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DIABETES AND TUBERCULOSIS

“A full life despite diabetes” is the theme for World Health Day this year for remembrance and rededication to fight the scourge. The slogan is most appropriate not only because diabetes is an important health problem but 1971 happens to be the golden jubilee year of the discovery of Insulin by Banting and Best of Canada.

Diabetes can neither be cured nor eradicated but its ravages can be greatly reduced by early diagnosis and proper treatment. It is also fortunate that the diagnostic method is rather simple and management by diet, drugs and exercise is comparatively easy with the patient's cooperation. The patients can also have normal span of life if the disease is kept under control. The onset of the disease is insidious and most of the cases remain undetected till the disease reaches an advanced stage. This is the greatest problem as undetected or uncontrolled diabetes can not only endanger life but may have many serious complications. Tuberculosis is one of them in which we are vitally interested.

In the fitness of things, this year should mark the start of a nation-wide campaign for early detection and to bring as many cases as possible from the unknown to the known pool, whose ratio may be even 10 to 1 today in India.

Epidemiological data should be the basis for proper planning of a campaign of this type. To our knowledge, no comprehensive national study on diabetes has yet been made. The following data on fairly limited studies on the prevalence of the disease are, however, available. Delhi (1961) Central Health Service employees 1.10%, their families—0.44%. Nine rural Health Centre population (1955-58)—0.31% to 0.66%.

Among all hospital admitted patients—Calcutta (1928-68)—0.71 %, Bombay—0.98%, and Medical College Hospitals in Calcutta, Agra, Jaipur, Nagpur and Mysore taken together from 1955-59 (Editorial, IJMA—1960) is—0.8%. The prevalence rate may, therefore, be roughly regarded as 1.0%. A special drive for diabetes detection in Bombay, however, indicated a much higher rate—2.5% to 7.0%.

Taking advantage of the knowledge that diabetes is mostly concentrated in the older age-groups and of the above mentioned limited studies, a case-finding programme may be started without delay, along with a mass educational programme to improve community awareness for early diagnosis. Urine examination for sugar for all the employees above the age of 35 years

in all large industrial and civil establishments may be organised with some financial and technical help from a central organisation. This should not be expensive or difficult as the blood test has been excluded and the work will need Technicians only with a few medical men for supervisory purposes. Urine may be collected after about 2 hours of a meal and examined at the establishment itself to avoid transport and other difficulties. The study may be extended later for school and college leaving age-groups and for the blood-relations of the diagnosed diabetes.

Attempts should also be made to make an extensive and thorough national study under a well designed common protocol like that of the "National Sample Survey" for Tuberculosis (56-57). Such a study should be easier to organise and less expensive for diabetes than for tuberculosis because of simpler diagnostic procedures and predominant prevalence in older age-groups. The study on Tuberculosis was undertaken by the Indian Council of Medical Research. The same council should be the pioneer in planning and organising this nationally important survey. Research on many unsolved basic problems of Diabetes should be encouraged by suitable grants.

The prevalence of tuberculosis among the diabetics is not precisely known. It appears to be 4 to 5 times more than the others from studies made abroad. The "Tuberculosis Sub-Committee of the Council" may also move to integrate a suitable plan of investigation for tuberculosis in the diabetes detected in this survey. The findings should be most useful for the control programme of both the diseases.

With the advent of potent anti-TB drugs, this unholy alliance of Diabetes and Tuberculosis is no longer so dangerous. Under the influence of Diabetes the character and evolution of Tuberculosis may have many adverse changes, but for controlled diabetes the ultimate prognosis of tuberculosis does not differ in any way. Since Tuberculosis too can be cured in almost all cases, a Diabetic with Tuberculosis can also expect "A full life despite both the diseases."

AWARD OF TAI GOLD MEDAL

The Tuberculosis Association of India awards every year a Gold Medal to a doctor who has done outstanding work in the tuberculosis field. The Association awarded the 1977 Gold Medal to Dr. K.N Rao, a distinguished colleague of all of us.

Dr. Kamarazu Narasimha Rao, was born on 31st January, 1907 at Gudivada in Andhra Pradesh, Dr. K.N. Rao took his M.B.B.S. in 1930. He had several distinctions in the Medical College, prizes in Physiology, Pathology, Medicine and Surgery, Medals for Clinical Surgery and Mid-wifery, Gy-



DR. K.N. RAO
naecology and diseases of the new-borns, diseases of children, Johnstone Medal and the Blue Ribbon as the best outgoing student. He joined the Indian Medical Service in 1935 in the military wing. He was a Prisoner of War in Singapore from 1942 to 1945. In 1946 he was transferred to the Civil Branch of Indian Medical Service. In 1948-49 he was Professor of Medical Jurisprudence in the Christian Medical College, Vellore, and in 1951 Professor of Tuberculosis in Stanley Medical College, Madras and the Tuberculosis Adviser to the Government of Madras.

Dr. Rao has published several books on Public Health and Medicine. Special mention may be made of his books on Medical Education, Nation's Health, Philosophy of Medicine, and India and World Health. Students of Public Health will recall his numerous lectures in various Universities. His papers on Surgical Treatment of Pulmonary Tuberculosis, Modified Thoracoplasty Operation and Tuberculosis Control and Role of General Practitioners are read with esteem and respect.

Dr. Rao was made Emeritus Professor of Tuberculosis in 1955. He was Director of Medical Services of Andhra from 1954 to 1963

and Director General of Health Services in the Government of India from 1964 to 1968. He was Chairman of the Expert Committee of the W.H.O. on Tuberculosis in 1964, Chairman of the Executive Board of W.H.O. 1967-68, First President of World Federation of Public Health Association, Consultant in Medical Education of the WHO/PAHO for Latin America in 1968, W.H.O. Visiting Professor of International Health at the Toronto University and WHO Consultant in Medical Education in Sierra Leone in 1970. As an authority on Family Planning and Population Control, Dr. Rao has contributed valuable papers for the guidance of the lay people and medical profession. He was a member of numerous Committees, Commissions and Councils in India and abroad, and is the recipient of coveted awards like Dr. P.N. Raju's Oration Award of the I.C.M.R., Sarabhai Oration Award of the Association of Physicians of India and B.C. Das Gupta Oration Award of the Indian Public Health Association. Honorary L.L.D. was conferred on him by the Shree Venkateswara University, Tirupathy.

As Chairman of the Tuberculosis Association of India, while he was the Director-General of Health Services, he did a great deal to expand the activities of the Association in various ways. He presided over the National Tuberculosis Workers' Conference in 1966. He initiated the compilation of a Text-Book on Tuberculosis and is its Chief Editor. For nearly 40 years Dr. Rao has served the cause of health, especially Tuberculosis with rare devotion, foresight and leadership. It is in the fitness of things that the Tuberculosis Association honours this great son of India with its Gold Medal. On behalf of the Tuberculosis Association of India, workers in the Tuberculosis field and on my own behalf, I congratulate Dr. Rao and wish him several years of service to humanity.

HEAT KILLED BCG VACCINE AS A "TUBERCULIN TEST" COMPARED WITH PPD-RT-23 WITH TWEEN 80 AND OLD TUBERCULIN

N. L. BORDIA

Introduction

Tuberculin test is an important tool for the diagnosis of infection with the mycobacterium tuberculosis especially in children. Various tuberculins have been used. At present ITU of PPD-RT-23 with Tween 80 is in common use. However in many instances it gives negative or weak reactions even among bacteriologically confirmed cases of pulmonary tuberculosis (1). Stronger strengths of the tuberculin (PPD-RT-23 with Tween 80) are not commonly available in India. Supply of Old Tuberculin is irregular. Even PPD-RT-23 1 TU with tween is available only to specialised agencies.

Can heat killed BCG Vaccine be used in place of 1 TU PPD RT 23 or Old Tuberculin? Comparative response to Old Tuberculin and PPD-RT-23 with tween has been reported (2) but not in India. Similarly heat killed BCG Vaccine has not been used as a tuberculin in India though it has been reported elsewhere (3, 4, 5). Using heat killed BCG Vaccine in different dilutions Frappier and Guy (3) reported that it was more specific than the tuberculins in common use. In these studies (3, 4, 5) reaction to 'BCG Vaccination' was measured but BCG was not used for a Mantoux test. The present study was undertaken to see if BCG could be used as (an antigen for) a Mantoux test for detection of infection. If so, unused vaccine which is now thrown away, could become available for general use or for use to those who are unable to get any of the standard preparations of tuberculin.

Objective of the Study was to study the comparative sensitiveness of 1 TU of PPD-RT-23 with tween 80, 0.1 cc of Old Tuberculin (O.T.) 1/1000 and 0.1 cc of heat killed BCG vaccine (freeze-dried).

Methods and Materials

Two consistent BCG technicians for testing and reading of the Mantoux tests were selected and were used for the entire study.

New syringes and needles were colour coded and used exclusively for the same

preparation throughout the study. Four amber coloured similar bottles were filled with

- (a) PPD-RT-23 with tween 80 in the strength of 1 TU in each 0.1 ml.
- (b) O.T. 1/1000.
- (c) Freeze-dried BCG, dissolved by solvent as done commonly in BCG programme and
- (d) For dummy vaccination carbolised normal saline solution was used.

These four bottles were labelled with different colour codes. The corresponding syringes were given the same colour codes. The same syringe was used throughout the study for the same antigen and testers and readers had no access to the colour-code for the different antigens.

As far as possible, only fresh PPD-RT-23 with tween 80 1 TU and freeze dried BCG vaccine were used. Old Tuberculin (O.T.) was procured from 'Burrows Welcome', only fresh dilutions in carbolised normal saline were used. Freeze dried BCG diluted to standard strength vaccine, and boiled in a test tube for 15 minutes. To make up the water loss due to boiling more saline was added to the required level in the test tube.

The boiled contents were emptied into the amber coloured bottle.

Bacteriological testing of the viability of heat killed BCG was not done, nor were the sterilization tests on other biologicals nor carbolized saline for dummy vaccination. It was presumed that boiling the reconstituted vaccine for 15 minutes killed all the living BCG organisms.

The study was conducted between 28-7-1970 to 14-8-1970 in Indore City. M.P.

Four intradermal tests were given simultaneously, two on the left and two on the right front forearms of 162 proved patients of tuberculosis or patients under investigations in

the Tuberculosis hospital and sanatorium; for 161 patients test results are available.

271 patients of both sexes in a general hospital were also given four tests, 236 test results are available.

School children were given only two tests each, with either PPD-RT-23-1 TU or heat BCG or O.T. 999 students aged between 6 and 16 years were tested but only 620 students are considered after excluding all those with previous BCG vaccination scar.

0.1 cc of each antigen was injected by the Mantoux technique at different sites on the forearms. Tests were read after 48 hours and in a few cases later but always before 72 hours.

During the course of readings of the tests it was found that reactions to heat killed BCG vaccine were uniformly very strong in comparison to other tests. There were too many blister reactions with febrile

response. Then the contents of the coloured bottle containing BCG was reduced to $\frac{1}{2}$ the standard strength by addition of an equal quantity of saline without the knowledge of the testers or readers. Thus the standard dose of BCG was used among the patients of TB hospital and the sanatorium; $\frac{1}{2}$ the standard dose of BCG was used among patients of the General Hospital and among school children.

Results

Only the results of the three antigens used are presented; results of testing with the placebo are neglected.

Chart 1 shows the frequency curves of the size of reactions to PPD-RT-23-1 TU, 0.1 cc of O.T. 1/1000 and 0.1 cc of heat killed BCG vaccine among 161 patients of TB hospital and sanatorium. It is obvious that the frequency curve for BCG tends towards the right hand side as compared to those of O.T. or PPD-RT-23. The frequency curve of PPD-RT-23 tends always to the left hand side of the other two curves. All the three curves appear to be

CHART 1

FREQUENCY CURVES SHOWING REACTIONS TO P.P.D- RT-23-ITU WITH TWEEN 80

0.1 cc. OF O.T. 1/1000 AND 0.1 CC OF HEAT KILLED B.C.G AMONG 161 " PATIENTS" OF T.B. HOSPITALS AND SANATORIUM

NOTE —○— P.P.F.- RT-23-ITU WITH TWEEN
 ——— 0.1CC OF O.T.1/1000
 - - - - - 0.1CC OF HEAT KILLED B.C.G. [FULL STRENGTH]

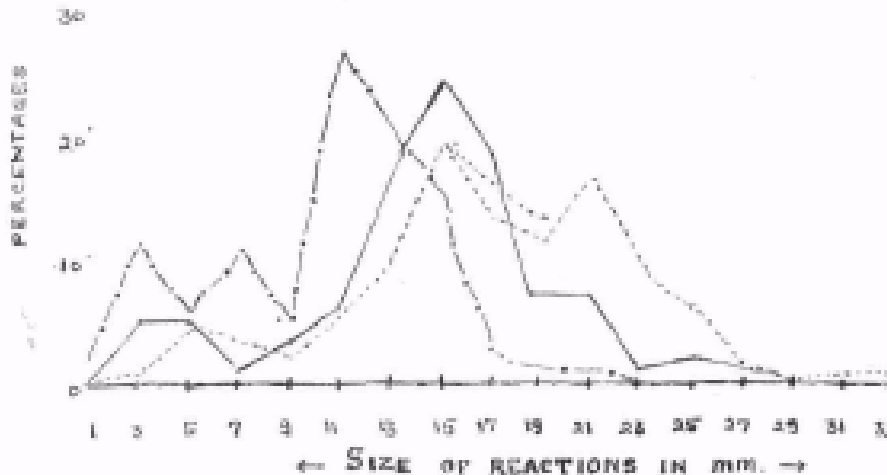
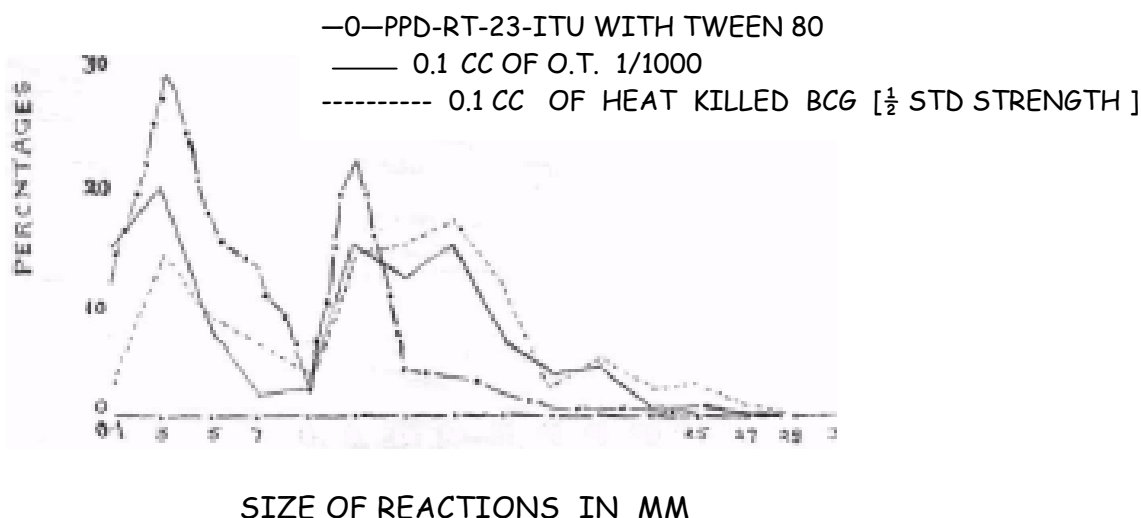


CHART-2

FREQUENCY CURVES SHOWING REACTIONS TO P.P.D - RT-23- ITU WITH TWEEN 80

O-1CC OF O.T. 1/1000 and 0.1cc OF HEAT -KILLED B.C.G
AMONG 236 PATIENTS IN THE GENERAL HOSPITALS



fairly similar. If one considered those with 10 mm and bigger reaction as reactors then only about 10% are *non-reactors* to BCG whereas about 13% to O.T. and 34% to PPD-RT-23. i.e. PPD RT 23 has given the smallest number of reactors, while BCG the highest.

