total toxic reactions were significantly higher ( $P > 0.001$ ) among patients weighing less than 40 Kg. than among the patients weighing 40-49 kg. viz. 37.8 and 24.9% respectively while such difference among patients of latter group (49-49 kg) and patients with heavier weight (50 kg or more) was not significant viz 24.9. and 21.8.% ( $P > 0.5$ ) respectively. When the toxic reactions were further analysed on basis of their types (gastrointestinal, dermal or giddiness) in relation to body weight same pattern of difference was observed in gastrointestinal reaction and giddiness but not in dermal reactions.

TABLE 1 Age and Sex distribution of the Study Material

Time of Inclusion in study	Age in years										Total
	15—24		25—34		35—44		45 and above		All		
Sex:	M	F	M	F	M	F	M	F	M	F	
September 1968 to August, 1971	167	63	281	74	210	17	162	12	820	166	986
September 1971 to March 1972	49	13	55	13	55	4	46	4	205	34	239
All	216	76	336	87	265	21	208	16	1025	200	1225

TABLE 2 *Incidence, type and degree of thiacetazone toxicity among 1225 cases of pulmonary tuberculosis*

Type of toxicity	Incidence of toxicity		Intensity of toxicity			
	Total		Moderate		Severe	
	No.	%	No.	%	No.	%
(A) Gastrointestinal including Hepatic						
(1) Nausea/Vomiting	77	6.4	39	3.2	38	3.2
(2) Pain abdomen	59	4.8	53	4.3	6	0.5
(3) Diarrhoea	51	4.1	39	3.2	12	0.9
(4) Anorexia	47	3.9	39	3.2	8	0.7
(5) Dyspepsia	13	1.0	13	1.0	—	—
(6) Jaundice	4	0.3	—	—	4	0.3
Total	251	20.5	183	14.9	68	5.6
(B) Dermal						
(1) Pruritus	36	2.9	17	1.4	19	1.5
(2) Rash	21	1.7	2	0.1	19	1.5
(3) Exfoliative dermatitis	3	0.2	—	—	3	0.2
(4) S.J. Syndrome	15	1.2	—	—	1.5	1.2
Total	75	6.0	19	1.5	56	4.5
(C) Giddiness	29	2.3	26	2.1	3	0.2
Grand Total	355	28.9	228	18.6	127	10.3

TABLE 3

*Period of onset of various types of toxicity to thiacetazone*

Type of toxicity	Intensity of toxicity	Period of onset in weeks							
		0—4		5—8		9—13		Total	
		No.	%	No.	%	No.	%	No.	%
Gastro-intestinal	Severe	52	78.0	11	16.2	4	5.8	68	100
	Total	180	72.5	53	21.1	18	6.4	251	100
Dermal	Severe	28	50.0	23	41.0	5	9.0	56	100
	Total	30	40.0	43	44.0	12	16.0	75	100
Giddiness	Severe	—	—	1	33.0	2	2.0	3	100
	Total	8	28.6	16	57.2	4	14.2	28	100

TABLE 4

*Thiacetazone toxicity in relation to body  
Weight*

Weight of patients in kg.	Total Patients to start with	Amount of thiacetazone (approx. per kg. body Wt. of patient)	No. and %	Toxicity (all forms)				Gastrointestinal		Dermal		Giddiness	
				S	T	S	T	S	T	S	T	S	T
Less than 40 kg.	418	4 mg	No %	64	158	41	114	21	27	2	17	15.3	37.8
40-49	661	3-4 mg	No %	52	165	22	117	29	38	1	10	7.9	24.9
50 kg and above	146	3 mg	No %	11	32	5	20	6	10	—	2	7.5	21.8
						3.4	13.6	4.1	6.9	—	1.4		

S—Severe      T—Total

TABLE 5

*Influence of simultaneous use of antihistaminics on incidence and onset of thiacetazone toxicity*

Simultaneous use of anti-histaminics	Patients taking treatment	General toxicity				Onset of toxicity in weeks				
		S	T	0-4		5-8		9-13		
				S	T	S	T	S	T	
With anti-histaminics	No.	986	103	284	60	166	33	89	10	29
	%	100	10.5	28.8	58.2	58.5	32.0	31.3	9.8	10.2
Without anti-histaminics	No.	239	24	71	21	52	2	14	1	5
	%	100	10.0	29.6	87.5	73.2	8.5	19.7	4.0	7.0

Incidence of toxic reactions has been analysed (not tabulated) according the calendar months of their appearance. This analysis reveals that mean values of general incidence of total and severe toxic reactions during six months from February to July were 9.3 and 3.4% compared to 6.8 and 2.3% during remaining six months, but the above variation was reflection of increased incidence of gastro-intestinal reactions during this period while dermal reactions and giddiness remained almost constant throughout the year.

Comparison of incidence of toxic reaction between "Antihistaminic" and "Non antihistaminic" groups of patients reveals that —

(1) The general incidence of total and severe toxic reactions was almost the same viz. 28.8% v/s 29.6% and 10.5% v/s 10.3% among the patients of these two groups respectively.

(2) Proportion of severe and total general reactions appearing during first four weeks was

significantly lower in antihistaminic group than non-antihistaminic group viz. 58.2 v/s 87.5 ( $P < 0.001$ ) and 58.5 v/s 73.2 ( $P < 0.02$ ).

### Discussion

The present study deals with various aspects of the problem of toxicity attributable to thiacetazone, a drug which is being very commonly used as companion drug, to isoniazid particularly in developing countries where resources available are very limited (Canetti, 1962 and Fox, 1964).

Total of 1225 hospitalized and previously untreated pulmonary tuberculosis cases were included in this study. About 80 percent of them could be observed for 8 weeks and 56 percent for 13 weeks.

#### I. General incidence of toxic reactions

Overall incidence of toxic reactions was 28.9 % of which 18.6% were moderate and 10.3% were severe in degree (table 2). The cooperative study (Pamra, 1971) revealed that the incidence of the severe toxic reactions was 4.1 percent, compared to 10.3% of the present study. TCC Madras (1967), Sen et al (1968) and Muthuswami (1969) observed that incidence of severe toxicity to thiacetazone was over 10 % whereas Deshmukh and Master (1962), Sikand et al (1963), Menon (1965), Gothi et al (1966) and Bhatia and Thind (1967) observed severe toxic reactions to be almost absent. Shah et al, (1968) and Khanna (1969) reported the toxic reactions to be about 4% or less. Similarly the results of East African/BMRC Investigations (1960, 1963, 1966 and 1970) also reveal that the incidence of severe toxic reaction attributable to thiacetazone was at lower level than the present study.

Following factors may possibly explain the higher incidence in the present study compared to many of the studies mentioned above.

(1) Patients were hospitalized for initial period of eight weeks when most of the toxic reactions appeared, where there was practically no chance of missing any toxic reaction, particularly severe ones.

(2) Factors like exposure to sunlight, malnutrition and extremes of climate may be more marked in this part of the country compared to many other places.

#### II. Type specific incidence of toxic reactions

Among all the toxic reactions the commonest were gastrointestinal followed by dermal reactions,

Among the gastrointestinal toxicity commonest was nausea/vomiting followed by pain abdomen and diarrhoea. Of the dermal reactions commonest was pruritus followed by rash. These observations were similar to those reported by others (TCC Madras, 1967; Jaswant Singh, 1967 and Shah et al, 1968 and Aquinas 1968). Giddiness was the commonest toxicity reported by Gothi et al (1966) and Miller et al (1966). This was the least common toxicity in the present study.

Similar to the observations of cooperative study (Pamra, 1971) there was no toxic effect on haemopoetic system in the present study.

#### III. Onset of toxic reactions

Similar to other trials (East African/BMRC investigation, 1960, 1963; Miller, et al, 1966; TCC Madras, 1967 and Pamra 1971), most of the toxic reactions (more than 90 %) appeared by the end of 8 weeks. Analysing the incidence of toxic reactions of different types, the maximum incidence of gastrointestinal toxic reactions was during first four weeks while that of dermal and giddiness was observed during next four weeks (5 to 8 weeks). Thus gastrointestinal reactions were earliest to appear followed by dermal and giddiness. But Miller et al (1966) observed that dermal side effects were earliest to appear followed by gastrointestinal and then by giddiness.

#### IV. Age and sex wise incidence of toxic reaction

The present results indicate that the incidence of toxic reactions was not modified by age or sex of the patients. Miller et al (1966) and Pamra (1971) also made similar observations except vestibular symptoms.

#### V. Correlation of toxic reaction with initial body weight of patients.

In general the incidence of toxic reactions with thiacetazone was significantly (table IV) higher in the patients having low weight (less than 40 kg) and consequently getting higher dose (more than 4 mg per kg) of thiacetazone as compared to those having higher weight (40 kg or more) and getting lower dose of thiacetazone (less than 4 mg per kg). Our results are in agreement with the observations of Pamra (1971).

This difference in general incidence of toxic reactions was seen particularly in case of gastrointestinal upsets. On basis of such observations it seems advisable that the dose of thiacetazone should be individualized on basis of body weight (Deshmukh, 1969) or of body surface area as suggested by Dingley (1969).

#### VI. *Seasonal variation of thiacetazone toxicity*

It was observed that general incidence of total and severe toxic reaction was higher during the six months from February to July as compared with the incidence during remaining six months. Above variation was observed only in gastrointestinal toxicity while incidence of dermal toxic reactions and giddiness remained almost constant throughout the year. Narayan Sen (1969) also observed higher incidence of toxic reaction during the same period i.e. February to July. The high incidence of the toxic reactions during this period of six months was probably due to the combination of high temperature and low humidity which may lead to

- (1) Some kind of electrolytic imbalance or
- (2) slow excretion of drugs through the kidneys due to increased perspiration or/and
- (3) some mucosal changes in gastrointestinal tract making it more vulnerable to untoward effects of the drug.

#### VII. *Influence of simultaneous use of Antihistaminics on the incidence and onset of toxic reactions to Thiacetazone*

Frequency of severe and total reactions in general was almost the same among the patients of Antihistaminic and Non antihistaminic groups. This observation was not in conformity with the experience of some of the previous workers (Domagk, 1950; Deshmukh & Master, 1962; Dashmukh et al, 1963; Patel et al, 1965; Shah et al, 1968; Dashmukh, 1969 and Sen et al, 1970) who believed that most of the toxic reactions of thiacetazone were allergic in nature and could be easily controlled with antihistaminics. But WHO report (1970) also concluded that antihistaminics and vitamins did not reduce thiacetazone—induced side effects. Similarly BMRC study (Miller et al, 1972) did not show any overall benefit following the use of additions as prophylaxis for preventing side effects except gastrointestinal ones.

