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A Community-Wide Tuberculosis Study in a South Indian Rural Population, 1950-1955

J. FRIMODT-MØLLER, dr. med. (Copenhagen) [1]

An investigation carried out under WHO auspices in a small area of South India in 1950-55, and which covered a population of approximately 60 000, has not only shed light on various aspects of tuberculosis epidemiology, but has also served as an exercise in the practical conduct of a control campaign in a less developed area.

The programme was based essentially on systematic case-finding by mass miniature X-ray and tuberculin testing and the hospitalization of infectious cases. Its most dramatic effect on the community consisted in the great reduction of mortality—from 200 to 21 per 100 000 in less than four years—due no doubt to the advent of the newer antituberculosis drugs. This and other findings are discussed at length in the present report, which covers such topics as tuberculin sensitivity, infection rate, prevalence, incidence, and the results of a BCG control trial.

One of the conclusions reached as a result of the campaign was that domiciliary drug therapy had much to recommend it in an area such as this, given the reluctance of patients to enter hospital and thus be deprived of their earning capacity.

I. OBJECT OF INVESTIGATION

INTRODUCTION

With a view to investigating the prevalence and incidence of tuberculosis in a rural population in India, a Field Research Centre was established in 1950 at Madanapalle, South India, by the WHO Tuberculosis Research Office (TRO) in co-operation with the Government of India and the Union Mission Tuberculosis (UMT) Sanatorium, Arogyavaram. The purpose of the investigation was, first, to determine the prevalence of tuberculosis by studying the level of tuberculin sensitivity and by carrying out a community-wide X-ray survey, and, secondly, to study the incidence of fresh cases of tuberculosis by following up the initial survey through yearly tuberculin testing and X-raying of the same population. Another aim of the investigation was to see if it would be possible, within a relatively short period, to reduce significantly the community load of infection as well as to decrease the morbidity and mortality. To this end it was decided to isolate the infectious cases and to vaccinate the non-infected cases with BCG. While the infectious cases were isolated they would be treated as effectively as possible in order to render them non-bacillary. The study population selected consisted of the people living within a 10-mile radius of Madanapalle; the size of the study population was estimated to be about 50 000.

REVIEW OF EARLIER WORK

As tuberculosis is not yet a notifiable disease in India, no official data are available with regard to the occurrence of fresh tuberculosis or the number of deaths. From the impression gained by observing the number of tuberculous patients attending government and private hospitals, it has generally been thought that tuberculosis constitutes a major health problem. Since, however, tuberculosis institutions in India are few, they must necessarily draw their patients from very large populations. The impression that the incidence of tuberculosis is very high may therefore not be correct. Most surveys in the past

[1] Medical Superintendent, Union Mission Tuberculosis Sanatorium, Arogyavaram, South India; Chief, WHO Tuberculosis Research Office Madanapalle Field Research Station, Madanapalle, South India

have been concerned with ascertaining the number of infected persons by means of tuberculin testing. Ukil (1930), Benjamin (1938, 1952), Benjamin et al., 1939, Rao & Cochrane (1943), and Lal, Majumdar & Ahmed (1943) reviewing the results of tuberculin testing prior to BCG vaccination all over India, found the rate of reactors high, even in childhood, so the conclusion was that tuberculosis was widespread and formed an important health problem.

X-ray surveys with modern mass miniature equipment have been introduced only since the last war. They have been confined mainly to selected groups of persons such as labourers, students, military recruits or refugees. Aspin (1946) found pulmonary tuberculosis in 3.1% of labourers and 0.8% of Gurkha recruits. Hertzberg (1952), in a group composed of schoolchildren, factory workers and sections of Trivandrum, South India, found 1.2% with pulmonary tuberculosis; Sikand & Raj Narain (1952) found 1.4% active tuberculosis in Faridabad near Delhi; and Philip (1952) found 2.3% with pulmonary tuberculosis among industrial labourers in Madras, and estimates the prevalence of tuberculosis in an urban community to be 1.5%.