Chart 2 shows the frequency curves of size of reactions to PPD-RT-23-1 TU, 0.1 cc of O.T. 1/1000 and 0.1 cc of heat killed BCG tests among 236 patients in General Hospital. All the three curves are bimodal and the bifurcation of the two distributions could be made at 9 mm level which means that those with 10 mm and larger reactions could be considered as reactors and those with 9 mm could be regarded as non-reactors. The modes of distributions of reactors of O.T. and heat killed BCG appears at 15 mm whereas for PPD-RT-23 appears at 11mm. Further, the frequency curve for reactors of the heat killed BCG (half the standard strength) tends to be above and to the right hand side of the other two curves. For non-reactors the frequency curve for the heat killed BCG tends to be below and to the left hand side of the other curves and modes of all the three curves are at 3 mm. Separation between PPD-RT-23 is

sharper as compared to either O.T. or heat killed BCG.

Again PPD-RT-23 has given the smallest number of reactors and BCG the highest.

Chart 3 shows the frequency curves of reactions to PPD-RT-23 1 TU, 0.1 cc of O.T. 1/1000 and 0.1 cc of heat killed BCG tests among school children. All the three curves appear to be bimodal. The point of separation between two distributions of all these three curves appear at 9 mm. Again it is clear that those with 7, 10 mm size of reaction could be regarded as reactors. Modes for all the three distributions of reactors appear at 11 mm and the curve for heat killed BCG is on the right hand side and above those of O.T. and PPD-RT-23, Modes of the distributions of non-reactors for O.T. and PPD-RT-23 appear at 3 mm whereas for heat killed BCG appear at 5 mm. Again, number of reactors is highest with BCG.

In Table 1 patients have been divided into 4 groups by size of their reaction to PPD-RT-23. For each group the Mean size of reaction to BCG is the largest and for PPD-

CHART-3

FREZQUENCY CURVES SHOWING REACTIONS TO P.P.D - RT-23- ITU WITH TWEEN 80
 O-1CC OF O.T. 1/1000 and 0.1cc OF HEAT KILLED B.C.G AMONG
 417, 419 AND 404 SCHOOL CHILDREN RESPECTIVELY

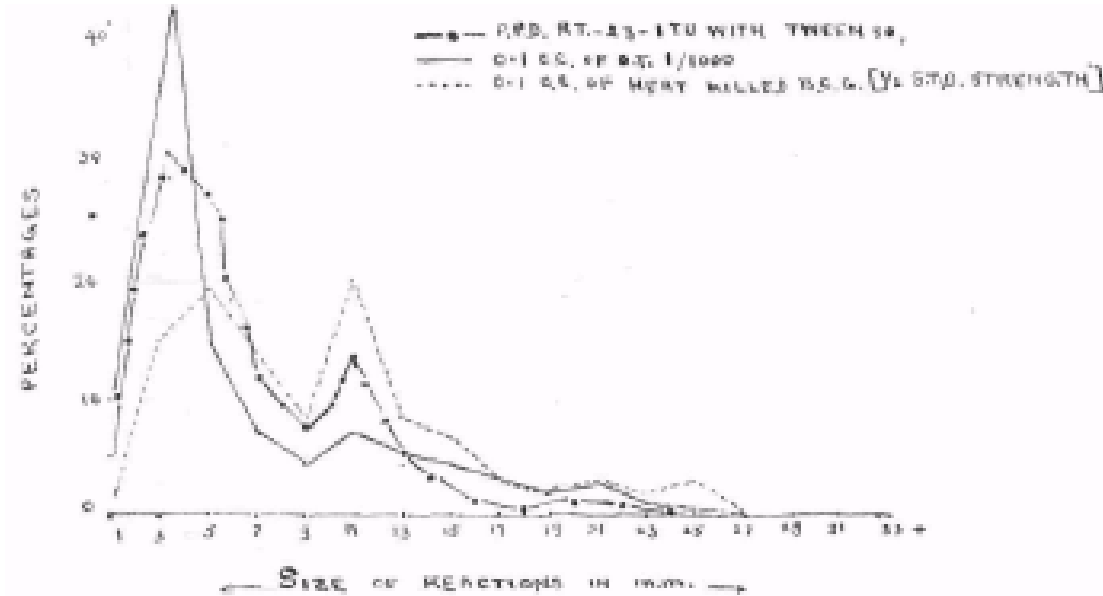


TABLE I

Size of mean reaction to O.T. and heat killed B.C.G. test among 'patients' in the TB hospital and sanatorium for different belts Of reaction to PPD-RT-23-1 TU

Reaction to PPD-RT-23-1 TU (in mm)	Number test read	Size of mean reaction (in mm) to	
		O.T.	BCG (Standard strength)
0-5	30	8.13	9.87
6-9	25	13.12	16.08
10-15	98	14.94	17.18
16	8	19.75	23.75
Total	161	13.63	15.98

RT-23 the smallest, (This is evident from the table for the 1st 3 groups and it is so, though not shown, for the 16 mm belt).

Table 2 shows similar findings for General Hospital patients except for those with 16 mm to PPD-RT-23 which may be due to small

TABLE 2

Size of mean reaction to O.T. and heat killed B.C.G. test among the patients in the general hospital for different belts of reaction to PPD-RT-23-1 TU

Reaction to PPD-RT-23-1 TU (in mm)	Number test read	Size of mean reaction (in mm) to	
		O.T.	BCG (half the standard strength)
0-5	129	6.05	8.36
6-9	35	9.14	12.00
10-15	65	12.83	14.77
16	7	13.71	13.43
Total	236	8.60	10.81

TABLE 3

Size of mean reaction to O.T. and heat killed BCG test among school children for different belt is of reaction to PPD-RT-23-1 TU

Reaction to PPD-RT-23-1 TU (in mm)	Number test read	Size of mean reaction (in mm) to O.T.	Number test read	Size of mean reaction (in mm) to heat killed BCG half the standard strength
0-5	132	3.64	119	6.71
6-9	37	4.81	38	9.11
10-15	45	11.47	36	13.83
16	2	22.00	8	17.25
Total	216	5.64	201	8.86

number of patients in this group.

Table 3 shows that the mean size of reaction of BCG among school children is larger than that due to O.T. The group with 16 mm reaction to PPD-RT-23 should be neglected due to small numbers in this group.

Further mean size of reaction to both O.T. and BCG recorded a gradual increase, from lower belt of reaction size to higher belt of reaction size to PPD-RT-23 in all the three tables.

Discussion

Any tool of diagnosis should be (i) sensi-

tive (ii) easily available and (iii) cheap. PPD-RT-23 1 TU with tween is in common use in India to detect infection with tuberculous mycobacterium. But even proved tuberculosis cases do not react to this test on many instances. Stronger strengths of PPD-RT-23 are not commonly available to test further such non-reactors. To decide the level of size of separation between reactors and non-reactors the point of separation on a frequency curve is not sharp even among young children, the group in which interpretation of a tuberculin test is most accurate.

It has been shown in chart 1 that the heat killed BCG appears to be sensitive in detecting the infected ones as all the persons included

were either tuberculosis patients or with symptoms of tuberculosis disease under investigation. The BCG used in this group was of standard strength which gave blister reaction and febrile response. If lower strengths of BCG had been used what the results would have been is not easy to answer without a certain amount of speculation. However, from the results in the patients of the general hospital and particularly from school children one would be inclined to think that the results would not have been different ; only blisters and febrile response would have been avoided. Further the frequency curves in Chart 1 are all fairly similar thereby showing that the study population is a homogeneous group and all are most likely to be infected with mycobacterium tuberculosis. Reaction to BCG is comparatively larger and the proportion of those with less than 10 mm is relatively small. The test therefore appears to be more sensitive than either O.T. or PPD-RT-23 in finding the infected.

The sensitiveness of BCG is further confirmed for reactors as seen through charts 2 and 3 in the patients of the General Hospital and school children. In both the cases the point of separation between reactors and non-reactors is the same as those for O.T. and PPD-RT-23. Further the frequency curve for heat killed BCG is on the right and above the other curves. However for non-reactors also the heat killed BCG gives larger reactions, best seen in chart 3. The mode is at 5 mm as compared to 3 mm in case of other two distributions. Further, frequency curve appears to the left and below the other two curves. Also tables 1, 2 and 3 show that the heat killed BCG gave larger reactions at all the levels. The heat killed BCG no doubt divides the population into two groups namely reactors and non-reactors but gives larger reactions for both reactors and non-reactors. Similar finding has also been reported from Thailand (5).

Thus, heat killed BCG appears to satisfy the primary condition of a tuberculin test as a specific test as it gives relatively larger reactions among infected persons quite distinct from those among the uninfected persons, with only a small number of intermediate reactors. It may be possible to improve the results with heat killed BCG by using weaker solutions than half strength and a suitable strength could be evolved for a diagnostic test. The great advantage is that it is easily available and the stuff which is normally thrown away can be utilised.

However there is one snag with the BCG test. Even killed BCG vaccines give rise to scars and post vaccination allergy. Thus BCG as a tuberculin test could be used only once. If it is negative, a later positive test will have no significance.

The main purpose of this investigation is to stimulate further study of the use of heat killed BCG test in different dilutions. It has been observed that many children who had been BCG vaccinated some years ago reacted much better to this antigen than to any of the tuberculins used. However this has to be confirmed by a separate study. There is no doubt that the BCG dilutions which are normally thrown away have a useful place to confirm clinical diagnosis where usual tuberculin test is negative.

ACKNOWLEDGEMENT

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REFERENCES

1. Raj Nirain, S.S Nair, K. Naganna, P. Chandrasekhar, G. Ramnatha Rao and Pyare Lal. Problems in defining a "case" of pulmonary Tuberculosis in prevalence surveys. *Bull. Wld. Hlth Org*, 1963, 39, 701-729.
2. F.B Siebert and E.H. Dufour. Comparison between the intradermal standard tuberculin PPDS and old tuberculin. *Amer. Rev. of Tuberculosis*, 1954, 69, 585-594.
3. A. Frappier and R. Guy. A new and practical BCG skin test (BCG Scarification test) for detection of total tuberculous allergy. *Canad. Journ. Of P.H.* 1950, 41, Page 72.
4. T. Egsmose. BCG vaccination with special emphasis on the feasibility of vaccinating also tuberculin positive persons and of using the vaccination lesion as an indicator of tuberculous infection, *Acta Tuberc, Scand*, 1965, 46, 220-264.
5. Boonsong Sunakorn and Y. Azuma. A Trial of BCG Vaccination without preceding tuberculin test. *WHO TB Tech. Information/66.47*.

INDIAN FREEZE DRIED B.C.G. VACCINE—ITS PROPERTIES AND ADVANTAGES

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(From B.C.G. Vaccine Laboratory, Guindy, Madras)

The BCG Laboratory at Madras, established in 1948, has to date prepared and supplied over 480 million doses of BCG Vaccine for use in India and some of the neighbouring countries. Till the end of 1967, the Laboratory was supplying only Liquid BCG vaccine. Freeze Dried BCG Vaccine was introduced on a regular basis in December 1967. However, even today the bulk of the BCG Vaccine produced is being issued as Liquid Vaccine.

Liquid BCG Vaccine has certain inherent drawbacks, such as :

1. Liquid Vaccine has a short "life" of two weeks from the date of manufacture.
2. Liquid Vaccine has to be continuously refrigerated to preserve its potency; even for this short period of two weeks.
3. Liquid Vaccine has to be transported in special insulated containers with ice to avoid deterioration.
4. Because of the very short life of liquid vaccine the Laboratory has to make a fresh batch of vaccine every week, as no reserve stock can be built up to meet the fluctuating demands from the BCG Teams.

The disruption or lowering of production in the Laboratory due to causes like scarcity of water, interruption of electricity, contamination etc., leads to short supply/no supply of vaccine to many BCG Teams, resulting in serious dislocation of the schedule of vaccination in the whole country.

Due to these reasons, the replacement of Liquid Vaccine with Freeze-Dried Vaccine was considered very desirable. It was also presumed that the introduction of F.D. Vaccine would be accepted with enthusiasm by the BCG Vaccination teams and the administrators of the campaign. However, from the large number of enquiries received from them, it soon became evident that F.D. Vaccine has failed to satisfy fully their expectations of a stable vaccine. The questions most often asked have been :

1. Why the freeze dried BCG Vaccine should be stored at +4°C ?

2. Why is the life of the dry vaccine limited to three months ?
3. Why should reconstituted dry vaccine be used up within 4 to 6 hours ?
4. Should reconstituted vaccine be kept on ice ?
5. Why should the dry vaccine be protected from sun light ?
6. In the field, when ice or other refrigeration facilities are not available, within how many days should the F.D. Vaccine be used up ?
7. What are the advantages of dry BCG Vaccine ?

In this paper, we have tried to provide rational answers to these questions. In many cases, special experiments were undertaken in the Laboratory to find these answers. The results of these experiments are also recorded.

Materials and Methods

The potency of BCG Vaccine (Liquid or Freeze-dried) depends on the number of living units of BCG in the vaccine. The viable Units Count of the Liquid Vaccine falls with passage of time, even when it is stored at 4°C. This fall is greater and more rapid when the vaccine is exposed to temperatures higher than 4°C. Therefore, in the experiments reported below, "Viable Units Count" test has been used to estimate the loss in potency of F.D. Vaccine on exposure (Storage).

Strain of BCG : BCG Strain "Danish 1331" has been used for preparation of Dried as well as Liquid BCG Vaccine.

Technique of "Viable Units Count" Test

Serial dilutions of the samples of vaccine are made in diluted Sauton (Sauton medium 1 part + distilled water 3 parts). The last 3 dilutions are adjusted to obtain, for the middle dilution, an estimated optimum count of 50 colonies per bottle of medium, the first dilution 100 colonies and the 3rd dilution 25 colonies.