Secondly, proportions of toxic reaction in general appearing in first four weeks of the treatment was significantly ( $P/ 0.001$ ) lower among antihistaminic group compared to other group. Thus the onset of toxic reactions was delayed in this group. This delay can be explained by the fact that antihistaminic neutralized effect of liberated histamine & masked the effect of toxic reactions for sometime.

The present study indicated no advantage of adding antihistaminics to the combination of thiacetazone and isoniazid.

#### Summary

This study deals with 1225 previously untreated cases of pulmonary tuberculosis who were observed for toxic reactions attributable to thiacetazone for a period of 13 weeks of which 8- weeks was in the hospital. The patients were treated with 150 mg thiacetazone plus 300 mg isoniazid. In addition to these all were getting vitamins and 986 (admitted during first three years of the study) were also getting an antihistaminic namely buclizine hydrochloride. Various aspects of the problem of thiacetazone toxicity were studied.

General incidence of such toxic reactions was 28.9 % of which 18.6% and 10.3 % were moderate and severe in degree respectively. The commonest moderate and severe toxicities were gastrointestinal. Among gastrointestinal toxic reactions the commonest was nausea/vomiting followed by pain in abdomen while among dermal reactions commonest was pruritis followed by rash.

More than 60% of all the toxic reactions appeared in 1st four weeks and about 90% in 1st eight weeks. Among them gastrointestinal reactions were earliest to appear followed by dermal reactions and giddiness.

No evidence was available for any correlation between toxic reaction and age and sex. While there were more frequent toxic reactions among patients weighing less than 40 kg than among the remaining patients.

Incidence of toxic reactions attributable to thiacetazone particularly gastrointestinal ones showed seasonal variation being higher during hot months (February to July) than during remaining period of the year.

Comparison of incidence and onset of toxic reaction amongst patients with antihistaminic and patients without antihistaminics revealed that use of antihistaminics failed to reduce incidence of toxic reactions of any type. The onset of reactions was delayed in the former group of patients with antihistaminics.

#### ACKNOWLEDGEMENT

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## CASE REPORTS

### SPINAL SUBDURAL TUBERCULOMA

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(From Govt. General Hospital & Kurnool Medical College, Kurnool).

Tuberculous granulomas of the spine are encountered in every anatomical plane of the spinal cord and its coverings. Those of the extradural space, arachnoid and intramedullary ones are the common forms. The least frequent is the subdural variety. Dastur (1972) found only four subdural granulomas among 74 cases of tuberculous granulomas of spine. Apart from the above review there is no specific report of a case of subdural tuberculoma in the Indian literature. In addition to the rarity, the present case merits recording because of the rapid postoperative recovery, both clinical and biochemical and also illustrates the value of corticosteroids in the rapid amelioration of the condition. The necessity of treating primary tuberculosis with a complete course of antituberculous drugs and the risk of developing CNS tuberculosis with inadequate therapy are also exemplified.

#### Case Report

A 32 year old woman was admitted with a history of numbness of the lowerlimbs and weakness of the right leg of one month duration. The weakness increased gradually and spread to the left lower limb and five days before admission she became totally paraplegic with retention of urine. There was no history of fever or trauma to the spine.

She was a married woman with four children. She was treated for "Tuberculous Abdomen" one year previously with antituberculous drugs, and was relieved of symptoms despite the fact that she did not receive a full course of the treatment.

*Examination* : Her general condition was good. Neurological examination showed absolute, flaccid paraplegia with loss of reflexes. The sensations were diminished below the tenth dorsal segment and lost below the first lumbar segment bilaterally. She had retention of urine and constipation. The spine was normal. Other systems including the abdomen were normal.

*Investigations*: Total white cell count: 14,000/cmm. Differential count: 60% neutrophils, 36% lymphocytes and 4% eosinophils. Sedimentation rate: 110 mm/1st hour. X-rays of the dorsal spine and the chest were normal. Lumbar Puncture: c.s.f. was xanthochromic, clotted instantaneously and contained 4.7

grammes of protein. Cisternal myelogram revealed a total block at D6, the appearances suggesting an intradural extramedullary compression.

*Operation*: Dorsal laminectomy of D5 through D8 revealed a tumor resistance under the dura which was thickened, lusterless and lacked pulsations. Dural opening disclosed a subdural granulomatous lesion ensheathing the cord all round. It was 3 inches long and its thickness varied from 0.1 to 0.3 inches. The dorsal and lateral portions were removed piecemeal. The spinal fluid flowed freely and the cord pulsations returned. The wound was closed. Postoperatively she was on antituberculous drugs (One gm of Streptomycin and 300 mgm. of INAH daily) and Inj. Betamethasone 4 mgm. 6th hourly with diminishing dosage.

Histologically the lesion was typical tuberculous granuloma (figure 1).

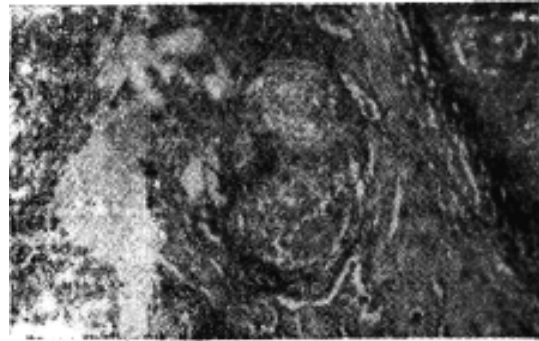


Fig. 1

Photomicrograph showing two tubercles with inflammation and fibrosis.

*Course*: Four days after operation she began to flex the left lower limb. Thereafter she showed a steady improvement in motorfunction. Her progress was impeded by severe cystitis which was satisfactorily managed by our urologist. Five weeks after operation she began to walk with support, having regained grade 4 to 5 power in the lowerlimbs, as well as sphincter control and sensations.

One week after surgery the CSF showed a fall in protein level to 2.7 gms. and 6 weeks later to 200 mgms % with no evidence of spinal block.

She has been discharged to continue antituberculous treatment at home.

### Discussion

There are two varieties of subdural tuberculomas of the spine. In the diffuse variety the dura is thickened all round and the granuloma of variable thickness surrounds the spinal cord. Dibble and Casino (1956); Jacoby and Koos (1961) and Jenkins and Hill (1963) have described such lesions. Some are localised and resemble benign tumors. (Arseni and Samitca, 1960; Slade and Glazer, 1955). The present lesion was of the diffuse type.

A preoperative diagnosis of the tuberculous nature of the lesion can be made with a reasonable amount of certainty when there is a history of tuberculous disease. Tuberculous meningitis preceded the development of the spinal granuloma in the cases reported by Slade and Glazer (1955); Arseni and Samitca (1960); Dibble and Casino (1956); and Jacoby and Koos (1961). Our patient was treated for tuberculous abdomen one year before she presented with signs of spinal compression.

Surgical excision is the treatment of choice followed by tuberculous chemotherapy. Two of the three patients of Arseni and Samitca (1960) showed improvement. The patient reported by Slade and Glazer (1955) showed some improvement and was able to walk with crutches. Dibble and Casino's case showed steady improvement from the 10th day after operation. The patient of Jacoby and Koos (1961) however did not show improvement in motor power.

The rapid clinical and biochemical recovery in our patient is attributed to the surgical decompression plus tuberculous chemotherapy and corticosteroids. While the former two are by themselves sufficient to effect a cure, it is felt

that the addition of steroids has hastened the recovery remarkably.

### Summary

A case of subdural extramedullary tuberculous granuloma treated surgically with rapid improvement postoperatively is reported. The value of postoperative corticosteroids in hastening neurological recovery has been stressed.

### ACKNOWLEDGEMENTS

We are grateful to the Superintendent of Government General Hospital, Kurnool, for permission to publish this case. Our thanks are due to Dr. N. Ramachandra Rao for referring the patient and to Dr. A.V.S. Reddy, for the management of the bladder.

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## PRIMARY TUBERCULOSIS OF THE CONJUNCTIVA

R.N. GANDHEWAR And P.J. MOKADAM  
(From Govt. Medical College, Nagpur)

Tuberculosis is not uncommon in India and this part of the country. But primary tuberculosis of the conjunctiva is rather uncommon. Various ocular manifestations of tuberculosis, either direct or allergic are commonly seen but primary tuberculosis of the conjunctiva is quite rare. During the last five years only one case of primary conjunctival tuberculosis has been recorded in this hospital. We are reporting a case of nodular type of primary tuberculosis of the conjunctiva in a child.

### Case Report

H.K.C. 5.1/2 years old Hindu male child attended the Eye O.P.D. Medical College Hospital, Nagpur, on 8.4.1972 with complaints of multiple swellings both lids, redness of both eyes and mucoid discharge from both eyes since six weeks. The patient was treated outside with various antibiotic ointments locally. The patient was not relieved of his symptoms. There was no history of any illness preceding the present complaints or illness in the past. There was no history of tuberculosis in the family or definite history of exposure to any tuberculous patient.

*On general examination* —The child was well built and developed. There was no pallor or oedema. Pulse, Respiration, B.P. was within normal limits. There was enlargement of the preauricular lymph glands on both sides. Generalised lymphadenopathy was absent.

*On Systemic Examination* —Live and spleen was not palpable. Respiratory system was normal. C.V.S. revealed no abnormality. C.N.S. was normal.

*On examination of the eyes* — The lids were swollen. At places marked local swellings (Fig. 1) similar to chalazion were present. There was conjunctival congestion. Palpebral conjunctiva was more congested than bulbar in both eyes. Multiple nodular swellings were present on both upper and lower palpebral conjunctiva in both eyes. Mucoid discharge was present. Cornea was normal. Visual Acuity in each eye was 6/6. Preauricular lymph nodes were enlarged, mobile and not tender. Rest of the eye examination was within normal limits. Fundus examination was normal.



Fig. 1

Clinical photography of the patient showing localised swellings.