THE MADANAPALLE SURVEY, 1948-49

The first community-wide X-ray survey for tuberculosis in India was carried out in Madanapalle Town from 1948 to 1949 (Frimodt-Møller, 1949). As this survey was a forerunner of the present one, it may be briefly reviewed. By means of a portable 35-mm X-ray apparatus, 10 691, or 76%, of the population of Madanapalle Town (approximately 14 000) were photographed. Pulmonary tuberculosis was found in 73, or 6.8 per 1000 X-rayed. Tubercle bacilli were found in 45 out of 54 examined bacteriologically. Assuming the same proportion of bacillary cases among the non-examined, this would give a rate of 5.7 bacillary cases per 1000. Another 226, or 21.2 per 1000, showed X-ray shadows suggestive of tuberculosis, 32, or 3 per 1000, showed calcified foci, and 29 cases appeared to be of non-tuberculous pathology. The people of Madanapalle were also tuberculin tested. Among 10 427 tested with 1 TU of PPD tuberculin, followed by 10 TU among those having reactions of 3-4 mm and 100 TU among those having 2 mm or less, 69% had positive reactions (i.e., indurations of 5 mm or more). This survey was carried out in conjunction with an investigation which served as a pilot study before BCG vaccination was introduced in India on a large scale. This was done at the request of the Government of India, which wished to carry out some trials with BCG before launching the wider campaign. The Government therefore requested the UMT Sanatorium to examine whether BCG vaccination could be given to Indian children without causing any harm. Consequently, 3010 of 3204 non-reactors to 100 TU were given BCG, and two-thirds were retested within the next three to four months. No harmful complications were encountered. The post-vaccination allergy was not as high as expected, only 69% showing a perceptible increase in allergy. Even revaccinations produced only a small increase in allergy. As a result of this observation, the dose of BCG vaccine (manufactured by the BCG Laboratory in Guindy, Madras) was increased in April 1949.

PRESENT SURVEY

The material collected in Madanapalle was scientifically valuable and rather unusual for India, since it consisted of people of whom the majority had been tuberculin tested as well as X-rayed, and included—for the first time in India—a group of BCG-vaccinated children; continued observation of this material was therefore held to be of great interest. However, as the population of Madanapalle Town seemed too small for a follow-up study, it was thought desirable to extend the survey to the surrounding villages. In December 1949 negotiations were begun between the TRO, the Government of India and the UMT Sanatorium to set up a joint research and control project. The facilities of the UMT Sanatorium were to be made available for the project. It was also thought that the goodwill of the population was assured as a result of many years' contact with the Sanatorium.

It was decided that the TRO should set up a Field Research Station and finance a field staff of three teams, consisting of a doctor, a nurse or health visitor, and clerks, as well as personnel for a mobile X-ray unit, transport, office and statistical staff and the necessary equipment, in particular a mobile X-ray unit. The Government undertook to maintain a special isolation hospital for the cases of tuberculosis detected by the mobile X-ray unit or otherwise found in the community. The UMT Sanatorium was asked to take over the management of the research and control programme in its various aspects with its Medical Superintendent as chief of the Field Research Station and as Medical Officer in

charge of the new isolation hospital. The research programme was to be under the guidance of the Director of the TRO. The Sanatorium undertook to provide the beds for the new isolation hospital. The expanded research programme started in 1950, the Field Research Station was set up in January, the isolation hospital in May, and the mobile X-ray unit began operations in September of the same year.

II. GENERAL DESCRIPTION OF STUDY AREA AND POPULATION

PLACE OF OPERATION

Madanapalle Town is located 160 miles (257 km) by road west-north-west of Madras, in Chottoor District, Andhra State (prior to 1953, Madras State). Its population was about 20 000 in 1955, having risen from an estimated 14 000 in 1948. As shown in Fig. 1, roads radiate out from it in many directions, like spokes from the hub of a wheel. The area is thinly populated, being scattered with small villages. The study area is estimated to cover 205 square miles (530 km²) with a total of 338 villages and small towns having a population of about 73 000. Excluding 143 villages and hamlets that were too far off the roads to be accessible to the X-ray unit, the actual study area covers only 130 square miles (336 km²) with a population of 60 000. The rural population under study amounts to 37 000, occupying nearly 200 villages. As shown in Table 1, 170, or 88 %, of the villages examined had less than 300 inhabitants.

The UMT Sanatorium, Arogyavaram, is situated 4 miles (6 km) north of Madanapalle.

Types of houses

The villages all consist of clusters of houses around a central open place or street; the houses are usually built closely together or with short narrow lanes between them. In the small villages about 95% of the houses are huts built of sun-baked mud or clay, with thatched roofs. Nearly all the huts are circular with a single room, usually with just one door and no windows (Fig. 2). Cooking is done either inside the hut or on an open fireplace in the courtyard. The floors are of beaten mud or clay and are smeared with cow dung. The water is drawn from one or two common wells, or from private wells dug in the courtyard. In larger villages, the proportion of mud houses to brick houses is about 50:50, and in the smaller towns about 30:70. The average number of persons per house is 4.5-5.5. As the family grows, new houses may be built in the courtyard, so that the joint family may occupy more than one house on the same compound. The poorer strata of society live as tenants in huts built close to one another that are easy and cheap to construct.

Geographical features, climate and communications

Madanapalle lies about 2000 feet (about 600 m) above sea level on the Deccan Plateau. It is surrounded by hills ranging from 800 to 2000 feet (about 240-600 m) in height. The area is very rocky. The few rivers which are found in the area are dry most of the year; the cultivation depends upon irrigation from rain-water stored in artificial lakes (tanks) or from wells.