With 1 ml. graduated pipettes, the three dilutions are inoculated into Lowenstein-Jensen

medium contained in 2 oz., flat sided white, screwcapped bottles, as detailed below :—

- 1st dilution : 0.2 ml into each of 3 bottles
- 2nd dilution : 0.2 ml. into each of 3 bottles
- 3rd dilution : 0.2 ml. into each of 6 bottles

The dilutions and inoculations are made in an air conditioned (22°C) room from which daylight is excluded. The inoculated bottles are kept flat overnight and then incubated upright at 37°C. The counting of colonies is done at the end of 4 weeks' incubation. The viable units are calculated based on the colonies obtained in all the 3 dilutions.

Results

- I. *Why the freeze-dried BCG Vaccine should be stored at +4°C or below ?*
- II. *Why is the life of the dry vaccine limited to three months ?*

Liquid BCG Vaccine has a "life" of two weeks only, when stored at 4°C. At 37°C, its life is much shorter. The dry vaccine is expected to be much more stable than Liquid Vaccine, both at + 4°C and at higher temperatures.

To assess the relative stability of dry vaccine on storage, a number of experiments were undertaken, in which "Viable Units Count" test was performed on batches of Liquid Vaccine and F.D. Vaccine at varying intervals after storage at 4°C (Refrigerator temperature) and at 37°C. (Incubator Temperature). The results obtained from these experiments are shown in tables 1 to 4.

It will be seen from tables I and 2 that when stored at 4°C, the Liquid Vaccine loses over 60 per cent of its viability in 4 weeks and when stored at 37°C, the loss is over 95 per cent. In F.D. Vaccine the corresponding loss in viable units is considerably less (12 per cent and 80 per cent).

In fact, in case of F.D. Vaccine stored at 4°C, the percentage survival (of viable units) varied from 80.0 per cent to 96.8 per cent at the end of four weeks. At the end of 24 weeks (approximately 6 months) the percentage survival varied from 49.1 per cent to 80.6 per cent (Table 3). It would appear that while majority of the batches of F.D. Vaccine retain high potency for more than six months when stored at 4°C, there may be some batches, where the potency of the vaccine falls to below 50 per cent. Further, it has to be expected that the storage conditions may not be ideal in many centres and the vaccine may be stored at temperatures higher than 4°C. Therefore, it has been considered safer to limit the "life" of the dry vaccine to 3 months from the date of supply, for the present.

Table 4 demonstrates the steep fall in viable units count of dry vaccine when the vaccine is exposed to 37°C. At the end of 4 weeks' storage, the survival rates of viable units was 24 to 33 per cent only. This clearly shows the deleterious effect of high temperature on Dry Vaccine. Therefore, to safeguard the potency of F.D. Vaccine it has been stipulated that Dry Vaccine should be stored at 4°C and not at room temperature.

- III. *Why should reconstituted dry vaccine be used up within 4 to 6 hours ?*

TABLE I

Effect of storage at 4°C on the "Viable Unit?" in BCG vaccine results are expressed as percentage survival

VIABLE UNITS %					
Liquid Vaccine			F.D. Vaccine		
Batch No.	Fresh	After 4 weeks	Batch No.	Fresh	After 4 wee2s
1192	100%	21.3%	121	100%	88.7%
1193	100%	55.0%	122	100%	81.8%
1194	100%	10.0%	123	100%	80.0%
1195	100%	36.2%	124	100%	96.8%
MEAN	100	35.9	MEAN	100	88.6

TABLE 2
Effect of storage at 37°C on the "Viable Units" in BCG vaccine results are expressed as percentage survival

VIABLE UNITS %					
Liquid Vaccine			F-D. Vaccine		
Batch No.	Fresh	After 4 weeks	Batch No.	Fresh	After 4 weeks
232	100%	4.5%	121	100%	10.4%
233	100%	2.7%	122	100%	25.5%
234	100%	1.6%	123	100%	13.0%
235	100%	4.8%	124	100%	29.0%
MEAN	100	3.4	MEAN	100	19.5

TABLE 3
Effect of storage at 4°C on Viable Units count of F.D. vaccine

F.D. Vaccine	Period of storage at 4°C— result of Viable Units Counts Test				
	Fresh Dried	4 Weeks		24 Weeks	
	Batch No.	Viable Units (mill/mg)	Viable Units (mill/mg)	Percentage Survival	Viable Units (mill/mg)
F. 121	11.5	10.2	88.7	7.3	63.5
F. 122	11.0	9.0	81.8	5.4	49.1
F. 123	10.0	8.0	80.0	7.7	77.0
F. 124	15.5	15.0	96.8	12.5	80.6

TABLE 4
Effect of storage at 37°C on the Viable Units count of F.D. vaccine

Period of Storage	Viable Units— Percentage Survival				
	Batch No. 103	Batch No. 111	Batch No. 115	Batch No. 122	Mean of batches
<i>At 37°C</i>					
0 hour	100.0	100.0	100.0	100.0	100.0
2 weeks	50.0	77.2	69.5	79.6	69.1
4 weeks	30.6	24.0	33.5	27.2	28.8
6 weeks	23.0	18.8	20.5	23.8	21.5
8 weeks	6.0	10.0	14.5	20.8	12.8
<i>At 4°C</i>					
24 weeks	80.2	86.9	78.6	49.1	73.7

TABLE 5

Stability of F.D. vaccine after reconstruction, as determined by the viable units count

Batch No.	Initial count % 'O' hour	Mean survival percentage when stored at					
		4 ^D C			37°C		
		3 hours	6 hours	12 hours	3 hours	6 hours	12 hours
F. 111	100	87.1	73.3	84.8	78.4	69.6
F. 124	100	89.9	84.8	79.8	73.5	61.5	48.7

IV. *Should reconstituted vaccine be kept on ice ?*

To find out the time within which the reconstituted dry vaccine be used up, 20 ampoules of dry vaccine were reconstituted in diluted sauton and their pooled contents distributed in a number of test-tubes. These samples were stored at 4°C and 37° C for varying periods of time, at the end of which viable units estimations were performed. Table 5 shows the results. All the samples were kept protected from sunlight direct and reflected.

When stored at 4°C, 73 to 84 per cent of the initial viable units survived at the end of 6 hours. Even after 12 hours storage the vaccine retained nearly 80 per cent of its viability.

The survival rates were slightly lower (61.8 to 78.4) when stored at 37°C for 6 hours. At 12 hours there was a tendency to a more rapid fall in viability, survival percentage being 48.7 to 69.6.

These results indicate :—

1. That the reconstituted dry BCG Vaccine can be used upto 6 hours after reconstitution without significant loss of potency.
2. During this period of 4 to 6 hours the vaccine maintains high potency even if it is not refrigerated, provided the ambient temperature is 37° C or below.
3. In view of the tendency for a more rapid fall at higher temperature (37° C), it is preferable to keep the reconstituted vaccine on ice for obtaining best results.

V. *Why should the dry vaccine be protected from sunlight ?*

Liquid BCG Vaccine is highly susceptible to sunlight, direct or reflected. F.D. Vaccine, though more resistant, deteriorates considerably when exposed to sunlight.

To obtain data on the effect of sunlight, dry vaccine in ampoules (colourless) was exposed to direct sunlight in the open and to reflected sunlight (day light) on the roofed verandah of the laboratory (on a bright sunny day in April) for different periods of time. Samples of the exposed vaccine were tested for viable units contents along with control vaccine stored in the dark at 4°C. The results are given in Table 6.

Direct sunlight killed 35 percent of the bacillary units in 10 minutes, 90 per cent in 30 minutes and nearly 100 per cent in 90 minutes.

The effect of daylight was less drastic, the fall in viable units being about 30 per cent in 2 hours, 53 per cent in 4 hours, and 60 per cent in 8 hours.

Once the freeze dried vaccine was reconstituted daylight had a more severe effect (Table 7).

When exposed to daylight the viable units count showed a decrease of 54 per cent in 2 hours, 88 per cent in 4 hours, and almost 100 per cent in 8 hours.

These results clearly emphasise the need for complete protection of F.D. BCG Vaccine from sunlight at all stages.

VI. *In the field, when ice or other refrigeration facilities are not available, within how*

TABLE 6

Effect of exposure to sunlight on the viable units content of dry BCG vaccine

DIRECT SUNLIGHT			REFLECTED SUNLIGHT		
Period of exposure	Viable units mill/mg.	Percentage survival	Period of exposure	Viable units mill/mg.	Percentage survival
0 hour	6.49	100	0 hour	6.49	100
10 minutes	4.20	64.7	2 hours	4.66	71.8
30 minutes	0.68	10.5	4 hours	3.03	46.7
90 minutes	0.016	0.02	8 hours	2.55	39.3

TABLE 7

Effect of day light on reconstituted freeze dried BCG vaccine

Period of exposure	Viable units mill/mg	Percentage survival
0 hours	3.85	100
2 hours	1.77	46.0
4 hours	0.43	11.2
8 hours	0.025	0.65

many (lays should the F.D. Vaccine he used up

Experiments in this Laboratory have shown the F.D. BCG Vaccine retains 70 to 80 per cent of its viability up to one week when stored at 37°C (protected from sunlight). Hence it may be reasonable to assume that the vaccine can be kept for one week at room temperature, provided the maximum ambient temperature is below 37°C. But considering the possibility of the vaccine being subjected to adverse effects of exposure to sunlight etc., besides higher temperature, it is advisable to limit the maximum period of keeping the vaccine at room temperature to 2 or 3 days.

VII. *What are the advantages of dry BCG Vaccine over Liquid BCG Vaccine ?*

The advantages of freeze-dried BCG Vaccine over Liquid Vaccine can be stated as follow :—

1. The significantly higher stability of the dry vaccine, both at 4°C and at 37°C is of decided advantage, especially in tropical countries like India, where ambient temperatures are high and

refrigeration facilities are often difficult to obtain. In such cases, even if the dry vaccine gets exposed to higher temperatures for short periods, it will retain sufficient potency to produce adequate immunity.

2. The longer life of the dry vaccine enables the state and district centres for BCG vaccination, where refrigeration facilities are available, to keep several weeks' stock of vaccine instead of obtaining vaccine every week or two as is done in the case of liquid vaccine.
3. This also minimises the wastage of vaccine due to time expiry.
4. Normally it takes 10 to 12 weeks to complete all the control tests on the vaccine. The longer life of the dry vaccine enables the production laboratory to complete all the tests and issue only batches of vaccine conforming to the standards.
- 5.. The longer life of the vaccine makes it possible to manufacture and stock

sufficient vaccine in the Laboratory to meet the fluctuating demands of the vaccination centres, thus assuring full supply at all times.

Discussion

The studies reported here confirm the superiority of lyophilized BCG Vaccine over liquid vaccine on three aspects—the longer life, the better heat stability and the higher resistance to the action of daylight. But these characteristics vary to a considerable extent, depending on the sub-strain used for the preparation of the vaccine.

Though all BCG cultures used for vaccine production are descendants of the original Calmette Strain of BCG, due to the different methods of maintenance in the various production laboratories, many sub-strains with distinguishable characteristics have evolved during the past few decades. Thus the Prague (Czechoslovakia) and the Moreau (Brazil) sub-strains produce less allergy in guineapigs than other strains. The French and the 809 Madras Strain grow faster in Sauton medium than the Copenhagen 1331 Strain. The Japanese sub-strain 172 is quite different in that, the bacilli are much smaller and are more resistant to freeze drying and distinctly more heat stable.

Due to these two advantages the Japanese 172 sub-strain is obviously the strain of choice for freeze dried vaccine. But recent studies in animals by the WHO (Christensen et al 1968) have shown that the Danish Strain 1331 affords better protection than the Japanese Strain. Hence the WHO has recommended the Danish 1331 strain for the production of BCG Vaccines. The national authorities in India have accepted this recommendation of the WHO and since January 1967 the BCG

Laboratory, Madras, is using 1331 strain for the production of Liquid and Freeze Dried BCG Vaccine.

The early expectations of a highly heat-stable F.D. Vaccine were based mainly on the work on Japanese Strain 172. Dr. T. Hashimoto et al (1969) found that under identical condition, the resistance to the trauma of freeze-drying and heat stability of vaccine made from Japanese Strain 172 was nearly double that of Danish Strain 1331. Since the Danish Strain 1331 is more susceptible to freeze drying and is less heat-stable, the Dry Vaccine produced in Madras has a lower viable count and is less heat-stable than the Japanese vaccine. The Madras F.D. BCG Vaccine has a mean survival rate of 28.8 per cent when exposed to 37°C for 4 weeks (see table 4) and when kept at 4°C, the survival rate is over 70 per cent even after 6 months (Table 4). Some of the batches tested after 12 months' storage at 4°C had a survival rate of 61.4 per cent.

The advantages of the F.D. BCG Vaccine enumerated above are of great help in the production, testing, distribution and handling of the vaccine during field campaigns. In spite of these advantages it has to be strongly emphasised that for the best results the dry vaccine still has to be stored under refrigeration and protected from sunlight at all times.

REFERENCES

1. K. Bunch Christensen, A. Ladefoged & J. Guld., *Bull. Wld, Hlth. Org.*-1968, 39, 821-828.
2. T. Hashimoto, K. Bunch-Christensen, K. Lund Nilsen and A. Ladefoged.

(Paper presented at the W.H.O. Symposium on BCG Vaccine Production Manila, Philippines 22nd to 26th September, 1969.

URINARY TRACT INVOLVEMENT IN PULMONARY TUBERCULOSIS

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Introduction

Tuberculosis is a systemic disease and likely to be wide spread. Even though the clinical presentation may suggest involvement of only one organ or one system, seldom if ever, the disease is so localized. Invasion of urinary tract by mycobacterium tuberculosis is, but one phase of the disease that later on can spread to many other parts of the body.

Tubercular Bacilluria: Cohnheim Colby: (1961) postulated the hypothesis that tubercle bacilli can be excreted by normal kidney, based on the observations that the organism could be demonstrated in the urine of patients who have no symptoms pertaining to the urinary tract. Medlar (1926) made a very careful study of the kidneys of patients who died of active caseating pulmonary tuberculosis, by serial sections. He conclusively demonstrated active tubercular foci, as well as healed scars, in kidneys of patients who had no symptoms attributed to the urinary tract during life. His observations made Cohnheim's theory of "Physiological filtration and excretion" untenable. Medlar's findings were subsequently confirmed by experimental as well as autopsy studies of Liberthol (1933) and Band (1935).

Tubercular bacilluria is known to be associated with tuberculosis of various sites in the body. Rosencranz (1940) reported it in 7% of patients of pulmonary tuberculosis, Medlar & Ordway (1942) in 7.7% and Band (1943) in 21.3%. Harris (1929) found it in 29% of osteoarticular tuberculosis and Maclelland and Davis (1942) in 18%. Medlar (1949) reported his findings of 5,424 necropsies and demonstrated tubercular lesions in kidneys in 26%.

Material

55 patients of proved pulmonary tuberculosis with presence of albumin, pus cells or R.B.C. and sterile 24 hour culture of urine were selected in the present work.

Methods

= *Collection* : Morning samples of urine were collected in sterile jars with aseptic precautions on three consecutive days and stored in refrigerator at 4°C till processed.