### Investigations

The total leucocyte count was 11,200/cmm. The differential leucocyte count was : Polymorphonuclear neutrophils 70%, Lymphocytes 28% and Eosinophils 2%. E.S.R. (Wintrobe) was 22 mm. at the end of first hour. Urine and stools examination was normal. Mx test was 3mm. only. X-ray chest was normal. Conjunctival smear showed presence of a few pus cells, epithelial cells and staphylococci. Culture was not done. Biopsy from the conjunctival nodule was typical of tuberculosis (Fig. 2). Animal inoculation was not done.

### Discussion

Primary Tuberculosis of the conjunctiva is uncommon. The first observation of tuberculous infection of conjunctiva was done by Arlt (1864). Tuberculomata occurring in the conjunctiva had been demonstrated by Koster (1873). But credit goes to Sattler (1874) who described the first clinical cases of tuberculous ulceration. Primary tuberculosis of the conjunctiva had been reported in most of the cases in the first two decades of life. The present case was also in a child. It might be exogenous or endogenous. In our case there was no definite history of contact. In most of the cases at the beginning of the primary lesion, it is associated with some fever, malaise and general symptoms (Duke



Fig. 2

Clinical photography of the patient showing nodular swellings of both lower palpebral conjunctiva.

Elder, 1965). But such definite history was absent in the present case. Probably such minor symptoms might have passed unnoticed. We thought it was a case of primary type of tuberculosis of conjunctiva because we could not find any other tuberculous focus in the body. Moreover the MX test was 3 mm. only which is taken as negative. Tuberculin test becomes positive in most of the cases after 6-8 weeks of tubercular infection. In the present case there was history of six weeks' duration only. Samuelson (1936) reported enlargement of regional lymphnodes in primary infection type only. In the present case also there was enlargement of the pre-auricular lymph nodes.

In primary tuberculosis of the conjunctiva palpebral conjunctiva was affected in 70 to 80% of the cases reported. Cassady (1965) reported in 70% of cases. In our case also there was involvement of the palpebral conjunctiva only. Clinically the condition had to be differentiated from all forms of Parinaud's syndrome, Ophthalmia nodosa, spring catarrh, trachoma etc. The present case was also like that of Parinaud's syndrome. Chandler and Locatcher Khorazo (1964) reported a case of primary tuberculosis of the conjunctiva with vernal like appearance with lymphadenopathy. Many clinical types of primary conjunctival tuberculosis have been described. The present case was that of nodular type. The histological picture (Fig. 2) was suggestive of nodular type of tuberculosis.

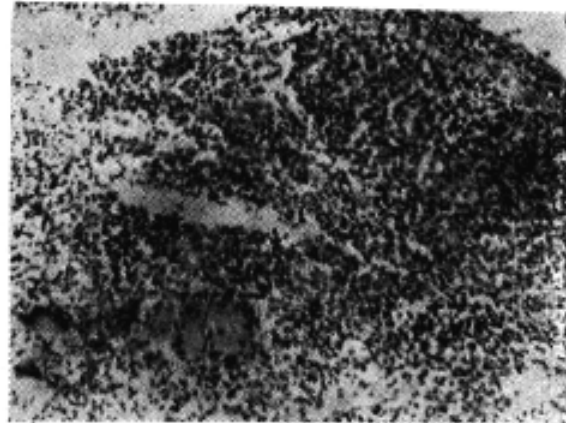


Fig. 3

Photomicrograph showing giant cells epithelied cells and lymphocytes.

### Treatment

The patient was advised antitubercular treatment.

### Summary

A case of Primary Tuberculosis of the Conjunctiva is reported because of its rarity.

### ACKNOWLEDGEMENT

We are thankful to Dr. Ishwarchandra, Professor of Ophthalmology, Medical College, Nagpur, for his guidance and encouragement. We express our thanks to Dr. V.B. Pathak, Dean, Medical College, ISfagpur, for according permission to publish the case. We are also thankful to our colleagues in the Department of Pathology and Shri Joshirao, the photographer, of the institution for his valuable help.

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## TUBERCULOSIS OF THE MANDIBLE

A.A. KHAN, ANSAR A. KHAN, And A.A. IRAQI  
(From Muslim University, Aligarh)

Mandible is affected by a variety of pathological lesions, but its involvement by tuberculosis is extremely rare. Chatopel (1930) claimed that up to 1922 only 50 cases of this lesion were described. An additional 14 cases were reported from 1922 to 1939 (Meng 1940). Since then occasional cases have been recorded by Stuteville and Hulswit (1948), Pekarsky (1954), Spilka (1955), Allan (1956), Taylor and Booth (1964) and Weidmann and MacGregor (1969). The lesion has predominantly been reported in the ramus of the mandible, which on roentgenography showed multiple cystic areas. We did not come across any report on the tuberculous osteomyelitis of the mandible in the available Indian literature and considered it worth reporting, because of its rarity,



Fig. 1

Shows multiple lytic areas in the body of the mandible.

### Case Report

R.W., a 22 year old female, was admitted on 20th April 1971 with the complaint of swelling of the lower jaw on the left side for preceding 9 months. To start with it was painless but later pain appeared in that swelling. One week before the admission she started having discharge from the mouth, which used to increase on pressing the swelling. On examination she was a well nourished lady. There was a diffuse swelling in the lower jaw on the left side, which was firm, nontender and fixed to the underlying bone. Intraoral examination revealed an opening on the inner aspect of the mandible with a greyish discharge coming out of it. The breath was foul smelling, and 1st and 2nd molars were missing on the left side. There were discrete, enlarged and tender lymph nodes in the neck on the same side. The erythrocyte sedimentation rate was raised to 60 mms for the first hour. The serum calcium, inorganic phosphorus and alkaline phosphatase were within normal limits. The chest skiagram showed no evidence of tuberculosis. The x-ray of the left lower jaw revealed multiple radiolucent areas in the body of the mandible (Fig- 1).

After a course of broad-spectrum antibiotics, lasting for 7 days she was operated and curettage was done. The cavity was full of soft cheesy and necrotic material, which on histological examination showed tuberculous granulation tissue. Antitubercular treatment was then started. After 2 years of follow up of the patient the lesion was found to be completely healed.

### Summary

A case of tuberculosis of the body of the mandible without pre-existing pulmonary focus, has been reported.

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## TUBERCULOSIS OF THE TONGUE

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(From Lady Hardinge Medical College & Hospital, New Delhi)

The primary tuberculosis of the tongue is very rare but usually lingual tuberculosis is associated with pulmonary or laryngeal tuberculosis.

The incidence of lingual tuberculosis reported or reviewed by several authors varies from .02% to 1.9% (Table I). Although there have been many reviews of the subject in the past (Weinstein 1914, Marrow and Miller, 1922, Finney and Finnsy, 1925 and Kanwar et al, 1970), we report here one such case of lingual tuberculosis.

### Case Report

Table 1

*Incidence of lingual tuberculosis according to different reports*

Author	Percentage
Farber <sup>5</sup> et al	0.1
D' Aunoy <sup>3</sup> and Associates	0.02
Titche <sup>13</sup>	0.3
Myerson <sup>2</sup>	0.3
Willek <sup>**</sup>	0.1
Fisher <sup>**</sup>	0.4
Chiari <sup>**</sup>	1.9
Chawson <sup>2</sup>	0.2
Katz	19.9*

\* } See discussion quoted in referenced.  
\*\* }

L.D. 40 years old female was admitted in this hospital on 28.6.73 with the chief complaints of fever off and on with evening rise of temperature, burning micturition, loss of weight for four months, painful nodule on the tip of the tongue for last three months. She denied symptoms referable to respiratory system.

On examination she looked chronically ill and thin built, lymphnodes not palpable, pulse

regular good in volume 100/min. Temperature ranged between 103-105° F. B.P. 110/70 mm Hg. Examination of the respiratory system revealed scattered crepts over both apices and mid zones. On the left side of the tip of the tongue pea size nodule firm in consistency (fig., 1), no evidence of inflammation. Fundi showed multiple tubercles.



### Investigations

Hb. 8.2m %, TLC: 7700/cu mm., P84%, L13 %, E1 %, M2 %. ESR was 66 mm in the 1st hour. Examination of the sputum for AFB was positive. Blood urea 30-38 mgm%. Urine full of pus cells and culture revealed heavy growth of pseudomonas pyocyaneus sensitive to gentamycin. Skiagram of the chest showed bilateral apical infiltration with cavity in the left mid zone.

Biopsy was taken from the tongue lesion and histopathological report revealed lesion to be tubercular in nature. She was put on gentamycin and antitubercular treatment, her temperature settled and she was discharged on antitubercular treatment on 17.7.73. She was next seen on 18.9.73; the nodule on the tongue was smaller in size and less painful. Patient expired on 7th November 1973 at home after a bout of severe haemoptysis.

## Discussion

The incidence of lingual tuberculosis is less than 1 % of oral tuberculosis (Komet et al 1965). This low incidence is probably because of the use of modern powerful antitubercular agents for the treatment of primary tubercular focus in the body.

Tuberculosis of tongue is more common in men than in women. It is generally accepted that this condition is usually secondary to tubercular involvement of the other organs principally the lungs. Tubercular infection of the tongue usually occurs due to direct contact with the infected sputum. (Ghose 1966) but the other routes of infections mentioned are lymphatic spread, hematogenous spread and extension from the involved neighbouring tissues.

Pathologically, Aird(1957) has described five types of lesions (i) Tubercular ulcers, (ii) Tuberculoma, (iii) Tubercular fissure, (iv) tubercular papilloma, (v) tubercular cold abscess. Earlier authors have also observed the frequent association of lingual tuberculosis with far advanced pulmonary disease and tuberculosis of the larynx and intestine. (4,2, 5,13, 9) Among those detected clinically the edge and the tip of the tongue were affected most (5,13,15) often clinically it is difficult to diagnose lingual tuberculosis but the only positive method of diagnosis is by biopsy. The condition has to be differentiated from carcinoma, gumma and chronic non-specific ulcers of tongue.

The prognosis as to life depends largely on the underlying tuberculosis in other organs. The treatment of lingual tuberculosis is that of tuberculosis in general. However surgery in the form of local resection may be required if the lesion persists or a cold abscess forms.

## Summary

A case of tuberculosis of the tongue is reported and the literature is reviewed.