TABLE 1

DISTRIBUTION OF VILLAGES IN STUDY AREA ACCORDING TO NUMBER OF INHABITANTS

Number of inhabitants	Number of villages examined 1950	Villages added since 1950	Inaccessible villages not investigated
Below 100	81 [a]	3	92
100–	60	2	39
200–	25	2	8
300–	12	1	3
400–	5	—	1
500–	1	—	—
600–	—	—	—
700–	—	—	—
800–	—	—	—
900–	1	—	—
1000–	3	—	—
2000-	—	—	—
3000–	—	—	—
4000–	1	—	—
5000–	—	—	—
Total	189 [a]	8	143

[a] Three villages were dropped later: one was abandoned owing to fire, and two became inaccessible.

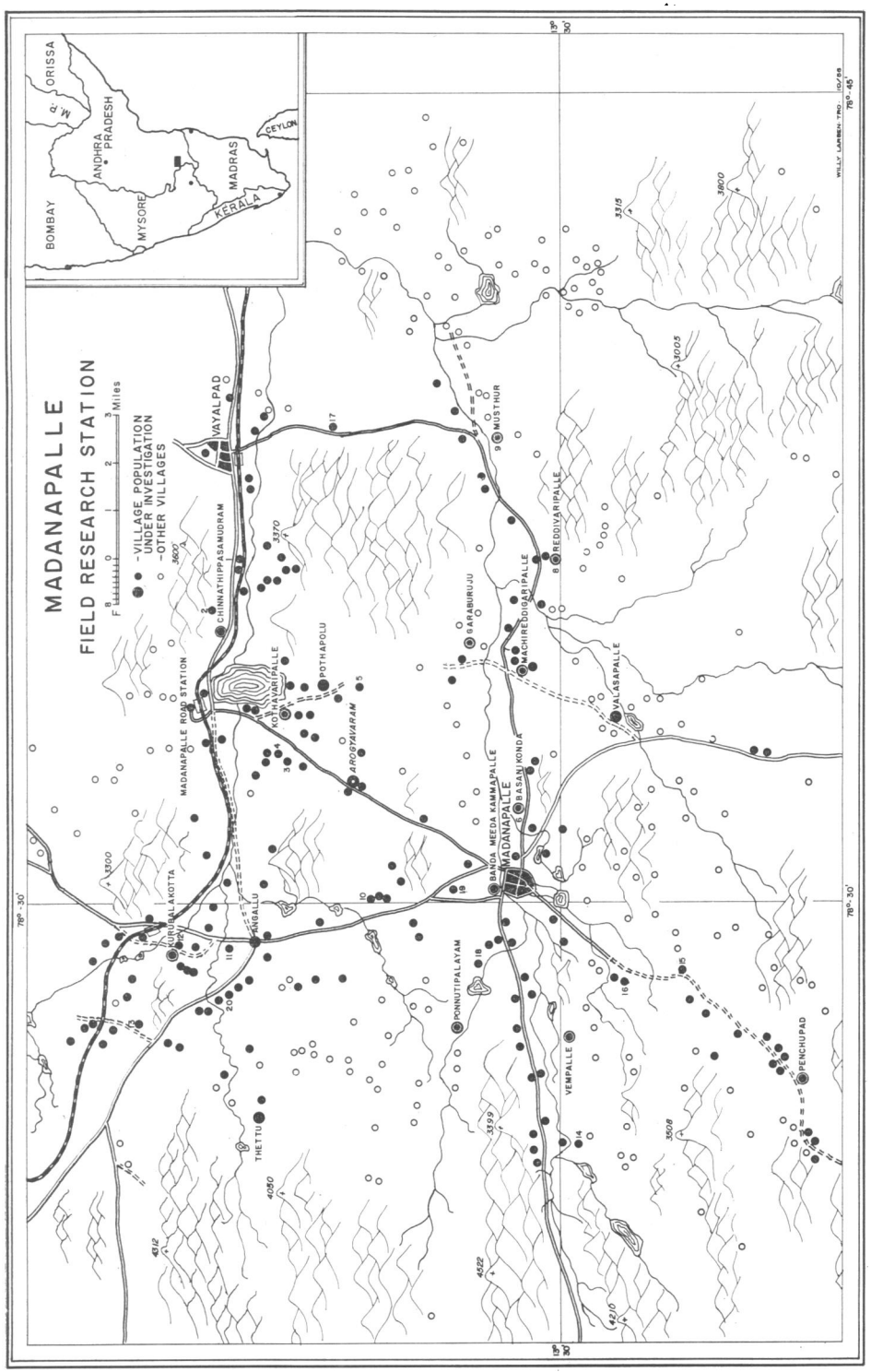
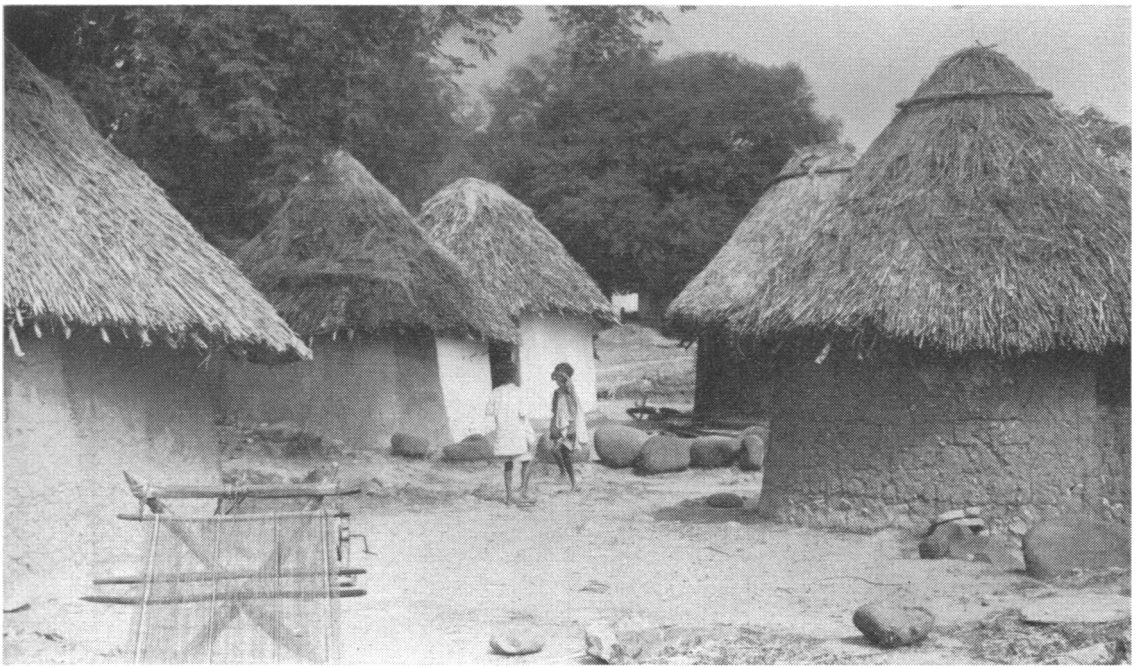