= *Concentration* : The pooled urine was centrifuged at 3,000 rpm for 30 minutes (Hill: 1966). The supernatant was discarded and the deposits used for bacteriological study. In group C (vide infra) the deposits were further washed thrice with saline before processing.

= *Smear* : A smear was made from the deposit and stained by Ziehl Nealsons technique for the presence of acid fast bacilli.

= *Culture* : The urine is so processed as to eliminate contaminants and to bring it to a suitable PH for plating on L.J. Media. This is achieved by treating the urine with 4% sodium hydroxide solution in ratio of 4 : 1 and incubating at 37°C for 30 mts.

Then 80% Hcl is added to bring the PH to 7 (Hill : 1966), using phanophathaline as an indicator. The mixture is then centrifuged at 3000 rpm for 30 minutes.

The deposit is now ready and is cultured on Lowenstein Jensen's media which was prepared as advised by the International Union against Tuberculosis. This was done in culture chamber to avoid contamination. After plating, the sample is incubated at 37°C for 6—8 weeks and periodically inspected for growth.

Grouping of case material : Depending upon the technique employed, the 55 patients were divided into following three groups: —

Group A: Consists of 15 cases where anti-tubercular drugs were continued during study.

Group B: Consists of 20 cases where anti-tubercular drugs were stopped for 7 days prior to the study of urine.

Group C: Consists of 20 cases where the drugs were stopped as in group B plus the urine was washed with normal saline thrice to remove any trace of the anti-tubercular drug which might still be in it.

Observations

The age and sex incidence of cases is given

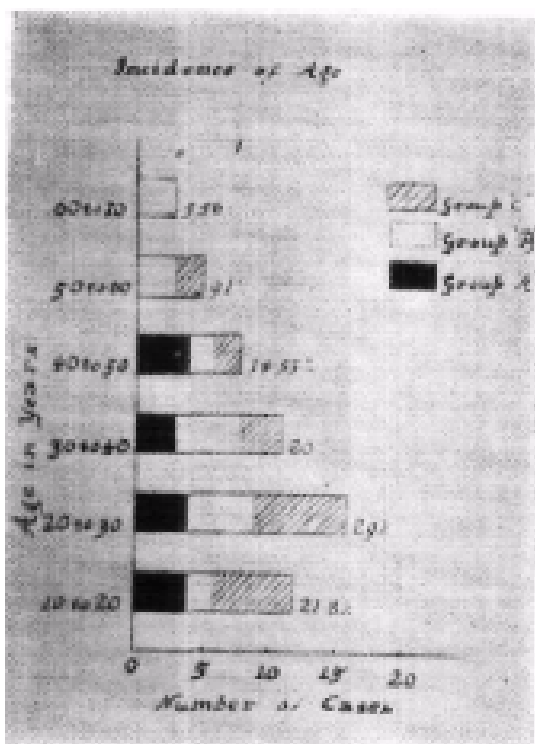


Fig. 1 Age Incidence

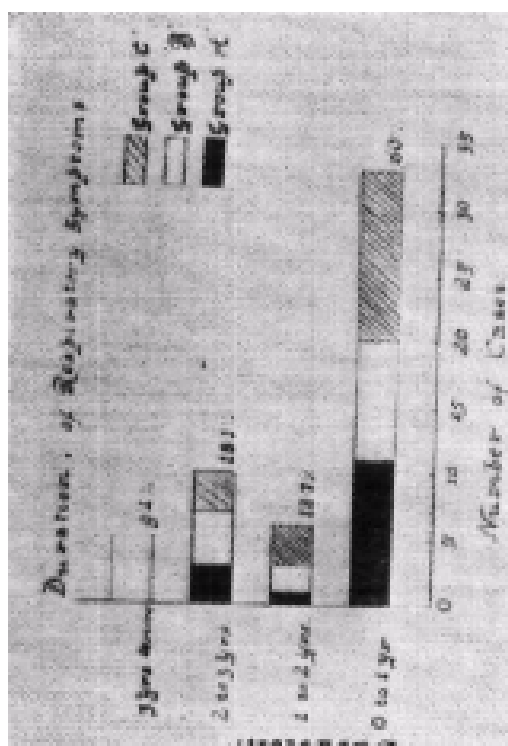


Fig. 3 Duration of pulmonary tuberculosis

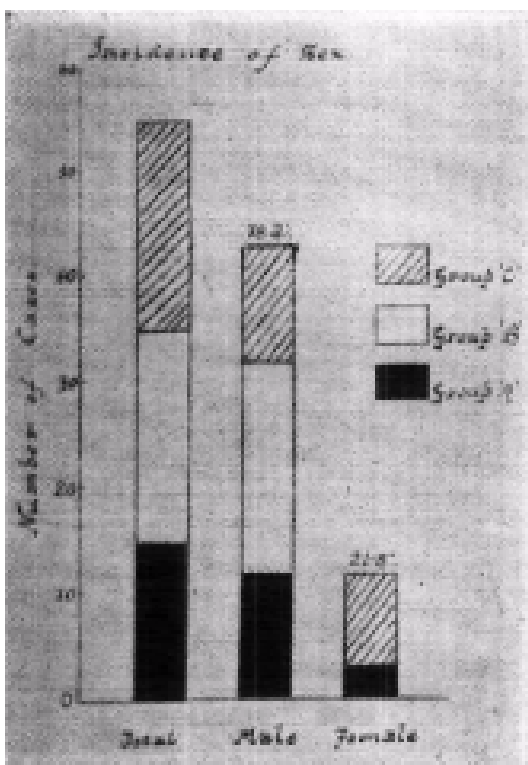


Fig. 2 Sex incidence

in Fig. 1 and 2 respectively and the duration and distribution of pulmonary tuberculosis in Fig. 3 and 4. Fig. No. 5 shows the anti-tubercular chemotherapy of the patients.

The routine examination of the urine of these patients, as shown in Fig. 6 revealed acidic reaction and pus cells in all the cases, albuminuria in 80%, microscopic haemnturia in 30.9% and casts in 5.4%.

Smear examination revealed positive identification of A.F.B. in 9.09% Table J shows the breakdown of positive smear findings in respect of the three groups of patients.

Culture of urine for A.F.B. revealed positive results only in 3.8% of the patients

TABLE 1

	A	B	C	Total	%
No. of cases	15	20	20	65	100
No. of positive smears	2	1	2	5	9.09%

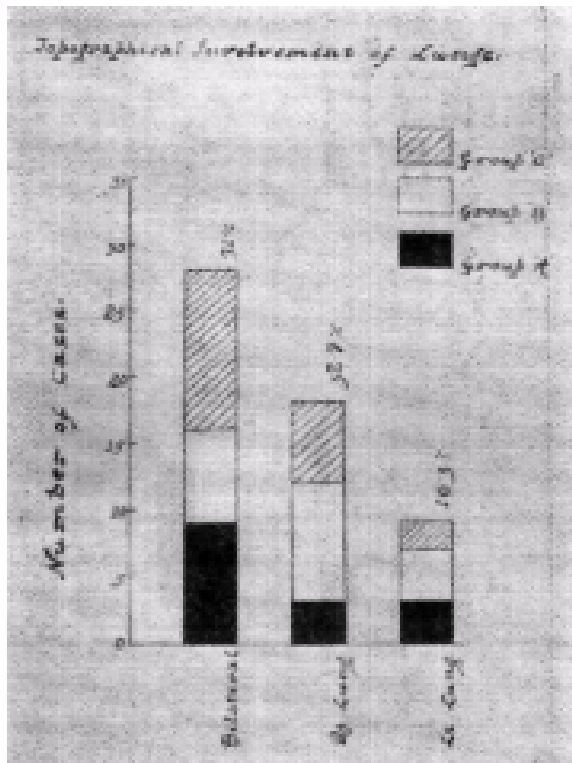
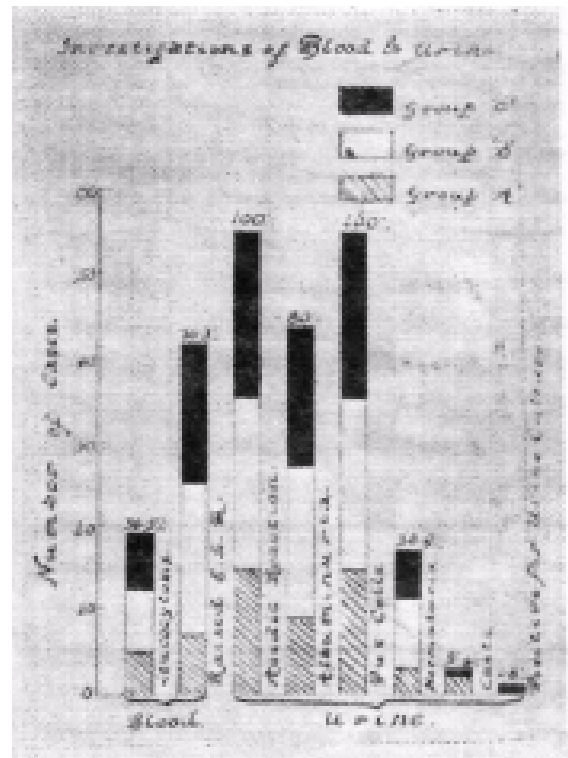


Fig. 4 Distribution of pulmonary tuberculosis



Fir, 6 Blood and urine analysis

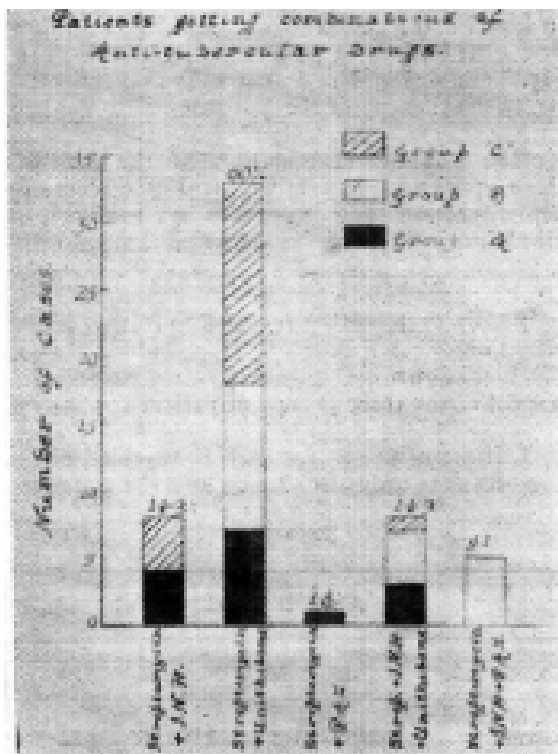


Fig. 5 Antitubercular chemotherapy schedule

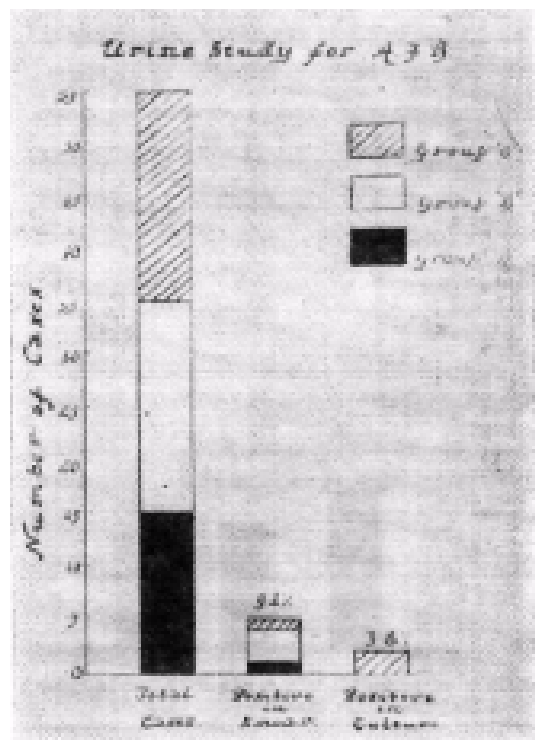


Fig. 7 Smear and culture report

studied (see Fig. 7). All these patients belonged to group C i.e. where the antitubercular therapy was not only stopped for 7 days prior to testing but the centrifuged deposits were also washed with normal saline repeatedly taking away the traces of drugs which still may be getting excreted by the kidneys. In group C alone positive culture was in 10% cases.

Comments

Urinary tract is involved in cases of pulmonary tuberculosis. As the urinary component can be asymptomatic, it is likely to be missed even when special attention is given to detect it, because it is becoming increasingly difficult to demonstrate tubercle bacilli in urine. In the present series of 55 patients of lung TB with pus cells in urine only 9.1% gave positive findings in smear examination and 3.8% on culture. Even in confirmed cases of genito-urinary tuberculosis this very problem is encountered.

Kenney(1960) observed that introduction of antitubercular drugs has made the demonstration of tubercular bacilluria difficult. This could be either due to the drugs causing healing of renal focii or to their presence in urine inhibiting the growth of A.F.B. in the culture. In this series also positive cultures were detected only in Group-C i.e. where the drugs had been stopped for a week prior to the test and the centrifuged deposits of urine were washed with normal saline prior to plating. No positive results could be obtained in group A or B.

The failure to culture organism can also be attributed to intermittant discharge of bacilli or to their being present in very low concentration in the urine. Repeated testing

in the same patient is therefore likely to give better results.

Summary

Results of bacteriological examination of 55 case of pulmonary tuberculosis with "sterile pyuria" has been presented. Problems in the culture of A.F.B. from urine have been discussed.

ACKNOWLEDGEMENT

We are extremely grateful to Professor R.M.L. Mehrotra, M.D. Ph. D (London), Head of the Department of Pathology, for the help received in conducting this study.

REFERENCES

1. Band, D: *Edin. Med.J.*, 42: 162, 1935.
2. Band. D: *Postgrad. Med. J.*, 19 : 266, 1943.
3. Colby, F.H: *Essential Urdogy*, 4th Ed; 552, 1961.
4. Harris, R.I: *Brit. J. Surg.*, 16; 464, 1929.
5. Hill, C.A. & Gow, J.G; *Brit. J. Urd.*, 48; 163, 1966.
6. Kenney, M., *Am. Rev. Resp. Dis.*, 82: 564, 1960.
7. Lieberthol, F., Huth, F., *J. Urd.*, 30: 153, 1933.
8. Maclelland, J.C & Davis, K.F., *J. Urd.*, 47: 320, 1942.
9. Medler, E.M, *Am. J. Path.*, 2: 401, 1926.
10. Medler, E.M., *Rev. No. Tub, Assn.* 7: 579, 1949.
11. Medler, E.M., Ordway, W.H., *J.A.M.A.*, 119: 937, 1942.
12. Rosencranz, E., *J. Urd* , 44: 498, 1940.

TUBERCULOSIS OF TONGUE

(A case report)

B.K. KHATRI and G. S. JHALLA

(From Medical College, Ajmer)

The occurrence of tuberculosis of tongue as a primary lesion is quite rare and invariably the condition is associated with pulmonary or laryngeal tuberculosis.