## ACKNOWLEDGEMENT

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**REPORT  
ON  
TERMINOLOGY FOR PULMONARY PHYSICAL SIGNS**

R. VISWANATHAN

**Introduction**

It is often said that "chest is difficult", meaning thereby the physical examination and interpretation of signs. "Chest" on the other hand, should not be difficult if only systematic methods of physical examination sanctified by ancient physicians like Hippocrates and subsequently amplified by Laennac who introduced the method of auscultation for the first time, are systematically followed.

One of the important reasons for "Chest" being difficult is the confusing terms used by different authors. Even Laennac, for instance, has used the word 'rhonchus' to indicate all forms of added sounds heard during auscultation. He has also used the word "rales" to represent the rattling sounds of impending death. Now-a-days "creps" and "crackles" are the commonest medical slang used both by physicians and medical students.

Modern text books on Diseases of the Chest give very little importance to physical examination. On the other hand, chapters are devoted to other methods of examination like Radiology, Tomography, Bronchography, Bronchoscopy, Scintigraphy etc. No doubt such sophisticated procedures may be required in a few problem cases. They are without question necessary methods of investigation in specialised Chest Institutes, which act as the appellate court for problem cases and which are centres for post-graduate training.

However, such sophisticated methods are not available to the vast majority of chest physicians working in the districts. For them, the diagnosis of chest diseases depends almost entirely on physical examination, with or without radiology. No doubt examination of sputum is a simple procedure which ought to be conducted by all chest physicians in India where tuberculosis continues to be the most important public health problem.

In order to facilitate the recording and interpretation of the data obtained by routine examination, uniformity of nomenclature is essential.

A Committee of Experts was appointed to rationalise the terminology pertaining to physical examination of the Respiratory System. Their recommendations were later circulated to some of the leading chest experts in different States for

their comments. The Committee's report, the expert's comments as well as the recent report on 'Pulmonary Terms and Symbols' published in May 1975 issue of "Chest", have been taken into consideration in formulating the following terminology :

In order to facilitate communication between members of the medical profession and in particular between examiners and examinees, it is considered eminently desirable to use common terms for pulmonary physical signs. Adoption of common terms will obviate necessary confusion and facilitate understanding. It is hoped that the suggested terminology will be adopted by all students, teachers and practitioners of medicine.

**Importance of physical examination**

While recognising the usefulness of the more modern methods of instrumentation techniques, it should be emphasised that such methods can only supplement and not supplant routine systematic physical examination. This consists in employing the physician's senses—sight, touch, and hearing. The time-honoured system of inspection, palpation, percussion and auscultation should be adopted.

*Inspection* : Every patient should be examined with chest stripped to the waist. The subject should be made to sit in relaxed state on a revolving stool. This will facilitate the inspection of the patient from all sides by rotating the stool. The patient may be made to sit sideways, particularly during auscultation. This is done mainly to avoid the patient breathing or coughing on the physician's face. It is necessary to examine the patient, lying down as well.

*Palpation* : Apart from eliciting tenderness or rigidity, ascertaining the position of cardiac impulse, position of the trachea, abnormal pulsations, skin temperature and swellings, assessing of voice vibrations felt during palpation, will be of use. The term recommended for such vibrations is "*vocal fremitus*". It may be 'absent', 'normal', 'diminished'. The term *friction fremitus* may be used to indicate tactile vibration felt in dry pleurisy.

*Percussion* : The technique to be adopted for percussion cannot be over-emphasised. What is heard on percussion is to be called "*percussion note*". Percussion note can be 'normal',

'diminished' or 'increased'. The term '*tympani-tic note*' can also be used in describing the sound heard while percussing over pneumothorax, large cavity or stomach distended with air.

#### *Auscultation :*

(1) In order to elicit voice sound during auscultation, the subject may be asked to say 'ninety nine' if English speaking, and 'teen teen' if Hindi speaking. The sound heard is to be called "*vocal resonance*". It may be 'absent', 'normal', 'diminished' or 'increased'.

(2) Normal sounds heard on auscultation during breathing is to be called '*vesicular*'. When breath sound over any part of the chest resembles the sound heard when auscultating over the trachea, it is to be called '*bronchial*' which is ordinarily a high-pitched sound.

Bronchial breath sound is a "loud, harsh, high pitched, snorting type of sound with a distinct pause between inspiration and expiration, the latter being even longer, more harsh and higher pitched than the former."

When the breath sound has a hollow, reverberating quality commonly heard over a large empty cavity, communicating with a bronchus, it is to be called "*amphoric breathing*".

(3) *Added sounds* :- All extraneous sounds heard during auscultation are to be called "added sounds". Added sounds may be either interrupted or uninterrupted.

Fine, constant, clear-cut high-pitched interrupted sounds heard chiefly at the end of inspiration, uninfluenced by coughing, resembling the sound heard when rubbing a lock of hair near the ear, are to be called "*crepitations*." They are usually due to separation of the walls of sticky alveoli.

The term "rale" is to be used for all other interrupted sounds, usually resulting from the bursting of small or large air bubbles in the bronchiolar or bronchial secretion. The rales may be medium or coarse.

(4) Uninterrupted added sound is to be called "*Rhonchus*" which is generally due to the narrowing of air passages. They may be divided into "wheezing or cooing", "medium" or "coarse".

The sound of "pleurisy" is to be called "*friction rub*". It is a to and fro grating type of sound.

The following terms are also recommended:

(i) "*Whispering Pectoralogy*" :- Whispered voice which is ordinarily inaudible over a normal chest, can be heard over solid area lying near a bronchus. It may either be consolidation, tumour or enlarged lymphatic gland.

(ii) "*Post-tussive Suction*" : It is the name given to a sucking sound heard immediately after the cough sound, over a cavity.

(iii) "*Succussion splash*" : This term is used to represent a splashing sound heard during auscultation, while the chest is jerked to and fro. It is generally heard in a case of hydro-pneumothorax.

(iv) "*Coin sound*:" This is a metallic sound heard while auscultating in front of the chest in a case of tension pneumothorax while percussing over back of the chest using two coins as plexor and pleximeter.

(v) "*Fibrotic rales*" : This term is suggested for interrupted sounds heard during auscultation in cases of interstitial fibrosis, with neither cough nor sputum.

(vi) *Leathery rales* : In some cases of bronchiectasis to and fro interrupted sounds with a grating quality are heard. They may be mistaken for friction rub. They are termed leathery rales.

Language is the means of communication between human beings. Certain terms are expected to have certain meanings. If multiple terms are used to convey the same meaning, there is bound to be confusion. Hence it is advisable to use only one term to convey one meaning.

### **Terms at a glance**

#### *Palpation :*

Vocal fremitus  
Friction fremitus

#### *Percussion :*

Percussion note  
(a) Normal; (b) Diminished; (c) Increased;  
(d) Tympanatic.

#### *Auscultation:*

Breath sounds:  
(a) Vesicular (normal); (b) Bronchial; (c) Amphoric,

REPORT ON TERMINOLOGY FOR PULMONARY PHYSICAL SIGNS

*Added Sounds :*

- |  |                                 |
|--|---------------------------------|
| (a) Crepitations                                   | (2) Post-tussive suction        |
| (b) Rales: (i) Fine; (ii) Medium; (iii) Coarse.    | (3) Succussion splash           |
| (c) Rhonchi: (i) Coarse; (ii) Medium; (iii) Coarse | (4) Clicking or Crunching sound |
| (c) Friction rub.                                  | (5) Pericardial rub             |

*Additional Terms:*

- |                            |                           |
|----------------------------|---------------------------|
| (1) Whispering pectoralquy | (6) Pleuropericardial rub |
|                            | (7) Coin sound            |
|                            | (8) Fibrotic rales        |
|                            | (9) Leathery rales.       |

## REPORT ON TB CONTROL PROGRAMME IN LIBYA

M.D. DESHMUKH

On the recommendation of our Ambassador to Libya — Shri Homi J.H. Taleyarkhan and at the invitation of the Health Ministry of the Arab Republic of Libya, the Government of India deputed Dr. G.D. Gothi and myself to visit Libya for a little over two weeks in the first half of December 1974. The object of the visit was to review the Libyan National Tuberculosis Programme and to make suitable recommendations for improvement.

We visited the two main Tuberculosis Regional centres at Tripoli and Bengazi as also a number of Tuberculosis Control Centres, Tuberculosis Hospitals and allied institutions, held discussions with officials at different levels, studied documents supplied by the Health Minister and then made a detailed report to the Government of Libya.

### Libyan Arab Republic

Libya is roughly square in shape, with the Mediterranean forming the northern border. Egypt and Sudan are to the east, Chad and Niger south and Algeria and Tunisia to the west. Although the surface area is over 1.1/2 million sq. meters, 4/5th of it is a sandy desert. The total population is only about 2.1/2 million, 90 per cent of people living in the narrow fertile strip along the Mediterranean. It was here that the early Phoenicians followed by Greeks and Romans settled. There are some spectacular excavations of their early settlements which we had the opportunity to see during our tour (Leptis, Sabratha, Cirene etc.).

The climate in the coastal region is mild and sunny (Mediterranean) with summer temperature of 35° to 48° and winter temperature of 2.6° to 5° C. Rainy season is from December to February.

The climate in the Southern desert region is of extremes of temperatures ranging from 1° to 2° to 40° C and with frequent dust storms.

### Socio-Economic Pattern

Although some agricultural projects and small scale industries are being established, the main activity appears to be housing projects both in cities and villages. Modern concrete blocks are coming up everywhere.

The only exports in old days used to be olive oil and dates but now, of course, Libya is fore-

most among the oil producing countries. When the petrol boom started in 1961, per capita annual income was 88 Libyan Dollars. By 1970, it had zoomed up to 549 and is rising year by year. The Libyan dollar, by the way, is worth about Rs. 25.00. Ungainly sights of the new riches are the numerous grave yards of discarded cars outside the cities. The people do not strike one as typical Arabs, most of the city dwellers wearing western dress. The complexion ranges from very dark as in the Barbers to fair as in the southern European races. The religion is Moslem and language spoken Arabic. The people are well disciplined and law abiding. The incidence of crime is low probably because of 'total prohibition' on alcoholic drinks and severe punishment for crimes. But there is also no class distinction. All live in brotherly fraternity. Even the drivers of the cars are treated like equals, never being left alone in the front seat. Health Minister used to drive himself to his office in his Volkswagen.