Although there have been many reviews of the subject in the past (Weinstein 1914, Morrow and Miller 1922, Finney and Finney 1925 and Kanwar et al 1970), it was considered worth while to report a case of lingual tuberculosis seen recently by us.

Case Report

L.C. 38 yr. H.M. (Reg. No. 14369) was admitted in J.L.N. Hospital, Ajmer on 18.4.70 with the complaints of a painful ulcer on the tip of the tongue for the last 3 months. He also complained of loss of weight and occasional fever off and on for the last 3 months. On examination, an ulcer about $\frac{1}{4}$ " x $\frac{1}{4}$ " in size was found on the tip of the tongue extending on the ventral surface of the tongue. The ulcer was painful and lined with pale granulation tissue.

On general examination he was found to be poorly built and nourished. Submental and submandibular cervical glands were enlarged.

Examination of the respiratory system revealed occasional crepitations at both bases.

Investigations done were Hb 8 gm per cent, TIC 900/cu mm. P 60 per cent, L 35 per cent, E 3 per cent and M 2 per cent. ESR was 40 mm in the 1st hour. Examination of sputum for A.F.B. was negative.

Skiagram of chest showed evidence of bilateral miliary tuberculosis.

Biopsy was taken from the tongue lesion and histopathological report (653/70) revealed lesion to be tuberculous in nature.

Anti-tubercular treatment was started and there was evidence of remarkable healing of the ulcer.

Discussion

The incidence of secondary lingual tuber-

culosis is less than 1 per cent of the oral tuberculosis (Komet et al 1965). This low incidence is probably because of the use of modern powerful anti-tubercular agents for the treatment of primary tubercular focus in the body.

Tubercular infection of the tongue usually occurs due to contact with the infected sputum (Ghose, 1966) but it may also occur by blood spread, lymphatic spread or by direct contamination from the neighbouring tuberculous focus in the oral cavity.

Pathologically, Aird (1957) has described five types of lesions : —

(i) Tubercular Ulcers :—It usually develops as a small tubercle which later on softens to form an ulcer. Typically, they are shallow, often multiple, ovoid and lined with pale grey granulation tissues. They are quite painful and seen near the tip of the tongue.

(ii) Tuberculoma :—It originates as a lump anywhere in the tongue. The lump in due course of time softens to form an ulcer. Clinically, tuberculoma resembles a lingual gumma.

(iii) Tuberculous fissure :—They usually occur on the side of the tongue and their extent can be appreciated only by separating their edges.

(iv) Tubercular papilloma :—is due to an overgrowth of the margins of tuberculous fissures.

(v) Tuberculous cold abscess is due to break down of a tuberculoma.

Clinically the disease is more common in males and particularly seen in persons under treatment for advanced pulmonary or laryngeal tuberculosis.

The bed side diagnosis is rather difficult. However, the following features may prove helpful in diagnosing the tuberculous nature of lesion.

(i) The condition is quite painful.

(ii) Edges of the ulcer are sloping. If

carefully examined, each ulcer will be seen surrounded by a ring of minute "sentinel" tubercles.

(iii) Clinical evidence of pulmonary, laryngeal or genito-urinary tuberculosis.

(In our case, associated Koch's lesion in the chest and cervical lymphadenopathy was suggestive of the nature of the lesion).

The condition has to be differentiated from a carcinoma, gumma and chronic non-specific ulcers.

The final diagnosis, however, depends upon histopathological examination.

Management and prognosis

Anti-tubercular treatment should be insisted upon, once the diagnosis has been established. Usually the lesion heals well under conservative treatment.

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 tongue is reported. The literature has been reviewed briefly.

Acknowledgement

Thanks are due to Dr. M.N. Kathju, Principal, J.L.N. Medical College, Ajmer for his permission to publish this case report.

REFERENCES

1. Aird Ian: A Companion in Surgical studies. E & S Livingstone Ltd. Ed and London, 1957.
2. Finney, J.M.T. and Finney, J.M.T. (Jr.) : Tuberculosis of Tongue. *Surg. Gynec. and Obst.* 40 : 743., 1945.
3. Ghose, S.M. "Ulcers of tongue". *Ind.Joun. Med.Assos.* 41: 377, 1966.
4. Kanwar et al "Tuberculosis of Tongue" *Raj. Mcd. Jom-n.* Vol. X., No. 1, 1970.
5. Komet et al.: *A.M.A. Arch. Otolaryngol.* 82 : 649, 1965.
6. Morrow and Miller : "Tuberculosis of tongue" *J.A.M.A.* 83 : 1483, 1924.
Weinstein, J. : Tuberculosis of tongue. *New York, M.J.* 100: 162., 1914.

A CASE REPORT OF PULMONARY COMPLICATION OF AMOEBIC LIVER ABSCESS WHICH EXAGGERATED THE TUBERCULAR LESIONS IN THE LUNG

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1. T.J. 45 years, Muslim male Agricul turist attended the out-patient on July 31st 1969 with complaint of cough with expecto ration of 4 ounces with certain amount of foul smell. Fever with rigor pain in the right side of the abdomen for one month. Having haemoptysis and breathlessness since a week. He had an attack of dysentery for which he took treatment for 3 days, 3 months ago, in his village. Since then he is not keep ing good health. He was keeping good health before the attack of dysentery.

2. On examination patient was found an adult male under-nourished and anaemic. Clubbing of lingers and signs of toxoemia were present in the right infrascapular and inframammary area. Signs of consolidation with cavity in the right infrascapular area were present. Tenderness in the right hypochondriac region was present. Liver was palpable for 3 fingers breadth and was tender.

3. 1271, Figure 1 : X-ray chest taken on 31-7-69 shows dense infiltration and cavities with fluid levels in the right mid and lower zones. An horizontal fluid level seen under

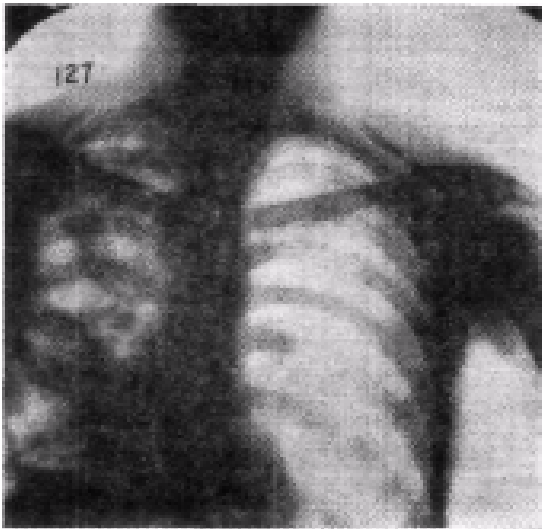


Fig. 1

X-ray Chest taken on 31-7-69, shows dense infiltration and cavities with fluid level on the right side. An horizontal fluid level under the right diaphragm.

the right diaphragm. Suggestive of liver abscess bursting into the right lung, producing Bronchohepatic fistula. Treatment started with amoebicidal drugs with general treatment (1) Dehydrometine 60 mg. I.M. daily for 10 days and later followed with chloroquine 300 mg. daily in two doses for 5 days and later followed 150 mg. after food. (2) Terramycin S.F. 500 mg. twice and daily for 3 days by mouth.

4. On repeated examinations of sputum, for acid fast bacilli, was negative. Sputum was positive for active amoeboid trophozoites. Motion was positive for cysts of *Entamoeba histolytica*. Urine for sugar nil.

5. 1320, Figure 2 : X-ray chest taken on 6-8-69 shows slight improvement and still

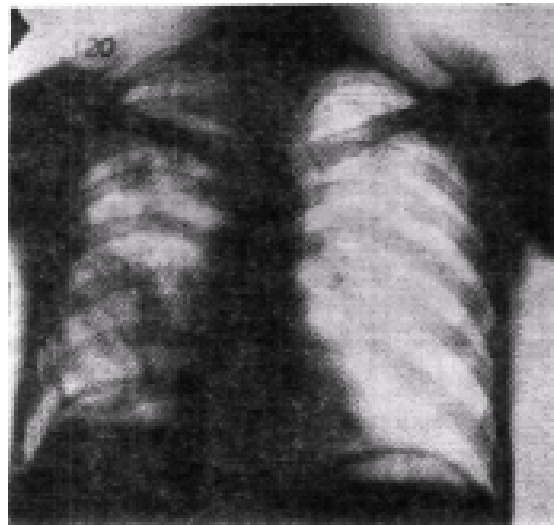


Fig. 2

X-ray chest taken on 6-8-69, shows dense infiltration and cavities with fluid level on the right side. An horizontal fluid level well seen under the right diaphragm.

dense infiltration, and cavity with fluid level seen. But the horizontal fluid level under the right diaphragm seen very well, better than figure 1.

6. 1404, Figure 3 : X-ray chest taken on

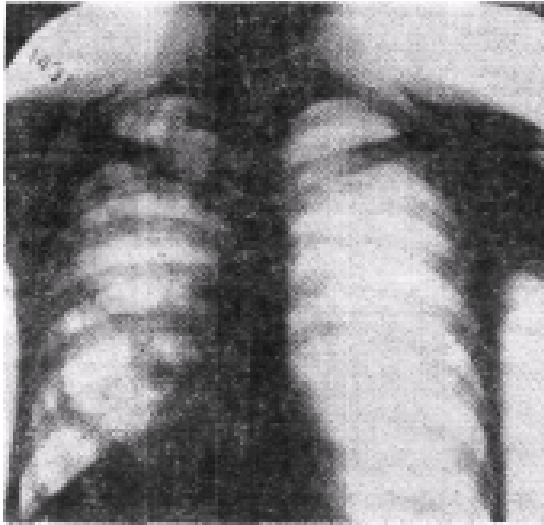


Fig. 3

X-ray chest taken on 14-8-69, shows **infiltration** right upper zone peaking of (he right diaphragm and a gap in the peak, looks like a **volcano**.

14-8-69 shown very much improvement compared to figures 1 and 2. The cavity with fluid level has disappeared. Even the horizontal fluid level under the right diaphragm has disappeared. But only infiltration is seen. Peaking of the diaphragm in the centre and a gape also seen in the peak of the diaphragm looks like a volcano. Suggestive of opening in the diaphragm through which liver abscess has ruptured.

7. 1507, Figure 4 : X-ray chest taken on 25-8-69 shows good improvement and further clearing of lesions. Gaping in the diaphragm has become smaller, but still some infiltrations seen in the right upper zone.

8. Hence pulmonary tuberculosis was suspected and the treatment of INH 300 mg. was advised for a period of one year, as his sputum was negative for AFB at this stage also. Advised checkup at every 3 months interval. Unfortunately patient never came for checkup.

9. On June 24th, 1970 the patient attended outpatient with complaints of cough with expectoration of one ounce daily, fever, chest pain, loss of weight since 3 months.

On examination the patient was undernourished, amoemic generalized oedema. No clubbing of fingers were present. Signs of bilateral infiltrations with cavities were

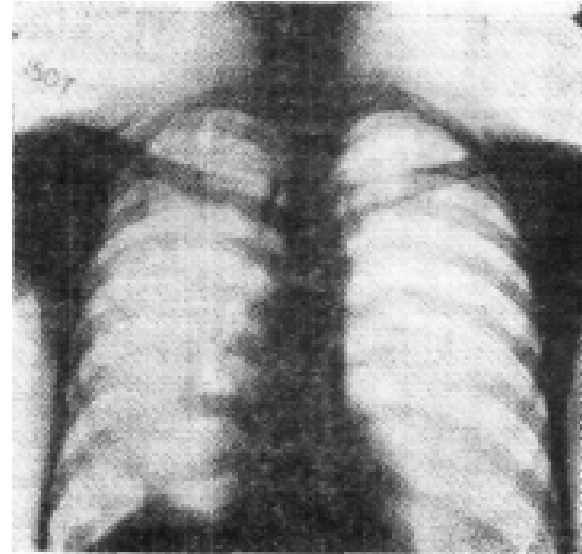


Fig. 4

X-ray chest taken on 25-8-69, shows infiltration in the **right upper zone** and a gap in *the* peak of the right diaphragm,

present. No tenderness in the right hypochondriac region and liver was not palpable. Sputum for acid fast bacilli was positive (+++) on spot collection and examination. Sputum for amoebic trophozoites or for cysts, was negative. Motion also was negative for cysts of *Entamoeba histolytica*. Urine for sugar was nil.

Figure 5 : X-ray taken on 25-6-70 shows extensive bilateral infiltrations with cavities. Right dome of the diaphragm normal and on screening the movements of the right diaphragm confirmed.

The pulmonary amoebiasis resulting from the direct extension due to the rupture of amoebic liver abscess, producing dense infiltration and cavities with fluid level in the lung seen in the Figure No. 1 and 2. It was diagnosed on history clinical examination presence of enlarged tender liver. Evidence of X-ray specific shadow of horizontal fluid level under the right diaphragm and the diagnosis was confirmed by the presence of amoeboid trophozoites in the sputum and cysts in the motion.

In this case the horizontal fluid under the right diaphragm seen in figure No. 1 and 2 is only due to the entrance of air through the bronchial-fistula caused by the rupture of

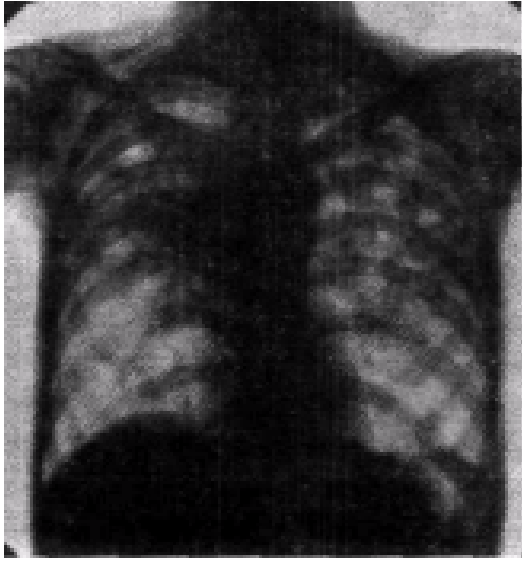


Fig. 5

X-ray chest taken on 24-6-70, shows extensive bilateral infiltration with cavities contour of the right diaphragm normal.

the abscess, as the liver abscess never aspirated at any time.

When once pulmonary complications occurs the case may be misdiagnosed either as pulmonary tuberculosis, lung abscess or as bronchogenic carcinoma, because the signs symptoms and also some of the X-ray shadows of the above conditions are alike. Hence the diagnosis should be confirmed on demonstrating the specific aetiology.

The case was diagnosed and confirmed by demonstrating the amoeboid trophozoites and cysts. Bronchography could not be done to demonstrate the bronchohepatic fistula. Pneumoperitonium not done to demonstrate the adhesions at the rupture point. This may be a case of bronchogenic spread of *Entamoeba histolytica*, as the major portion of the right lung is involved, seen in figure No. 1 and 2. An interesting point in this case that complete disappearance of clubbing of the fingers after treatment. With the persistence of slight infiltration in the right upper zone in figure No. 4 after 25 days treatment, associated condition of pulmonary tuberculosis with liver abscess was suspected. Sputum was negative for AFB and Mantoux test was positive. Anti-T.B. treatment was advised.