Health and education facilities are rapidly expanding, both being completely free for all subjects. But there is a great shortage of technicians and teachers. Most of the technical work is done by imported technicians. In 1972 there were only 74 Libyan doctors and many of them were pursuing higher studies abroad. Medical College at Bengazi started only 4 years ago and the one in Tripoli 1 year back.

### Health Services

The country is divided into 10 Governates (Mohafidats) each having Governor responsible administratively for implementation of all nationally approved programmes. The Governor is assisted by a Director for each department.

In the central Ministry, there is a Health Minister with an Under Secretary and six Health departments namely (1) Preventive (2) Curative (3) Endemic Diseases (4) Medical equipment and supplies (5) Planning and Follow up (6) Administration and Finance.

The Endemic Diseases Department has 5 sections responsible for Prevention and Control of the following —(1) Tuberculosis (2) Trachoma (3) Schistosomiasis (4) Malaria (5) Leprosy.

### Tuberculosis Control Programme

In 1965, there were only 19 doctors working in the field of tuberculosis. A total of 612 beds

Were available for institutional treatment — 305 in general hospitals and 307 in the two specialised tuberculosis hospitals.

In 1963, a Pilot Project was undertaken jointly with WHO help at Bengazi. This led to subsequent planning of National Tuberculosis Control Programme.

In 1968, N.T.P. was expanded to cover the whole country. The accepted principles were (a) diagnosis to be confirmed bacteriologically (b) treatment to be mainly on domiciliary lines. The main difficulty was not financial, for the country was by now affluent, but shortage of technical staff both medical and paramedical.

### Organisation

The tuberculosis section, headed by the section chief, Dr. Ashraf of Pakistan, is responsible for planning, organising and supervising the TB Control Programme. He is also responsible for assessment and evaluation of progress and coordination of the anti-tuberculosis services with other departments, particularly the I.N.A.S. which is something like our Employees State Insurance Scheme or E.S.I.S. and also with Army Health Institutions to ensure uniformity of T.B. Control Programme throughout the country.

### Regional Tuberculosis Centres and Peripheral Tuberculosis Control Centres

The western and eastern regions have each a Regional Tuberculosis Centre at Tripoli and Bengazi respectively. The Tripoli centre has under its jurisdiction eight Tuberculosis Control Centres (Zamia, Zavera, Khoms, Mirurata, Yefron, Gharian, Tarhima, Sabha) and 2 Tuberculosis Hospitals (Abu Sitta and Ben Ghasir).

Bengazi Regional centre has six T.B. Control centres — (Tobrauk, Derna, Bieda, AlMarj, Ajdabia, Sirt) and three TB hospitals (Shahat, Gwareha and Kwafa).

Both regional centres are well equipped with M.M.R. (1 stationary and 4 mobile) bacteriological laboratories and B.C.G. section. The staff consists of 4 or 5 T.B. specialists, x-ray technicians, health visitors and other auxiliary staff.

At both the regional centres and control centres two main categories of patients attend — (a) Symptomatics and (b) workers for fitness certificates. The attendance of symptomatics did not strike us as very heavy but the work in the other category was voluminous. At Tripoli

an average of 350 workers attend every day for M.M.R.

The peripheral centres appeared to have very few patients on the register for treatment. In one centre catering for about 50,000 population there were only 35 TB cases in 1973. Standard forms were used for recording and were meticulously filled to the extent of re-duplication of some of the registers. Most of the forms used are, by the way, like our N.T.P. forms. The WHO Expert in Bengazi project had worked at N.T.I., Bangalore, before going to Libya.

Streptomycin (1 Gm. daily for 3 months), INH & PAS for 2 years, was the standard regimen. In case of resistance, Ethionamide, Pyrazinamide and Cycloserine are used and if these fail then only Ethambutol and Rifampicin are used. All Anti-TB drugs are strictly controlled by the State and are not available in the market. They are given to the patients after due registration at the TB Centres.

Although theoretically sputum positivity has to be established before starting treatment we saw many sputum negative and even x-ray negative symptomatics put on drug therapy. The drug regularity appears to be good (80 %) and recovery rate also high (60-70%). This is probably due to the fact that TB patients on treatment get a generous financial grant which can be stopped if they are irregular.

### Regional Laboratories

These laboratories not only deal with the work from the Regional centres but get specimens of sputum from all the TB Centres and TB Hospitals in the region. Vehicles are sent regularly once a week to collect these specimens. Culture and sensitivity tests are undertaken against primary drugs. Specimens are flown to Edinburgh for sensitivity tests against 2nd and 3rd line drugs.

The Control Centres of course have a small laboratory for direct microscopic examination of sputum specimens.

### Tuberculosis Hospitals

These are well staffed and well equipped, very spacious and scrupulously clean. Directors of Regional centres are also consultants in hospitals under their jurisdiction. Thoracic surgery is done in some hospitals regularly and only sporadically in others.

The basis of priority of admission are acute disease, complications and surgery.

The admissions are usually through the clinic.

The average stay is 5-6 months.

### Training

The training of various categories of staff is in service training' at the Regional Centre. Various training manuals prepared jointly by the Health Ministry and WHO are used for training e.g. (1) Principles and Methods (2) Manual for x-ray technicians (3) Manual for laboratory workers (4) Manual for BCG Technicians (5) Manual for Reporting and recording.

BCG is taught to nurses in their training course.

### B.C.G. Vaccination

BCG policy is very successful achieving nearly 100% cover for children under 15 because of the following steps :

1. BCG is made compulsory by law. It is obligatory in the first month after birth. No birth certificates is given unless certificate of successful BCG vaccination is produced. All maternity hospitals give BCG to the new born within 48 hours of birth.

2. For those who miss it at the maternity hospitals, Maternity and Child Welfare centres which are in profusion, give BCG Vaccination.

3. School Medical Services also give BCG Vaccination in schools.

4. Tuberculosis control centres send techni-

cians to schools every year to do tuberculin test on the new entrants and give BCG Vaccination to negative reactors.

5. All adults attending for fitness certificates, if found clear, are given BCG vaccination.

6. Contacts of known Tuberculosis and Leprosy patients are given BCG vaccination.

We verified the fact that BCG policy was very successful by stopping some school children on their way to school. All had BCG scars.

### Tuberculosis Position in Libya

There are no reliable data available on the basis of well planned National Surveys. It is believed that tuberculosis prevalence is comparatively higher in coastal belt than in the interior. In 1957 a survey in the Southern desert region was undertaken when 8,917 persons were clinically examined. Only two cases of pulmonary tuberculosis were found.

### Tuberculosis Infection Rate

In 1960, tuberculin testing was carried out in the age group 15-18 years around Tripoli where 80 per cent were found positive. In the Southern desert region in the same age group the rate of conversion varied from 19 to 47 per cent.

A limited tuberculosis survey was carried out in 1959 by the Government of Libya with the help of WHO. 2808 persons of all ages selected from nine urban and rural areas of the north eastern part of the country were examined by tuberculin test, x-ray and sputum examination.

The following table gives the findings :

Areas	Tuberculin Positivity		X'ray shadow of TB Active & Inactive	Sputum positive rate
	10-14 years	All Ages		
Rural	43.0 %	31.0 %	4.7 %	0.8 %
Urban	46.5 %	52.6 %	6.7 %	2.7 %
Both	—	48.6 %	5.8 %	1.8%

As the survey was limited to a small part of the country and sample size was less than 0.2 % of the total population, it would be obviously incorrect to apply these findings to the whole country for estimation of the total tuberculous problem.

A study of tuberculin positivity in school children (6-9 years) of Tripoli and Bengazi compared to North Eastern study in 1959 gives following results :

Age	Bengazi 1969	Tripoli 1971	Bengazi and Cyranimica 1959
6—9	7%	8%	21.9%

The difference observed in these two studies suggests that either the epidemiological position has changed or technique adopted in the two studies was not identical. There is no information about low grade sensitivity due to mycobacteria other than tubercle bacilli.

#### Estimation of the Extent of Tuberculous Disease

The prevalence of sputum confirmed disease was reported to be 2.7% in urban areas and 0.8% in rural areas. The (average) combined prevalence was believed to be 1.8% of the total population. Thus there should be in the whole country about 20,000 sputum positive cases in the age group 15 and above. This would indicate that tuberculosis is a serious public health problem but the number of newly detected tuberculosis cases annually is about 1200 to 1300. The big gap may be due to either that the observed prevalence rates apply only to survey areas and not to the whole country or that Tuberculosis centres do not cover adequately the entire population and are unable to find large proportion of cases. Personal discussion with other specialists such as pediatricians, gynaecologists, maternity and child welfare workers, Chest physicians, E.N.T. specialists, dermatologists etc. gives the impression that there is little tuberculosis among their patients and the problem of tuberculosis in Libya may not be as serious as suggested by the limited survey of 1959.

The nature of the disease as seen by perusal of some x-rays taken in T.C.C. was not different from that seen in the Indian tuberculous

patients. A quick appraisal of the newly detected cases suggested that many tuberculous patients were elderly males.

#### Trends of Tuberculosis

With large scale direct BCG vaccination of infants and children, trend of infection could not be assessed. There appears to be a gradual reduction of the number of cases diagnosed: yearly 9.4 per 1000 in 1971, 5.3 per 1000 in

1973. The trend is despite intensified case finding activities since 1971 (In 1971, 1,24,377 and in 1973, 5,42,470 x-ray examinations). Information about prevalence of tuberculosis in southern part of the country is not available.

Excellent BCG cover, intensive case finding programme, higher proportion of cases in higher age groups, paucity of disease in infants, very little extra-pulmonary tuberculosis suggest that the anti-tuberculosis measures along with sound economic situation have favourably influenced the trends of tuberculosis.

#### Recommendations

Some of the important recommendations are given below :

1. Tuberculosis prevalence survey to obtain precise information on the tuberculosis problem should be undertaken.

A project may also be undertaken to study the trends of infection by tuberculin testing of unvaccinated school children year by year.

2. General Health Institutions should be involved in case finding and treatment programme. This should enhance case finding considerably. All patients with chest symptoms should be referred to T.C.C. for investigations.

3. Case-finding and treatment should be implemented in southern parts of the country at the general health institution level under the guidance and supervision of T.C.C.

4. Regional Tuberculosis Centres should regularly supervise the work of Tuberculosis Control Clinics with the help of a well trained supervising team consisting of a senior TB Specialist, laboratory technician and public health nurse.

5. Medical Officer incharge of T.C.C. should regularly review working procedure of his own centre and discuss with his staff ways and means to improve the work qualitatively and quantitatively.

6. Simpler record card for x-ray and sputum results should be evolved. Manuals for training different categories of workers need to be brought upto date.

7. Records on register may not be maintained. Cards and forms should be filled properly as per Manual recommendations.

&. Instead of maintaining case register at T.C.C. it would be better if each R.T.C. maintains a register regionwise. Statisticians could then help in timely evaluation of TB problems, monitoring of operational aspects and guidance of necessary action. If this is done, case index number could be given region-wise.

9. There are 600 TB beds in the country, These appear to be sufficient but if the proposed policy of increasing beds is implemented, these could be used for non-tuberculous chest disease.

Unduly prolonged stay in hospital should be looked into to ensure maximum utilisation of the available beds.

10. To boost the possibly fading immunity obtained from BCG Vaccination early in life it may be worthwhile to consider revaccination at school leaving age.

11. Thiacetazone may be used in place of the bulky doses of PAS after appropriate trials.

Intermittent (biweekly) regime of Streptomycin and high doses of Isoniazid may also be instituted after acceptability trials.

It is recommended that PAS in the 3-drug regimen may be replaced early by one of the 3 newer drugs — namely Pyrazinamide, Ethambutol and Rifampicin if response is not satisfactory. After 6 months if sputum is still positive, the remaining two drugs must be added. Timely surgical intervention will also reduce pool of resistant infectious cases.

12. Tuberculin positive children of young

age group in contact with open cases of tuberculosis may be considered for Isoniazid chemoprophylaxis.

13. It is recommended that research by individual groups as also coordinated multi-institutions research should be encouraged.

14. It is recommended that the Libyan National Tuberculosis Association be formed and steps taken to get it affiliated to the appropriate regional body of the International Union Against Tuberculosis.

15. A team of Libyan Nationals consisting of Medical Officers, Laboratory technicians, statisticians and nurses could be deputed to India for Programme Management Training at N.T.I. Bangalore.

With the interesting and instructive experience of the Libyan visit, the author has to put the following important observations for our Government to note

1. That B.C.G. was compulsory by law in the first month of life. No birth certificate was issued unless BCG Vaccination certificate was produced.

To implement this law —

(a) B.C.G. was given within 48 hours of birth in maternity hospitals.

(b) B.C.G. was given to children at home and to other preschool age children at Maternity and Child Welfare Centres which were profusely distributed in cities.

(c) School Medical Services also gave BCG to school children.

(d) TB Centres sent B.C.G. technicians to schools to vaccinate new entrants.

B.C.G. was supplied in 10 dose ampoules. The B.C.G. cover was thus made 100% for children.

(2) Anti-TB drugs were strictly under control of TB Centres and were not available in the market. All diagnosed cases whether by General Medical Practitioners or General Hospitals or Insurance Centres were referred to TB Centre for drugs. This prevented any possible misuse of drugs.

3. All labour force was subjected to M.M.R. examination. Unless a fitness certificate was obtained no employment was possible,

## NEWS & NOTES



Prime Minister Indira Gandhi

### PRIME MINISTER INAUGURATES SEAL CAMPAIGN

Prime Minister, Smt. Indira Gandhi, inaugurated the 26th TB Seal Campaign. She made a token purchase of 1,000 Seals at a special function at her residence on 3rd October. Inaugurating the Campaign, the Prime Minister stressed the need for making the people aware of the fact that tuberculosis is preventable and curable. She underlined the need for health education. The function was organised by the Delhi TB Association and Seals were bought by Shri Krishan Chand, Lt.-Governor, from Shri C.B. Khandelwal, President of the Delhi TB Association.

**West Bengal:** The Campaign was inaugurated in Calcutta by Dr. (Smt.) Phulrenu Guha on 2nd October, 1975 at a colourful function organised by the Bengal Association. Shri G. Saha, Sheriff of Calcutta was the Chief Guest. The Programme included presentation of Trophies and Plaques for meritorious services, presentation of Silver Manpatra to Dr. L.B. Banerjee, prizes to winners of the Arts & Crafts Exhibition essay competition, Flag Day collection, Award of Dr. A.C. Ukil Memorial Gold Medals and auction of a ten-rupee note autographed by Prime Minister Smt. Indira Gandhi. Sri B.M. Cariappa Secretary-General, Tuberculosis Association of India, addressed the gathering and opened the 19th Exhibition of Arts & Crafts by TB and ex-TB patients.

**Uttar Pradesh :** Under the auspices of the U.P. TB Association the Campaign was inaugurated in Lucknow by the Minister of Health, Shri Prabhu Narain Singh. The Minister assured full assistance of Government and Health Services for the success of the Campaign. The Association intends to raise Rs. 5 lakhs from the present campaign.

**Maharashtra :** In Maharashtra, the State Anti-TB Association in collaboration with the Lions Club of Wadala organised the Campaign along with the Joint Project of Immunisation for Children in Wadala. Sri B.G. Deshmukh, Commissioner, Municipal Corporation of Greater Bombay was the Chief Guest.

**Pondicherry :** In Pondicherry the Campaign was combined with the Sixth Rural Development Week sponsored by the Director of Health & Family Planning Services, Pondicherry. The programme included distribution of clothes to the patients and opening of the hospital Mahatma Gandhi Govt. Leprosorium.

**Andhra Pradesh :** The Campaign in Andhra Pradesh was inaugurated by Shri Kodati Raja-mallu, State Minister for Medical & Health, at a function organised by the TB Association of Andhra Pradesh in Hyderabad. Shri Rajamallu in an address stated that he would be intensifying the BCG Campaign in the State with the help of the State TB Association.

**Gujarat :** Srimati Hemaben Acharya, State Health Minister, inaugurated the Campaign in Ahmedabad at a programme organised by the Gujarat State TB Association.

**Jammu & Kashmir :** In Jammu & Kashmir the Campaign organised by the Jammu & Kashmir TB Association was inaugurated in Srinagar by the State Governor.

### EXPERT COMMITTEE

It was reported in the July 1975 issue of the Journal that representatives of the Association headed by Dr. M.S. Chadha presented a Memorandum to the Union Health Minister. One of the suggestions made in the Memorandum was to appoint a Committee to review the working of the National TB Control Programme in India. The Indian Council of Medical Research on the suggestion of the Government of India has

appointed a Committee consisting of the following :

1. Dr. R. Viswanathan	<i>Chairman</i>
2. Dr. K.N. Rao	<i>Member</i>
3. Dr. M.D. Deshmukh	"
4. Dr. N.L. Bordia	"
5. Dr. H.B. Dingley	"
6. Dr. S.P. Tripathy	"
7. Dr. D.R. Nagpaul	"
8. Dr. G.V.J. Daily	"
9. Brig. J.C. Chatterjee	"
10. Dr. B.N.M. Barua	<i>Member-Secty</i>
11. Dr. S.P. Pamra	<i>Member &amp; Project Officer</i>

The Committee will review the aims and objects, achievements, deficiencies, etc. of the N.T.P. in general by undertaking on-the-spot first-hand assessment of actual working of the programme at the level of D.T.C. and PHI in one or two districts in each of the five zones of the country, the pattern of working, in large metropolitan cities, participation of general medical practitioners and voluntary organisations, etc. and suggest necessary steps to be taken to provide coverage in the entire country and enlist the support and involvement of all concerned in the programme. The Committee is expected to complete its assignment and submit its report by the end of December, 1975.

#### NATIONAL CONFERENCE

The 30th National Conference on TB & Chest Diseases will be held in Hyderabad (A.P.) from Saturday, the 8th to Wednesday, the 12th November, 1975. Dr. H.B. Dingley, Chairman of the Standing Technical Committee, is the President of the Conference. The State Governor will be inaugurating the Conference.

Subjects selected for discussions at the Conference include (1) National TB Control Programme, (2) Primary Drug Resistance, (3) Follow-up of sputum negative x-ray positive cases of Pulmonary TB, (4) Chemotherapy, (5) Pyogenic Infections of the lung, (6) Amoebic Infections of lung and Pleura, (7) Para-medical services and (8) Assorted papers.

#### OPEN-AIR TB SANATORIUM

The Karnataka TB Association which has been conducting anti-TB Shibir in the slum areas in Bangalore, has a scheme for building an open air Cottage type 'People's Sanatorium' in the suburbs of Bangalore to accommodate 200 patients on the lines of Madanapalli Sanatorium in Andhra Pradesh. The ward will be in the form of small tenement with 3-4 beds with necessary facilities of Sanatorium. The State Health Minister, Mr. H. Siddaveerappa, has constituted.

a Committee headed by Mr. Y. Ramakrishna, former Health Minister, for this purpose. Dr. T.Manickam, Honorary Secretary of the Association, has appealed for liberal donations towards the scheme from each factory—Rs. 10,000 in the first instance and Rs. 2,000 to Rs. 3,000 for maintenance. The ward would be named after the donor/industry and would be reserved for its employees.

#### ANTI-TB SHIBIR

The 68th Anti-TB Shibir of the Maharashtra Anti-TB Association was held at Maulasar, Dist. Nagaur in Rajasthan on 16th and 17th August, 1975. The Shibir was jointly sponsored by the Somani Trust and the Rotary Club, Bombay. The Maharashtra Association held its camp at the time of the Annual Mela at Maulasar. The team visited the TB Sanatorium, Shri Kalyan Arogya Kendra, which is run by the Somani Trust. The team consisted of Dr. S.S. Viridi, Medical Officer, Organised Home Treatment Clinic, Dr. J.C. Kothari, Dr. Parikh, Dr. Gaggar and Dr. M.D. Deshmukh. They held the Camp at Primary Health Centre. In the case-finding drive nearly 25 % of the total attendance were symptomatics and 50 % of those screened showed radiological evidence of TB.

#### MASS VACCINATION CAMP

District TB Association, Chikmagalur, Karnataka, organised its 4th Mass BCG Vaccination and Health Education Camp at Kalaspura on 19th and 20th September, 1975. The programme included talks on Health Education and Mass sputum survey and BCG Vaccination.