After 10 months gap the patients returned for treatment with an open case of extensive bilateral pulmonary tuberculosis seen in the figure 5. By comparing the figure 5 with the figure 1 to 4, it is evident that infiltration in right upper zone has spread the disease both sides. The left lung which was clear in figure 1 to 4 is extensively involved and also the right lung seen in figure 5 and the sputum which was negative has become positive for AFB.

Hence in this case the pulmonary amoebiasis may be factor for exacerbation of the tubercular lesions. However, many other factors might have played part in exacerbating tubercular lesions :—

1. Old age.
2. Nutrition.
3. Hepatocellular damage.

Summary :

Pulmonary complication of amoebic liver abscess was suspected on clinical and on chest X-ray and the diagnosis was confirmed by demonstrating the amoeboid trophozoites in sputum and cysts in the motion. Response to the amoebicidal drugs was very good. Associated pulmonary tuberculosis suspected and treatment advised. As the patient failed to take the anti-TB drugs and returned with open case of extensive bilateral pulmonary tuberculosis. In this case, pulmonary amoebiasis might be a cause in exacerbating the pulmonary tuberculosis by spreading the disease to other areas of the lung and converting the negative sputum for AFB into positive sputum for AFB. Further failure of continuing the INH treatment also a factor which assisted on exacerbating the disease.

ACKNOWLEDGEMENT

I am highly grateful to the Director of Health & Family Planning Services, Bangalore and the District Health & Family Planning Officer, Gulbarga for having permitted to utilise the materials to publish this paper.

REFERENCES

1. Deshmukh, M.D. (1969) Radiological diagnosis of chest diseases, Hand book of Anti-tuberculosis Association Aurangabad, 13.
2. Stephen S.J., and Uragoda C.G., Pleuro-pulmonary Amoebiasis. A review of 40 cases. *British Journal Dis. Chest* 1970, 64, 96.

AMEBIASIS OF LEFT LUNG-A CASE REPORT

S.K. SINGH, R.K. NARANG and S.K. JAIM
(From G.S. V.M. Medical College, Kanpur)

Amebic infection of the liver is frequently complicated by thoracic manifestations. Right lung and the pleura is commonly affected due to spread of infection from the right lobe of the liver. Involvement of left lobe of the liver and hence of the left lung is rare. This has prompted us to report a case of amebic abscess of the left lung.

Case Report

N.J., a 40 years old Hindu farmer was admitted to the hospital as an emergency case of hemoptysis. He was completely asymptomatic a fortnight before his admission. His illness started with cough, mucoid sputum and pain in the left side of the chest. Two days before he was admitted to the hospital he had an episode of hemoptysis. Past history was insignificant.

Physical examination revealed a thin built man with marked toxemia. Temperature was 101°F, pulse rate 110/mt., blood pressure 108/60 mm Hg. There was no cyanosis and no clubbing. Crepitant rales were present at the base of the left lung posteriorly and laterally. Liver and spleen were not palpable. Nothing abnormal was detected in other systems.

Hemoglobin was 8.0 gm. %, ESR (Wintrobe) 67 mm at one hour, total leucocyte count 10,600 cumm with neutrophils 62%, lymphocytes 30% and eosinophils 8%. Sputum smear was negative for AFB. Mantoux test was negative. Cysts of *E. Coli* and *entameba histolytica* were present in the stool.

A skiagram of the chest on admission (Fig. 1) showed an ill defined shadow obscuring the left cardiophenic angle. A lateral view (Fig. 2) showed the shadow to be situated above the left hemidiaphragm extending to the hilum (anterior basal segment).

The patient was treated with tetracycline for three weeks without relief in symptoms. The patient continued having recurrent attacks of hemoptysis. A chocolate coloured specimen of the sputum raised the possibility of the diagnosis of amebic lung abscess. Accordingly emetine hydrochloride 60 mg. I M. injection was given daily for 10 days. This resulted in marked symptomatic improvement. Toxemia disappeared completely. There was no cough

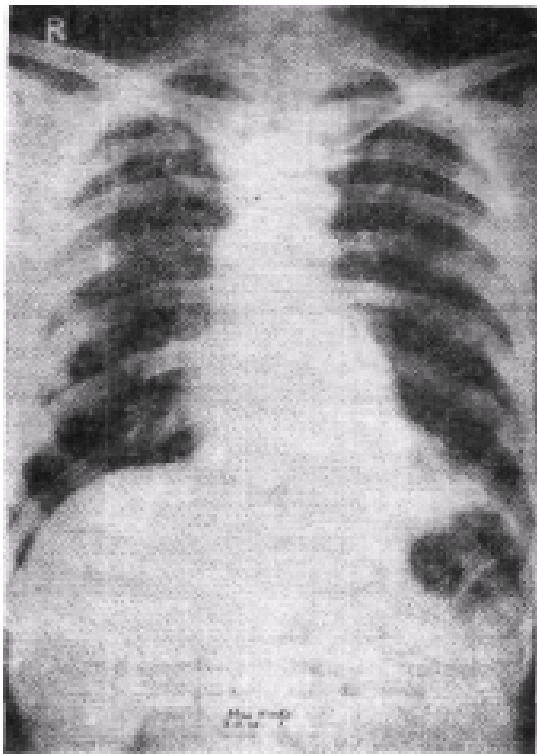


Fig. 1

X-ray Chest P.A. View. An illdefined opacity in the left cardiophenic angle.

and no hemoptysis. The shadow cleared on a repeat skiagram (P.A. view) but some residual lesion was still seen on the lateral view (Fig. 3).

Discussion

The diagnosis of amebic lung abscess was suspected when the patient passed chocolate coloured sputum and had failed to respond to tetracycline. The location of the lesion in the anterior basal segment should have put us on guard regarding the diagnosis. The diagnosis was confirmed by therapeutic response to emetine.

Pleuro pulmonary amebiasis usually in a complication of liver abscess (Vyas et al, 1953, Mat hew and Anathachari 1964). Since liver abscess effects the right lobe of the liver, chest lesions are nearly always present on the right side only. Involvement of the left pleural

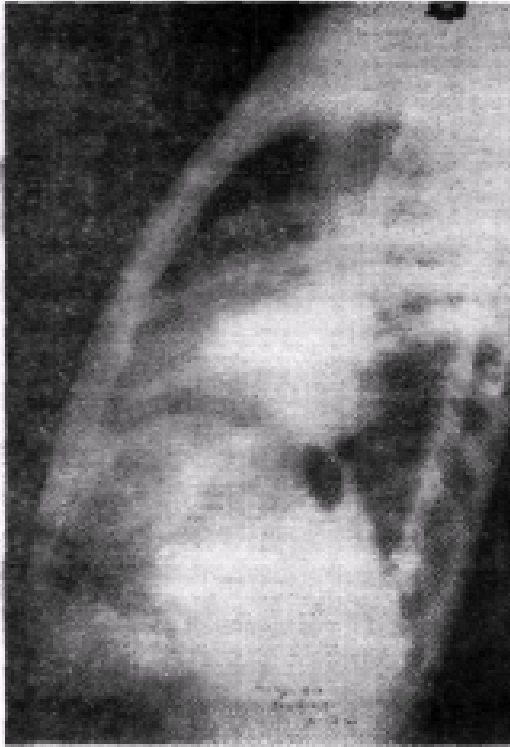


Fig. 2

X-ray chest left lateral view. Opacity situated in the anterior basal segment.



Fig. 3

X-ray chest left lateral view. After treatment with emetine, the lesion is much smaller.

cavity due to rupture of the amebic abscess of left lobe of liver has been uncommonly reported (Cort, 1951, Masse et al, 1957, Merchant et al, 1963, Mathew and Ananthachari 1964). In cases where pleural cavity is obliterated due to adhesions a left lobe liver abscess may rupture into the left lung (Chatterjee, 1962, Vyas et al, 1963).

In the present case there was no clinical evidence of a liver abscess. However, cysts of *entameba histolytica* were present in the stool. The spread of infection from the intestines to the liver and thence by lymphatics to the left lung was the possible sequence of events. Mullan and Williams (1965) report a case of amebic abscess of the left lung in which hepatic amebiasis was contacted by the patient 48 years previously. At autopsy there was no evidence of liver involvement. This extraordinary long gap between the attack of hepatic amebiasis and the lung infection may explain amebic involvement of the lung without clinical evidence of hepatic infection.

The diagnosis of amebic abscess of the lung is difficult especially when the left lung is involved. A chocolate coloured sputum,

location of the abscess in the anterior basal segment (an uncommon location for pyogenic abscess) and therapeutic response to emetine establishes the diagnosis.

ACKNOWLEDGEMENT

We are thankful to the Superintendent, L.L R. & Associated Hospitals for his kind permission to publish the case report.

REFERENCES

1. Chatterjee, P.K. (1962): *Indian J. Chest Dis.*,
2. Cort, E.C- (1951): *JAMA*, 90, 2005.
3. Masse, E., Mabitle, E., Merk, H. & Chebat, J: Quoted in *Trap. Dis. Bull.* 54, 431, 1957.
4. Mathew, N. T. and Ananthachari, M.D. (1964): *J. Ass. Phys. India*, 12, 839.
5. Merchant, H.C., Ramamoorthy, K., Choksy, M.D., Shikarpuri, N.K. and Shah, S.R. (1963): *Ibid*, 11, 583.
6. Mullan, D.P. & Williams, N.E. (1965): *Brit. Med.J.*, 1, 235.
7. Vyas, P.M., Bhargava, N.N. & Gopinath (1963): *Ind.J.Surg.*, 25, 141.

SUMMARY OF PROCEEDINGS OF TAIPEI CONFERENCE

(Seventh E.R.C. Conference)

The seventh Eastern Regional TB Conference of the International Union Against Tuberculosis was held in Taipei (Taiwan, the Republic of China) from November 16—21, 1970.

The conference was attended by about 100 delegates and of these nearly 70 were from overseas viz. Australia, Hong Kong, India, Indonesia, Japan, Republic of Korea, Malaysia, Singapore, Thailand and Republic of Vietnam.

The I.U.A.T. and W.H.O., were also represented.

The Indian Delegation consisted of the following :-

Shri B.M. Cariappa, Dr. S P. Pamra, Dr. S.K. Basu Chaudhuri, Dr. J.L. Bhatia, Dr. Y. Rajashekra, Mr. B.K. Shyara Singh and Dr. H.B. Dingley.

The conference was inaugurated by Mr. C.K. Yen, the Vice-President of the Republic of China, in Hole! Ambassador in Taipei and the closing session was held in the city of Sun Moon Lake.

The conference was well organised and managed. The scientific sessions were interesting and educative. The delegates were very well looked after and arrangements were par excellence.

There were at Homes by the Vice President of the Republic of China, the Mayor of Taipei city and Dr. C.W. Chao, the Director of Taiwan Provincial TB Control Bureau,

The Executive Committee and Council meetings were held on November 15, 1970, Mr. Cariappa was re-elected as a member of the Executive Committee. He was also chosen to serve on the programme and the budget committee.

The amended constitution was approved by the Council meeting.

A suggestion was made at the Assembly meeting that the Eastern Region should have a Technical Committee on Bacteriology. The proposal was that each National Association should appoint one person to serve on this Committee and this person should organise a

Committee on Bacteriology in his own country. We from India pointed out that we have a high power Technical Committee which advises the Association on all technical matters including bacteriology and generally a Technical Committee on Bacteriology alone did not seem to be necessary. We stated that the suggestion would be put to our Technical and Executive Committees and their decision would be forwarded to the Eastern Region.

The scientific session was inaugurated by the President of the Eastern Region of the International Union Against Tuberculosis on the afternoon of November 16th.

The whole afternoon was devoted to presentation of papers on "The Economic Development in Taiwan" by Mr. Y.S. Sun, Minister, Ministry of Economics, "The Development of Education in Taiwan" by Mr. C.C. Pan, Commissioner, Department of Education, and "Public Health in Taiwan" by Mr. T.Y. Lee,

Taiwan "Provincial Tuberculosis Control Programme" by Dr. C.W. Chao, "Tuberculosis Control Programme of the Educational Workers" by Dr. Meng and "Tuberculosis Control Programme of retired servicemen" by Dr. J.P. Lu.

The speakers gave an exhaustive review of the economic, social, educational and public health programmes and progress in Taiwan during the last 20 years. It was interesting to hear about the tremendous changes brought about over such a brief period.

"*Taiwan Provincial Tuberculosis Control Programme*", Dr. C.W. Chao stressed the three following aspects : (i) The epidemiology of tuberculosis in Taiwan (ii) the organisation of tuberculosis programme and (iii) the operation of the programme.

Dr. H.H. Meng : "*Tuberculosis Control Programme of Educational Workers*". It is a separate but an integral part of the nation wide TB control programme. It covers all the kindergarten primary and secondary school teachers and administrative staffs and also (he-normal school students and teachers.

Its activities range from health education X-ray chest of new entrants to the service and subsequently at regular intervals, treatment of

diagnosed cases, TB. seal sale contest among contacts etc.

Dr. J.P. Lu ; " Tuberculosis Control Programme of the retired servicemen". Its activities range from accurate diagnosis, to provide definite treatment, advances on job assignment and to supervise the work of the peripheral hospital.

Session On Standard Chemotherapy and its application in the Tuberculosis Programme November 17, 1910

Chairman, Dr. S.P. Pamra: while introducing the subject reviewed the concept and the present day status of chemotherapy. He stressed the judicious use of first line drugs in intensive initial therapy, the role of second line drugs in developing countries at present and the important problem of drug failure.

Dr. K. Kameda, Japan : Chemotherapy in Japan :- Three drug combination with SM , INH and P.A.S. is recommended at the start of the original treatment both for bacteriologically positive and negative cases. Thiacetazone is not used in Japan because of bitter experience of severe side effects.

The chemotherapy is continued for six months or one year after attaining therapeutic target point.

The default rate averages 30-40 per cent in one year of the domiciliary treatment.

Experience with three second line drugs showed 80 percent bacteriological conversion, 40-50 percent with two and 20 percent with one second line drug. In the chemotherapy with these drugs on cavitary cases, radiological improvement is little and relapse rate is higher.

Dr. C.C. Chang, China : Chemotherapy in Taiwan :- Experience with intermittent therapy showed 75.6 percent bacteriological conversion inspite of 100 percent regularity.

The primary drug resistance has increased from 18.1 percent in the second survey to 39.3 in the third survey. Similarly acquired drug resistance increased from 61.1 percent to 71.0 percent in third survey. Experience with the use of Thiacetazone showed higher incidence of toxic effects.

Dr. William Chan, Singapore : "Chemotherapy in Singapore" : Combination of streptomycin plus isoniazid followed by isoniazid is superior to streptomycin plus isoniazid and

isoniazid plus thiacetazone as regards toxicity and efficacy.