#### TB CAMP : KAKINADA, ANDHRA PRADESH

The District TB Association of Kakinada organised a TB week to launch large scale BCG Vaccination in rural areas. Sri K. Rajamallu, State Health Minister, addressing the meeting said that the Government had decided to combat TB on war footing and funds for this would be provided by the Government and Panchayat Samities. Dr. V. Govindarajan, Collector, presided.

#### REFRESHER COURSE IN UTTAR PRADESH

The U.P. TB Association organised a two-day Refresher Course in Lucknow on 28th and 29th October in collaboration with the Indian Medical Association, for the benefit of general practitioners.

#### MEXICO CONFERENCE

Drs. R. Viswanathan, New Delhi, K. Nagappa Alva, M.P., Bangalore, S.P. Pamra,

New Delhi, H.B. Dingley, New Delhi and M.L. Mehrotra, Agra attended the 23rd International TB Conference held in Mexico from the 22nd to 26th September, 1975. Drs. Viswanathan and Nagappa Alva represented India at the Council Meeting of the Union. Drs. Viswanathan and Pamra presented at the Plenary Session of the Conference the paper on "A controlled drug trial to determine the efficacy of short term chemotherapy of pulmonary tuberculosis", giving results of the studies now in progress by the Research Committee of this Association. They also represented the Tuberculosis Association of India at the Executive & Council meetings of the Eastern Region of the Union. Dr. H.B. Dingley presented the paper on "Prevalence of endo-bronchial TB and bacteriological determination and primary drug resistance in pulmonary tuberculosis in children", and Dr. M.L. Mehrotra presented the paper on "Role of neighbourhood clinics in management of urban TB problem" at this Conference.

#### **XTH EASTERN REGION CONFERENCE**

The 10th Eastern Region Tuberculosis Conference of the International Union will be held in Seoul, Korea from 11th to 15th October, 1975. The Korean National TB Association will host the Conference.

#### **AMRUT MODY RESEARCH FOUNDATION AWARDS—Rs. 10,000 EACH.**

UNI Trust invites Scientists and Research workers in the field of Basic Medical Services, to send in their nominations for any original and outstanding work done on any single topic after 1st January, 1968. For details about sponsors, method of Nomination, forms etc. write to Shri A.M. Research Foundation, Unichem Bhavan, S.V. Road, Jogeshwari (West), Bombay-60.

#### **MEMORIAL PRIZES**

The Indian Academy of Medical Sciences, will be awarding a number of medals and prizes during the year 1975-76. These include Dr. S.S. Misra Memorial Bronze Medal to be awarded for the best unpublished work in any field of bio-medicine. Sir Shri Ram Bronze Medal to be awarded for published paper during the proceeding 3 years on any clinical subject. Dr. R.M. Kasliwal Prize Medal to be awarded to the best worker in the field of "Colon and its Diseases".

The next Post-graduate Membership Examination (Part I & II) of the Indian Academy of Medical Sciences will be held in February 1976. For details write to the Executive Director, I.A.M.S., C-II/16, Ansari Nagar, New Delhi-16.

#### **INDIAN COLLEGE OF ALLERGY AND APPLIED IMMUNOLOGY**

The 9th Annual Convention of Indian College of Allergy and Applied Immunology will be held at the V.P. Chest Institute, University of Delhi, Delhi, from the 30th October to 2nd November, 1975. This will be preceded by a three day WORKSHOP for training teaching staff of Medical Colleges and department of Botany from different parts of India in Aero-Biology, identification of allergens, preparation of antigenic extract and investigation including antigen skin tests and clinic immunology for allergic diseases and their treatment. Research papers not only on allergy and allergens but also on interesting aspects of immunology of these diseases including immunology of tuberculosis will be presented.

#### **OBITUARY**

##### **DR. R. KRISHNA**

Dr. R. Krishna, 75, one of our well-known TB workers, passed away on 22nd October. Dr. Krishna was the Honorary Secretary of the Delhi TB Association for a number of years. He was Resident Medical Superintendent of the Silver Jubilee TB Hospital, Delhi from 1937-57 and also Tuberculosis Officer, TB clinic, Queen's Road, Delhi. He was TB Adviser to the Delhi State Government. He worked as Officer on Special Duty for Delhi Pilot Project in 1964-67. In his passing away TB workers have lost a friend, philosopher and guide. The Tuberculosis Association of India offers its sincere condolences to the bereaved family.

##### **DR. G. SAMUEL**

Dr. O. Samuel, a noted TB worker, died in July, 1975. He was Medical Superintendent of Wanless TB Sanatorium in 1939 and later took charge of Mahatma Gandhi Memorial TB Sanatorium in Thanjavur District, built it up into a modern 500-bedded Sanatorium between 1951 and 1974. He was awarded Kaiser-i-Hind Medal in 1945. He was a popular figure incur National Conferences. Dr. Samuel who went to U.S.A. in June this year died in Michigan on 21st July and his body was laid to rest at the cemetery in Madras on 31st July. We offer our sincere condolences to the bereaved family.

## MESSAGE



**President Fakhuruddin Ali Ahmed**

The Tuberculosis Association of India will launch the twenty-sixth Tuberculosis Seal Sale Campaign on the 2nd October-Gandhi Jayanti Day—the day on which every year we re-dedicate ourselves to the service of our people.

The Seal Sale Campaign has served a two-fold purpose; it has aroused public consciousness about this insidious disease and helped our TB Associations raise some funds to carry out their activities in support of the official tuberculosis control programme. I am extremely happy that this Campaign has come to stay in our country and I sincerely hope that year by year Tuberculosis Associations will improve upon their previous achievements.

I am glad to renew this year again my appeal to our people to buy TB Seals in large numbers as a token of their support to this humanitarian cause.

## MESSAGE



**Shri S. Ranganathan**

The annual Tuberculosis Seal Sale Campaign, which is being organised by the Tuberculosis Associations from 1950, needs no fresh introduction. Starting on the second of October and terminating on another important national day—26th January—the Campaign provides a unique opportunity to associate the people with the fight against tuberculosis—a disease which affects the entire community.

Being insidious in nature and having come to stay as an endemic entity, tuberculosis eats into the vitals of our national life. It claims at any given time about eighty lakhs of people as its victims of whom some twenty lakhs are said to be infective. One can imagine the problems it creates to the individual sufferers, to their families and contacts and to the community. Our Government's National Tuberculosis Control Programme aims at discovering and treating as many TB patients as possible and protecting the healthy population with B.C.G. against infection. These objectives can be achieved only if the people are deeply involved in implementing the programme. The activities of the Tuberculosis Associations are calculated to secure people's participation and the Seal Sale Campaign in particular further helps realise this objective. A TB Seal, moreover, is a symbol of mercy towards those who have the misfortune to catch tuberculosis. The quality of mercy, as you know, is twice-blessed; it blesses those that give and those that take.

The past twenty-five Campaigns have helped in spreading this message of mercy to an appreciable extent in our country. They have also helped our TB Associations to collect funds to carry on their activities. Their efforts should further increase in the coming years since from now the implementation of the control programme becomes a more direct responsibility of the States. I have every hope that our TB Associations will rise to the occasion and help their Governments and the Tuberculosis Association of India in implementing the control programme. They should intensify the Seal Sale Campaign and the propaganda efforts and also raise more funds than they did in the past. I appeal to our Associations and to the people to make the forthcoming Seal Sale Campaign a resounding success.

# The Indian Journal of Tuberculosis

## ABSTRACTS

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### **Glucose Intolerance in Pulmonary Tuberculosis**

*Michael B. Zack, Lynn L. Fulkerson and Emanuel Stein. Amer. Rev. Rssp. Dis.; 1973, 108, 1164*

Although increased incidence of tuberculosis in persons with diabetes is well documented, there is insufficient information on the incidence of diabetes in patients with tuberculosis. Two hundred and fifty six consecutive patients with positive sputum admitted to a sanatorium in New York from 1965 to 1970 were investigated for overt or latent diabetes. Their ages ranged from 16 to 79 years with a mean of 51 years. All except one were men. The blood glucose concentration two hours after ingestion of 100 grams of glucose ranged from 55 to 597 mg% (mean value 148.4 mg%). One hundred and twenty three patients had abnormal glucose tolerance test. In the case of 18 patients another factor such as corticosteroid or diuretic therapy or fever etc. could have been responsible for the abnormality and they were, therefore, excluded. In the remaining 105 patients (41%) no other factor could be found to account for the glucose intolerance. Their mean age was 51.5 years. Fifteen of these were known diabetics.

The greater incidence of glucose intolerance in tuberculous population probably reflects an increased association between the two diseases. With the prevalence of tuberculosis shifting to the higher age groups and diabetes also starting usually in the higher age groups, the increased incidence is significant. Diabetes may well be the factor which precipitates endogenous reactivation of healed unknown tuberculous lesions.

S.P.P.

### **Extramedullary hemopoiesis with multiple tumor-simulating mediastinal masses in hemoglobin E-Thalassemia disease**

*J.L. Da Costa, Y.S. Loh & E. Hanam. Chest; 1974, 65, 210.*

Intrathoracic tumor-simulating heterotopic marrow in hemoglobin E-thalassemia is described

for the first time. The characteristic feature of these extra-medullary hemopoietic masses is the uniform radiologic picture of rounded, often tabulated para vertebral soft tissue opacities in the posterior mediastinum usually below the 7th thoracic vertebra. When this picture is associated with chronic hemolytic anemia, preoperative diagnosis is possible making surgical intervention unnecessary.

The opacities have to be differentiated from neurogenic tumors, Hodgkins disease, paravertebral abscess, primary or secondary malignancy and extra pleural cysts.

S.P.P.

### **Primary Pulmonary Histiocytosis X**

*Marjorie Smith, Lawrence J. McCormack, Howard S. Van Orstrand and Robert D. Mercer. Chest; 1974, 65, 176.*

Primary pulmonary histiocytosis X is a disease of unknown aetiology. The clinical and pathological features of 11 cases diagnosed in Cleveland, USA by lung biopsy are reviewed. The disease was found more often in males and the age range was 3 months to 59 years. Children suffering from this isolated pulmonary disease have never been reported earlier. Electron microscopic observations in one case revealed rod-like intracytoplasmic inclusions in some histiocytes. Although previously described in skin, bone and lung lesions, nature of these inclusions is not known.