The combination of isoniazid plus ethambutol is effective and more acceptable than isoniazid plus P.A.S., but its high cost in relation to P.A.S. restricts its therapeutic role in routine practice.

Position of chemotherapy in various countries of the region was also presented by their representatives.

Chairman, Dr. R.S.A. Marshman, Australia

Dr. T. Nakajima, Japan : "A Follow UP Study of Pulmonary Tuberculosis" patients showed that prognosis of sputum positive cases was worse than that of negative cases. It was worse with far advanced cavitary disease with negative bacilli than that of the bacilli positive cases.

Though the minimal cases heal spontaneously without receiving treatment, the prognosis of far advanced cases is unfavourable and difficult to improve. The prognosis of moderately advanced cases has improved with advancement in chemotherapy and surgical treatment.

Dr. H.B. Dingley, India : "Management of drug failure cases": Specific treatment of drug resistant cases with anti-microbials is effective but not economical and has organizational difficulties. Surgical treatment, if applied at the most opportune time has a definite place in the management.

Dr. S.K. Basil Chaudhuri, India : Management of drug failure cases of pulmonary tuberculosis" : emphasized the role of surgical therapy in the treatment of drug resistant cases.

Dr. P.A.L. Horsefall, Hong Kong : presented the results of routine treatment with ethionamid, cycloserine and pyrazinamid. Discussion was headed by Sister Aquinas.

November 18th 1970, Session on case finding :

Chairman, Dr. Wong Hin Sun, Singapore.

Dr. J.S. Sodhy, Malaysia the main speaker introduced the subject by presenting material from Netherland, Sakeschwachen and the National Tuberculosis Institute, Bangalore .to prove that the contribution of mass miniature radiography to total disease discovered by examination of patients attending the specialised clinics and general health agency in the presence of symptoms is insignificant.

* *Dr. S. Sakamoto, Japan: "Case finding in Japan".* Of the total of 51.7 percent bacteriologically positive cases diagnosed, 41.7 percent were symptomatics, thus effective diagnostic methods of symptomatics will give a yield of nearly 80.7 percent of the new cases.

Of the newly registered TB cases 30 percent were detected by mass examination consisting of tuberculin test below 5 and the rest by M.M.R. The rest were diagnosed from amongst the symptomatics.

Dr. S.P. Pamra, India: "A critical appraisal of relative merits of radiology and bacteriology in case finding." In the absence of X-ray facilities direct microscopy of the sputum can help to detect all the highly infectious cases in the community easily, though not cheaply.

Where X-ray facilities are available, X-raying of the symptomatics followed by sputum examination of these with abnormal X-ray findings appear to be the most rational and rewarding case finding procedure.

Dr. S.W. Luan, Republic of China: "Case finding programme in Taiwan." Of the three ways of case finding, namely community wide mass chest survey, selective mass chest survey and direct microscopic examination. Selective mass chest survey is very effective both regarding yield and operational cost.

Dr. J.L. Bhatia, India, "How effective are the present control measures recommended for rural areas": He emphasised on the efficient working of the district TB. Control centre, which will attract majority of patients.

November 19th 1970, Session on B.C.G. Vaccination:

Dr. Y. Avzuma, Japan: B.C.G. Vaccination in Japan presented material showing the improved coverage of B.C.G. vaccination and about the productive effect of B.C.G. vaccination, which has brought down the tuberculosis incidence in the population.

The introduction of multipuncture method

of vaccination has reduced the complications of B.C.G. vaccination.

Dr. R.N. Roy, Malaysia: "B.C.G. Vaccination programme in the State of Sabah."

Dr. D. Song, Korea: "B.C.G. Vaccination programme in Korea:" In spite of nation wide intensive B.C.G. vaccination programme, it has not been possible to cover the entire child population, maintain standard technique and enthusiasm of nurses in charge of vaccination.

Dr. T. Sawada, Japan: B.C.G. vaccination by multiple puncture method employed in Japan: By the multiple puncture method of B.C.G. vaccination, the tuberculin reaction induced was comparable with that by the intradermal vaccination and the local lesion was much smaller than in the intradermal method.

Dr. W.C. Chou, Republic of China: Studies on post vaccination reaction in school children vaccinated with liquid and freeze dried B.C.G. Vaccination: The potency of liquid vaccine (Taiwan) was identical to freeze-dried vaccine (Japanese).

November 19th, 1970: Afternoon Session on "The role of voluntary tuberculosis organization and fund raising to support their activities:

Dr. Nakchin Chung, Republic of Korea: Community participation programme.

Dr. M. Yamaguchi, Japan: The role of women's society played in antituberculosis activities in Japan."

Mr. B.K. Shyam Singh, India: "Pilot Project in India: He stressed the role of voluntary worker in the development of TB. Associations, motivating the defaulters, health education etc.

Dr. Y. Rajashekhra, India: TB. control and family planning": With the increasing population the need to stress family planning among TB patients is more and therefore family planning must form an integral part of TB. control programme,
H.B.D.

NEWS AND NOTES

ANNUAL MEETINGS

The Thirty-second Annual General Meeting of the Tuberculosis Association of India was held on 16th April, 1971 in the Conference Hall of the Association. Dr. J.B. Shrivastav, Chairman of the Association, presided.

The Technical Committee of the Association met on 15th April and the Conference of the Secretaries of the State TB Associations and Seal Sale Organisations in India held their meetings on the 16th April, 1971.

SEAL SALE SHIELD-1971

The Association's Seal Sale Trophy for 1971 was awarded to the Tamil Nadu TB Association for the fourth successive year for the highest Seal Sale Collections. The Runners-up Cup was presented to the Kerala TB Association for the second highest collection. Dr. J.B. Shrivastav, Chairman of the Association, presented the awards to Shri A. Gopala Padayatchi and Dr. S. Sivaraman of the Tamil Nadu and Kerala Association respectively.

HEALTH VISITOR'S COURSE

The TB Health Visitor's Course will commence in New Delhi from July 1971 and terminate in March, 1972. Applications for admission to this course should reach the T.A.I, office on or before 31st May, 1971.

CASH AWARDS

The Tuberculosis Association of India will award a cash prize of Rs. 500/- to a Tuberculosis worker, preferably below 45 years of age, for an *original* article not exceeding 30 full-scape double-spaced typed pages (approximately 6,000 words) excluding charts and diagrams, on a subject relating to Tuberculosis in which he or she is specializing or has worked and adjudged best by a special committee of this Association. Papers may be sent in *quadruplicate* to reach on or before 31st October, 1971.

ESSAY COMPETITION

The Tuberculosis Association of India has decided to give another cash prize of Rs. 300/- to a final year medical student for an original essay on Tuberculosis adjudged best by a special committee of this Association. The competition will commence from 1972 and the

subject selected for the first competition is "Chemotherapy of Tuberculosis".

Manuscript should be typed in full-scape size double-spaced not exceeding 15 pages (approximately 3,000 words). Four copies of the manuscript should reach the Tuberculosis Association of India, 3, Red Cross Road, New Delhi before 16th October, 1971 through the Dean/Principal of the College.

22ND TB SEAL

The Tuberculosis Association of India has selected the design of a "ROSE BUD" for the 22nd TB Seal, designed by Shri Chintamani Vyas of New Delhi. The theme symbolises the happiness, the joy, living and cheer. The 22nd TB Seal Sale Campaign will commence, as usual, on 2nd October, 1971.

TB & CHEST DISEASES CONFERENCE: MAHARASHTRA

The ninth Maharashtra State TB & Chest Diseases Conference was held in Bombay from 9th to 11th April, 1971 under the auspices of the Maharashtra State Anti-TB Association. Smt. Pratibha D. Patil, Dy. Minister for Public Health & Prohibition, Government of Maharashtra, inaugurated the Conference. Shri Homi J.H. Taleykar Khan, Vice President of the Association, was the chief guest.

The Scientific session included Panel discussion on "Pitfalls in management of pulmonary tuberculosis" Dr. P.A. Deshmukh, Dr. S.P. Pamra, Dr. S.P. Tripathy and others took part in the discussion. Dr. M. D. Deshmukh acted as the moderator. Papers were also presented on "Surgical impressions of uro-genital tuberculosis", "Surgical management of bone and joint tuberculosis" and "Surgery in mediastinal tumours". There was also Panel discussion on "Non-Tuberculosis Respiratory Infections". Prof. N.H. Keswani, All India Institute of Medical Sciences, New Delhi, delivered the guest lecture on "Tuberculosis in Ancient India".

The Maharashtra Association also organised a TB Camp (Shibir) at Panvel during the Conference.

SEMINAR IN JAMMU & KASHMIR

A Seminar on Tuberculosis control will be organised by the Jammu & Kashmir TB

Association sometime in June this year. Dates and programmes for the Conference are being finalised now.

TEXT BOOK ON TUBERCULOSIS

The Text-Book on Tuberculosis which the Association has compiled under the General Editorship of Dr. KN. Rao is expected to be published by the middle of June, 1971. The publication is expected to cost about Rs. 50/-.

Messers Kothari Book Depot, Acharya Dhonde Marg, Parel, Bombay, are the publishers.

MOSCOW CONFERENCE

The 21st International TB Conference will be held in Moscow from 12th to 16th July, 1971. The Societe Des Phtisiatres, Moscow will be playing the host. Prof. B.V. Chebanov, President of the IUAT, will preside over the Conference.

Shri S.P. Sharma, Administrative Officer of the Association, passed away after a short illness on the 5th of April, 1971. Shri Sharma was on the staff of the Association from its inception. He was with the King George Thanksgiving Fund before 1939 and when this Fund was merged with the All-India Fund and the Tuberculosis Association of India was established on 23.2.1939 Shri Sharma was shifted to this Office. He was a very devoted worker. After becoming the Superintendent in April, 1963 he was promoted as Administrative Officer in March, 1966. He has left behind a large number of friends to mourn his loss. We offer our deepest condolences to the bereaved family.

ABSTRACTS

Vol. XVIII

April 1971

Abst. No. 2

The reactivation of tuberculosis in New York city in 1967.

John Edsall, J. Gary Collins and John A.C. Gray. Amer. Rev. Resp. Dis.; 1970, 102, 725.

A statistical sample of the reactivation cases of tuberculosis reported in 1967 was studied. 44.2% of the patients could be considered as true relapses. The disease had never been proved to be inactive in 54% and the remaining 2% were doubtful relapses. The relapses in 95% of the patients was bacteriological and/or radiological. In the remaining the proof came from autopsy or biopsy specimens. Reactivation occurred at the site of previous disease in 66%, new site in 10% and both at the old and new sites in 24%.

Relapse was noted in the first year after stopping treatment in 7.6%. Almost 50% of the relapses occurred in more than 5 years after the patient had reached inactive status. Relapses occurred most often among persons at the lowest end of socio-economic scale, those who live alone and were alcoholics. Negroes were more prone than whites. Inadequate chemotherapy appeared to be the most important factor but extent of disease was also a probable factor. Relapse was often associated with diabetes, peptic ulcer and pregnancy. Only 35% of the relapses were detected during routine follow up. The rest of them attended because of the presence of suggestive symptoms.

S.P.P.

Non-culturable Acid Fast Forms in the sputum of patients with Tuberculosis and chronic pulmonary disease.

Fredrick C. Warring Jr. and Urai Sutra-mongkole. Amer. Rev. Resp. Dis. ; 1970, 102, 714.

A total of 7,498 sputum cultures were examined from 1,242 hospitalized patients with tuberculosis and chronic pulmonary disease, and 2,755 specimens from 688 clinic patients

were examined. Non-culturable acid-fast forms occurred in the sputum of 24% of patients with active pulmonary tuberculosis, in 3% of the patients with quiescent or inactive disease and in 1% of persons with non-tuberculous conditions. Eight per cent of the sputum specimens from patients with active pulmonary tuberculosis were microscopically "positive" but culturally "negative" (MPCN). The incidence in patients with inactive tuberculosis was 1%, and in non-tuberculous patients it was 0.2%. Thirty two hospitalized patients and one clinic patient had three or more MPCN specimens.

The pattern of MPCN specimens was studied in detail in 32 hospital patients. Ten of them died ; in 6 of these the disease was inactive at the time of death ; in 1 quiescent and in 3 active. Autopsy was performed on 4 patients, all of whom had shown MPCN specimens within 6 months before death. Only one lung specimen could be put up for culture and the micro-organism did not grow.

Non-culturable acid-fast forms usually occur as pulmonary tuberculosis becomes quiescent or inactive and these bacilli are considered as true Acid Fast Bacilli that have been cast off from necrotic tissue and their viability is reduced. Isolated MPCN specimens from patients with non-tuberculous pulmonary disease or inactive tuberculous disease are more likely to be other bacteria. The fate of 2 patients with multiple MPCN specimens lends support to the theory of bacterial persistence during long-term chemotherapy.

Primary Drug Resistance : A continuing study of drug resistance in tuberculosis in a Veteran Population within the United States.

Gladys L. Hobby, Peggy M. Johnson and Valeria Boytar-Paptrnyik. Amer. Rev. Resp. Dis. ; 1970, 102, 347.

Between September, 1962 and September, 1969, 3183 strains of mycobacterium tuber.

culosis derived from an almost equivalent number of previously untreated tuberculous patients were tested for their susceptibility to anti-tuberculous drugs as part of a continuing survey of primary drug resistance amongst veterans in the United States.

Strains requiring more than 0.5 microgram INH, more than 5.0 microgram PAS, more than 10.0 microgram Ethambutol and more than 1.0 microgram Rifampicin per ml of medium for inhibition of 20 colonies or more of growth have been taken as showing "same degree of resistance". The study shows that primary drug resistance to streptomycin, INH and PAS did not exceed 1.6, 4.2, and 7.2% in 1968-69 as compared to 3.1, 3.9 and 2.9 respectively in 1962/63. Based on one year's experience only incidence of primary resistance to ethambutol was 15.8% and to rifampicin 0.4%.

S.P.P.

Mycetoma Formation in Cavitory Pulmonary Sarcoidosis.

Kenneth J. Gurske and Richard J. Fleming Radiology ; 1970, 95, 279.

Wide and varied manifestations of sarcoidosis are well known. Five cases of cavitory pulmonary sarcoidosis are presented. In 2 of them mycetoma was present within sarcoidosis cavity. The diagnosis of primary cavity sarcoidosis was made by elimination of other causes of cavitation viz, pulmonary tuberculosis, pathogenic fungi and those structural changes which often masquerade as cavities such as ectatic bronchi or emphysema tons blebs. Such patients are relatively asymptomatic in contra-distinction to other cavitory diseases and the cavity is relatively stable in its appearance over long periods of time.

The radiological appearance of the sarcoidosis cavities is not distinctive. The cavity is usually surrounded by diffuse infiltration process and its inner margin presents an irregular appearance. Varying degrees of hilar adenopathy may or may not be seen. Pleural reaction or effusion is conspicuous by absence. The exact pathogenesis of these cavities is in doubt. Because of propensity for production of hyaline material within sarcoid granulomata, it is believed that expulsion of this hyaline material accounts for cavitation. This view is supported by the finding of hyaline material in the sputum of some patients of pulmonary sarcoidosis. Another view ascribes cavitation to ischaemic necrosis of large conglomerate granulomata.