The skiagrams showed bilateral diffuse reticular and nodular infiltrations in most cases. Some patients had associated emphysematous changes. In one patient the only finding was a localized area of emphysema and reticular infiltrates developed later in both lungs. In two patients there was hilar prominence in addition to the parenchymal changes.

The clinical findings varied. Older children and adults usually had chronic non-productive cough, sometimes associated with shortness of breath and chest pain. Other symptoms included

fever, loss of weight, wheezing and cyanosis. In infants the usual complaints were vomiting, dehydration and failure to thrive. There was no polyuria, polydipsia, bone pain or tenderness.

Six of the 11 patients died. The treatment was mostly corticosteroids, radio-therapy and cytotoxic drugs either alone or in combination.

**Thymoma: Clinical and additional radiologic signs**

*Talma Rosenthal, Marjorie Hertz, Yeheskiel Samra, & Nazim Shahin. Chest; 1974, 65, 428.*

Thymic tumors are not rare. Clinically, thymoma may be accompanied by serious disorders like myasthenia gravis, red cell anemia and hypo — or agammaglobulinaemia, which may lead to severe secondary infections. Pancytopenia, Thrombocytopenia and Pernicious anemia have also been mentioned. Myasthenia gravis may be present in 50-75 % of cases of Thymoma and 8-15 % cases of myasthenia gravis are due to thymoma. Radiologically it may manifest itself in two ways. The first type which is more common consists of an oval or lobulated anterior mediastinal tumor which may show calcification. The second type is less frequent and more difficult to detect. It consists of a plaque-like band closely attached to the pericardium and large blood vessels. The tumor may extend as far down as the diaphragm. On fluoroscopy the tumor shrinks in size during deep inspiration. This sign is characteristic and is not present in any other tumor or enlarged lymph gland in the anterior mediastinum.

S.P.P.

**Multiple Primary Bronchogenic Carcinoma**

*Jay J. Rohwedder and Lee Weatherbee. Amer. Rev. Resp. Dis.; 1974, 109, 435.*

Five patients with bilateral primary bronchogenic carcinoma of different cell types were identified in a review of 926 patients with lung cancer. Incidence of multiple primary carcinomas ranges from 0.2 to 1.8% in different reports. The range for multiple primary disease in other organs is 2 to 4%. Among neoplasms with dissimilar histology, combination of epidermoid and oat cell carcinoma was more common. In 4 out of 5, the primaries were synchronous and in one the second primary appeared after an interval of 4 years. All were heavy smokers. Re-operation for a second primary is possible and immediate results and survival period are more or less similar to the resection for a single primary.

S.P.P.

**Treatment of Oat-Cell carcinoma of bronchus by pre-operative radiotherapy and surgery**

*Michael Bates, Victor Levison, Raymond Hurt, Maurice Sutton. The Lancet; 1974, i, 1134.*

A series of 29 patients with oat-cell carcinoma of the bronchus have been treated by pre-operative super-voltage radio-therapy followed by resection when technically possible. The diagnosis was confirmed by histopathological examination of the biopsy material in 28 cases and by sputum examination in one case. All cases were considered as operable on bronchoscopic examination.

Of the 29 patients, pneumonectomy was done in 24 after radiotherapy. Four were found inoperable at thoracotomy and one had become inoperable on clinical evidence during the radiotherapy. The pneumonectomy was carried out within 7 days of the completion of radio-therapy. No cyto-toxic drugs were given. The 4 years survival in the series was 24 % as compared to the rate of 3-7% in the BMRC study where the treatment was surgery or radio-therapy.

S.P.P.

**Pulmonary Arteriovenous Fistulas**

*David E. Danes et al. Mayo Clinic Proceedings; 1974, 49, 460.*

Over a 20 year period (1952 to 1972), 63 cases of pulmonary arteriovenous fistulas were seen at the Mayo Clinic. 41 had a single fistula and in 22 the fistulas were multiple. In 5 patients the fistulas were bilateral. 41 were females and 22 males. The mean age was 41 years, range being 4 to 70 years. Only 4 patients were less than 16 years old. The fistula was with arterial blood supply in 60 cases and with systemic blood supply in 3 cases. 35 of the 63 total cases (57 %) had neither symptoms nor any sign of fistula and its presence was detected on a routine chest x-ray. When symptoms did occur, the most frequent was dyspnea. Cyanosis and clubbing were present in about 15% of the cases. Bruit was heard in 37 patients (60 %). The bruit was continuous in 22 patients with a single fistula and in 15 with multiple fistulas. There was evidence of hereditary hemorrhagic telangiectasis in 38 patients (60 %). In patients with pulmonary arteriovenous fistula and hereditary telangiectasis there is an increased incidence of multiplicity in fistulas, an increased rate of fistula growth and an increased frequency of complications. Diagnosis is based on angiography and tomography. The main radiological feature of a fistula is a round shadow without any evidence of calcification,

connected to the hilum through a blood vessel. The treatment of fistula is discussed in detail.

**S.P.P.**

**A Controlled Clinical Trial of the Role of Thiacetazone containing Regimen in the treatment of Pulmonary Tuberculosis in Singapore : Second Report.**

*Singapore Tuberculosis Service jBrompton Hospital/British Medical Research Council Investigation, Tubercle, (1974), 55, 251.*

Results of 18 and 36 months of the treatment of Pulmonary Tuberculosis in Singapore with streptomycin plus isoniazid for six months followed by isoniazid alone (SH/H) and streptomycin plus isoniazid plus thiacetazone for six months followed by isoniazid plus thiacetazone (STH/TH) showed that at 18 months, 98 percent of 107 SH+H and 98 percent of 89 STH+TH patients bacteriological conversion and 36 months, 98 per cent of 100 and 99 percent of 83.

Two of seven patients on two drug regimen with initial drug resistance showed bacteriological conversion compared with all of six patients on three drug regimen. Side effects after 12 months occurred in 4 percent of 116 SH+H patients as compared with 20 percent of 105 STH+TH patients. The side effects were mild in SH+H regimen, but 11 (10 percent) of STH+TH had severe reaction. In all except one, these were due to thiacetazone.

The mean Haemoglobin concentration rose significantly during treatment with the SH+H regimen but not with thiacetazone regimen. However, an increase did occur for patients on the later regimen once treatment had been stopped.

H.B.D.

**Small Pox and B.C.G. Vaccination in the New Born: Follow up Study:**

*A.B. Desai and B.L. Kabra, Indian Fed. April 1975 Vol. XII No. 6.*

Two hundred and forty four children, who had simultaneous small pox vaccination and B.C.G. at birth were revaccinated for small pox at one year of age to assess the degree of protection. Ninety seven percent had major revaccination reaction

or an equivocal response indicating adequate protection. Three percent had primary type of reaction indicating lack of immunity. Similarly 121 babies were given tuberculin test at the age of six weeks and those who were negative were retested after a further period of six to eight weeks. By six months of age ninety seven percent had a positive conversion. It is concluded that simultaneous small pox and B.C.G. vaccination at birth confer adequate protection.

**H.B.D.**

**Use of B.C.G. as an Immunostimulant in the Surgical Treatment of Carcinoma of the Lung**

*F. Ronald Edwards and Francis Whitwell. Thorax, 1974, 29, 654.*

Cell mediated immunity to cancer cell would appear to exert some control over the extension of tumour growth and stimulation of this factor might result in increased survival after surgical treatment of the tumour. Of the various agents used as stimulators, a single dose B.C.G. = Glaxo (5,00,000 organisms) was given subdermally 10 days after excision of lung carcinoma. The length of survival was used as the index of the effect of the B.C.G.

The aim of the study was to assess the safety of B.C.G. and a survival in the B.C.G. group. Although results are encouraging but are not statistically significant.

**H.B.D.**

**The management and evaluation of the Solitary Pulmonary Nodule.**

*Gary Trunk, Douglas R. Gracey, and Richard B. Byrd. Chest, 66.3 Sept. 74.*

None of the nodules in 137 patients below the age of 35 years was carcinogenic on an analysis of case records and radiographic findings.

Definite, though small risk of thoracotomy, surgical removal is not justified in this age group of patients, particularly if previous chest films show that nodule has not enlarged over the preceding two years.

Most calcified nodules need not be removed.

H.B.D.

**Controlled clinical trial of four short course (6 months) regimens of chemotherapy for treatment of pulmonary Tuberculosis.**

*Lancet Nov. 9, Vol. II 1974*

Second East African British Medical Research Council Study. A comparison has been made of 4, 6 month regimens in the treatment of newly diagnosed cases of advanced pulmonary tuberculosis. The regimens were

**SHR**

Streptomycin plus isoniazid plus rifampicin daily for 6 months.

**HR**

As above for 6 months but omitting streptomycin.

**SHRZ/TH**

An initial intensive phase of streptomycin, isoniazid, rifampicin plus pyrazinamide daily for 2 months, followed by thiacetazone, isoniazid daily for 4 months.

**SHRZ/S<sub>2</sub>H<sub>2</sub>Z<sub>2</sub>**

The initial 4 drug intensive phase as above for 2 months followed by streptomycin, isoniazid plus pyrazinamide twice weekly for 4 months.

The object of this study were firstly to assess

the extent of streptomycin contribution to the success of SHR regimen.

Secondly to assess the efficacy of 6 months regimens based on a 4 drug intensive phase using either daily TH or twice weekly SHZ during continuation phase.

At 6 months, only 3 of 734 patients were classified as having an unfavourable response. There was very little drug toxicity.

The bacteriological relapse rate between 6 and 12 months were 5% of 170 patients on the two drug combination, 2% of 166 patients on the three drug combination, 6% of I&O patients on the regimens with thiacetazone plus isoniazid in the continuation phase and 4% of 161 patients on the regimens with intermittency in the continuation phase.

Most of the relapses occurred by 9 months and all except 1 of 31 patients who relapsed did so with sensitive organisms.

It is concluded that all the regimens were effective, that the streptomycin in the triple regimen has not made any important contribution to therapeutic success and that reducing the rifampicin to 2 months has left effective regimens even when followed in the continuation phase by a standard daily regimens or a twice weekly intermittent regimen.

H.B.D.