S.P.P.

Roentgen findings in Farmer's lung.

Howard J. Mindell. Radiology; 1970, 97, 341.

Farmer's lung is an acquired hyper-sensitivity reaction to glycopeptide or polysaccharide products of certain thermophilic actinomycetes which grow in mouldy hay. The lung lesion is usually described as granulomatous pneumonitis. The usual lesion in the acute phase is disseminated nodular densities, 1 to 3 mm in diameter, frequently concentrated in the central two-thirds or lower zones of the lung fields, occasionally described as 'sandstrom' appearance. The lesions may be so tiny and close together that alveolar confluence may be suspected. The hilar shadows are not accentuated and super-added alveolar exudate is unusual. On the whole radiological appearances are often less pronounced than the clinical picture. In the acute stage, the process tends to be self-limited and complete clearing is usual, generally in a few weeks but even as early as 10 days from the onset of symptoms. Repeated exposures may lead to irreversible pulmonary disease characterized by diffuse interstitial fibrosis, generalized or bullous emphysema and occasionally death. Rapid clearing helps to distinguish farmer's lung from other conditions producing similar radiological appearance e.g. pigeon breeder's disease, maple-bark disease, lequiosis, cave explorer's disease (possibly due to bat dung) and iatrogenic lung disease.

S.P.P.

Roentgen Manifestations of Pulmonary Nocardiosis.

Charles B. Grassman, David G. Bragg and Donald Armstrong. Radiology ; 1970, 96, 325.

Pulmonary Nocardiosis can occur both as a primary and as an opportunistic infective process. Twelve proved cases seen over a 9-year period in a New York Hospital are reported. It is seen more commonly in association with chronic and neoplastic diseases, particularly in patients on long-term adrenocorticosteroid therapy. Often it occurs as a complication of pulmonary alveolar proteinosis or in conjunction with active pulmonary tuberculosis and silicosis. Fever and cough were the most common presenting symptoms. Subcutaneous brain, hepatic and renal abscesses were often seen as a terminal complication

Radiological features consist of segmental or lobar infiltrative changes with rapidly occurring thick-walled cavities or cavities within the area of a nodule or mass. Empyema and

pleural effusions often co-exist. A "fungus ball" is not common and hilar involvement and calcification is seldom seen. Radiologically the lesion has to be differentiated from cavitation of a necrotic pulmonary neoplasm, tuberculosis, histoplasmosis, aspergillosis, actinomycosis etc. Sulphonamide drugs are by far the most effective agent in the treatment of Nocardiosis.

S.P.P.

Viral Pneumonia.

Patric Conte, E. Robert Heitzman and Bedros Markarian. Radiology ; 1970, 95, 267.

The number of known and unknown viruses which produce pulmonary abnormalities is fairly large. The evolution of viral pneumonia begins with destruction of ciliated epithelial cells, goblet cells and bronchial mucous gland cells throughout the respiratory tract. As these cells undergo necrosis, they are sloughed down to the basement membrane. Subsequently, the bronchial and bronchiolar walls become oedematous and infiltrated with mononuclear cells, primarily lymphocytes. This oedema and cellular infiltration extend from the peribronchial tissues into the interlobular septa of the lung. The pathological picture at this stage represents the so called "Interstitial viral pneumonia". Interstitial or focal inflammatory changes may eventuate into localized and generalized hemorrhagic pulmonary oedema. In this phase of the disease, the alveoli are filled with oedema fluid, marked hemorrhage and infiltration of neutrophils. Alveoli are often lined with a hyaline membrane. Thrombosis may supervene and eventually necrosis and abscess formation may result. As the process resolves, there is an epithelial regeneration, gradually changing into normal ciliated columnar epithelium of the respiratory tract. Some of these late changes resemble chronic interstitial fibrosis. Thus viral pneumonia although commonly considered to be interstitial often has a significant alveolar component or may present as pleuro-pulmonary reaction.

Radiological appearances conform to one of the following patterns :—

1. Interstitial viral pneumonia where presentation is that of a peribronchial infiltration.
2. Lobular or sublobular inflammatory reaction, which presents as patchy lobular pneumonia or bronchopneumonia.

3. Localized or generalized oedema where the appearance is identical to that of acute lobular or segmental pulmonary oedema of any cause. Radiological changes are rapidly progressing, often proceeding from a localized process to an extensive, confluent, bilateral involvement in a few hours.

4. Pleural reaction with or without free effusion. Whether the inflammatory reaction extends along the interlobular septa or merely extends from involved subpleural lobules is not clear. Resultant pain with splinting of the chest may produce poor basilar aeration and consequent linear atelectatic changes.

5. Chronic interstitial fibrosis. It is conjectured that viral pneumonia may be the cause for many of the chronic interstitial fibrotic processes now considered idiopathic.

S.P.P.

The Radiographic Manifestations of Alpha-1 Antitrypsin Deficiency.

Russel S. Bell, The Roenthenographic Findings in Alpha-1 Antitrypsin Deficiency (AAD), R.A. Rosen et al Radiology / 1970, 95, 19 & 25.

To-date, only two diseases have been associated with deficiencies or serum enzyme inhibitors :—

(a) Hereditary angioneurotic oedema with deficiency of the Alpha-2 globulin inhibitor of the first component of human complement.

(b) Chronic obstructive pulmonary disease (COPD) with Alpha-1 globulin antitrypsin deficiency (AAD). AAD is inherited as an autosomal recessive characteristic and, therefore, varies from one population to another. Pulmonary symptoms generally begin in the 3rd or 4th decade in contrast to the average patient with COPD presenting between 55 and 65 years of age. There is no sex variation in AAD, although male preponderance is generally noticed in emphysema arising as a result of COPD. Patients with AAD have no significant history of prior bronchitis or smoking or other factors commonly leading to emphysema. Pulmonary decompensation is the initial respiratory problem.

Radiographically, severe emphysematous changes are present, predominantly in the lower lobes in contrast to centri-lobular emphysema which primarily involves the upper zones. Bullous changes are usually absent. Evidence of pulmonary hypertension and right ventricular enlargement is often present. Decreased perfusion can usually be demonstrated by lung

scanning or by pulmonary augiography, with the changes most severe at the bases.

The authors hypothesize that in normal individuals serum antitrypsin activity increases markedly in the presence of infection. Deficient individuals have initially low antitrypsin activity levels which cannot be increased significantly. When challenged with a respiratory infection or other insult, such patients may autodigest their lungs as a result of the release of trypsin activity by the lysed defending leucocytes with subsequent emphysema,

S.P.P.

Pulmonary complications of drug therapy.

Alfred Brettner, E. Robert Heitzman and William G. Woodin. Radiology 1970, 96, 31.

Adverse drug reactions are becoming increasingly important and frequent in medical practice. The most common agents producing adverse pulmonary drug reactions are antibiotics and allied chemotherapeutic agents like penicillin, furadantin and madribon; anti-hypertensive agents like hexamethonium, inersine, and diiril; antimetabolites like methotrexate and myleran and few other drugs like dilantin, sansert and pronestyl. In some cases the reaction is an allergic manifestation while in some others reaction is the result of hapten-protein conjugation. In some the mechanism is still obscure or merely a manifestation of personal idiosyncrasy.

Clinically, the onset may be almost immediate or may occur months or years after the drug therapy was instituted. Acute onset is characterized by sudden development of chills, fever, cough and dyspnea. In some cases generalized hyperseusitivity reactions viz skin rash, lymphadenopathy and eosionphilia etc. may also be present. In the case of insidious reaction, usual complaints are cough and dyspnoea,

Radiologically the changes may present any of the following patterns :—

- (a) Acute (and often diffuse) alveolar pattern,
- (b) Acute and diffuse interstitial pattern.
- (c) Chronic interstitial pattern.
- (d) Pleura-pulmonary pattern.
- (e) Hilar adenopathy.

Alveolar pattern is the most common presentation and diagnosis is easy if radiological changes are accompanied by signs of hypersensitivity reactions. Reactions

associated with hypersensitivity usually clear promptly upon removal of the offending agent but in some cases chronic changes such as those produced by furadantin may take months to clear. In the case of chronic interstitial pattern, the changes may be permanent. A careful drug history should be as much a part of the evaluation of a patient with obscure pulmonary lesions as is the occupational history.

S.P.P.

Roentgenologic Observations of Lung Carcinoma in the Adult Health Study, 1950-1968, Hiroshima-Nagasaki.

Hajime Nakata, Keiichi Matsuura & Walter J. Russell. Radiology; 1970, 95, 623.

In an adult health study programme of the **Atomic Bomb** casualties in Hiroshima-Nagasaki, 29 cases of pulmonary carcinoma were detected and the speed of growth of the lesion was studied. In 6 of these, equivocal densities were evident at x-ray examination 23 to 62 months before subsequent establishment of the diagnosis of carcinoma. Thus 20 percent of the total cases had a relatively slow growth.

Two of them were males in 60—65 age group and 4 were females. The ages of the females were 50, 56, 58 and 68 years respectively. Four of the growths were Adenocarcinoma and 2 were undifferentiated.

S.P.P.

Widening of the Mediastinum Resulting from Fat Accumulation.

Edson Price and Leo G. Rigler. Radiology; 1970, 96, 497.

Increase in the width of the superior mediastinal shadow may be the result of many conditions such as tumour, lymph node enlargement, thyroid enlargement, dilated oesophagus, various vascular dilatations and mediastinal abscess. The presence of fat in the superior mediastinum is reported as an additional, unusual cause of such widening. This is a benign process, usually the result of prolonged steroid administration. It is also seen in cases of primary or iatrogenic Gushing Syndrome. Radiologically, mediastinal fat shadow is poorly defined and not clearly demarcated. It is less dense than other masses usually found in the superior mediastinum. Absence of tracheal compression is significant. Finding accumulation of fat elsewhere e.g. epicardial and supraclavicular areas is another important sign which will aid radiological diagnosis.

S.P.P.

B.C.G. vaccination : A comparison of post vaccination tuberculin sensitivity after oral and intra dermal vaccination of new born infants :

Hilde Kahn and Rolf Meyerheim. R.D. Azulay and Achilles ScorZelli., Tuberc., (1910), 51, 423.

Two groups of new born infants were vaccinated with B.C.G. soon after birth, one by the oral and the other by the intradermal route, a third group of infants were left unvaccinated. Tuberculin tests were done two, three and five months after vaccination.

All tests were completed in 148 of the oral group and 95 of the unvaccinated group.

Among the unvaccinated group 16 percent showed tuberculin conversion during the observation period.

Among those vaccinated by the oral route 82 percent became tuberculin positive, compared with 76 percent of those vaccinated intradermally. The difference was not significant.

Oral vaccination was as effective as intradermal vaccination in producing tuberculin skin sensitivity.

H.B.D.

Aspergillosis of (be lung—an eighteen year experience.

P.A. Aslam, C.E. Eastridge and F.A. Hughes. Chest Vol. 59, No 1, January 71.

The results of medical and surgical treatment of 21 patients with aspergillosis of whom nine were treated surgically, one by endocavitary infusion and 11 without any specific treatment have been reviewed.

H.B.D.

Open lung biopsy, a strong strand.

Benjamin L. Aaron, Sidney B. Bellinger, Barclay M. Shepard, and Donald J. Doohen. Chest, Vol. 59, 1, January 1971.

Triple biopsy (pleura, lung and hilar lymph nodes) was performed on 89 patients with diffuse pulmonary disease/and or hilar adenopathy and persistent pleural effusion. The result was a definite diagnosis in 62. In 25 patients diagnosis of tuberculosis was established which had escaped definite diagnosis by all techniques other than biopsy.

H.B.D.

Ind. J. Tub., Vol, XVIII, No. 2

Isoniazid with thiacetazone (thiocetazone) in the treatment of pulmonary tuberculosis in East Africa—second report of fifth investigation.

Tuberc., (1970), 51, 353.

A comparison of 18 months of treatment has been made for the following four regimens allocated at random, to East African patients with acute, extensive, bacteriologically positive pulmonary tuberculosis.

TH : Thiacetazone 150 mgm plus isoniazid 300 mgm daily in a single tablet.

S2 : The above TH regimen with an initial two weeks of daily streptomycin 1 gm.

S4: The above TH regimen with an initial four weeks of daily streptomycin 1 gm.

S8: The above TH regimen with an initial eight weeks of daily streptomycin 1 Gm.

87 percent of 146 TH, 87 percent of 157 S2, 93 percent 156 S4 and 96 percent of 156 S8 patients had a favourable response to treatment a statistically-significant trend.

Patients having severe toxic disease requiring streptomycin as a supplement to the Thiacetazone plus isoniazid regimen may be given a minimum of four and preferably eight weeks of daily streptomycin.

A cooperative study in East African hospitals, clinics and laboratories with the collaboration of the East African and British Medical Research Councils.

H.B.D.

Streptomycin plus pyrazinamide in the retreatment of pulmonary tuberculosis —second report.

Tuberc., (1970), 51, 359.

One hundred and nineteen African patients, who were failures of primary chemotherapy and who had a bacteriologically favourable response following a period of six months retreatment with various regimens of streptomycin plus pyrazinamide were allocated-at random to two regimens of continuation chemotherapy as out patients for a second six months.

S₂Z₂ : Streptomycin sulphate 1.0 g intramuscularly plus pyrazinamide 3.0 g orally, given together under supervision twice weekly.

S₂Z₆ : Streptomycin sulphate 1.0 g intra-

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muscularly plus pyrazinamide 1.5 g orally, given together under supervision, twice weekly and supplemented by pyrazinamide in a single daily dose of 1.5 g for self administration at home, except on Sunday on the days between the biweekly supervised chemotherapy.

43 S₂Z₂ and 58 S₂Z₆ patients were assessed at 12 months, 79 percent the S₂Z₂ and 90 percent of S₂Z₆ being culture negative, 19 percent and 7 percent having streptomycin—resistant cultures and 12 percent and 5 percent respectively pyrazinamide—resistant cultures.

84 percent of S₂Z₂ and 93 percent of the S₂Z₆ patients had a favourable bacteriological response.

Only two patients (both S₂Z₂) had treatment temporarily interrupted on account of toxicity, one for dizziness and ataxia in the seventh

months and the other for Jaundice in the eighth.

Patients with favourable response at 12 months were allocated at random to a further six months of continuation chemotherapy with streptomycin sulphate 1.0 g intramuscularly plus pyrazinamide 3.0 g orally, given together under supervision once weekly (S₁Z₁) or to no chemotherapy (Nil).

73 (38 S₁Z₁, 35, Nil) patients were assessed at 18 months, 97 percent of the S₁Z₁ and 94 percent of the — patients having negative cultures and 100 percent and 97 percent respectively a favourably response to treatment.

A cooperative study in East African hospitals, clinics and laboratories with the collaboration of the East African and British Medical Research Councils.

H.B.D.