FIG. 1
MAP OF STUDY AREA, MADANAPALLE, SOUTH INDIA

Altitudes are given in feet above sea level (1 ft = 0,3 m).
Nos. 1-20 indicate villages chosen at random for study of population movements.

FIG. 2
TYPICAL VILLAGE



The climate is dry. The average rainfall during 1946-55 was 30 inches (76 cm). About 80% of the rains fall during the two monsoons, the south-western in June-July and the north-eastern in October-November. The Madanapalle area, however, lies so far inland that the monsoons are irregular; the rains are often so insufficient that the tanks remain dry or become only partially filled. In such years cultivation of the fields by irrigation becomes impossible. From Fig. 3 it will be seen that during the period of the present survey there were years when the monsoons failed. When this happens two years in succession—as in 1951-52—many wells go dry. The rainfall during every quarter of the year from 1946 to 1955 has been worked out on the basis of observations by the Arogyavaram meteorological sub-station maintained by the UMT Sanatorium under the direction of the Government of India Meteorological Department.

The temperature at Madanapalle is usually lower than in the coastal plains near Madras. Fig. 4 shows the average monthly minimum and maximum temperatures based upon 10 years' observation at Arogyavaram.

The area is served by a single-track, narrow-gauge railway. In recent years the transport of goods by lorry has become very common. Buses ply several times a day from Madanapalle in all directions.

THE PEOPLE

The population are of the Dravidian race. The majority are Hindus, while a minority belong to the Moslem faith. The level of income is low, most of the people being labourers or poor tenant farmers. In Madanapalle Town and Vayalpad, the second largest township, are found merchants, craftsmen, government and municipal employees, police, etc.

General health

Being mainly farmers, the study population in general enjoys good health. The nutritional status is also quite satisfactory, but in times when rains are scarce, ordinary crops such as rice and ragi, which constitute the staple food, may become so limited that the poorest section may suffer considerably. Plague and cholera are endemic and cause some deaths every year. Malaria follows in the

FIG. 3
QUARTERLY RAINFALL, 1946-55, RECORDED AT UMT SANATORIUM, AROGYAVARAM

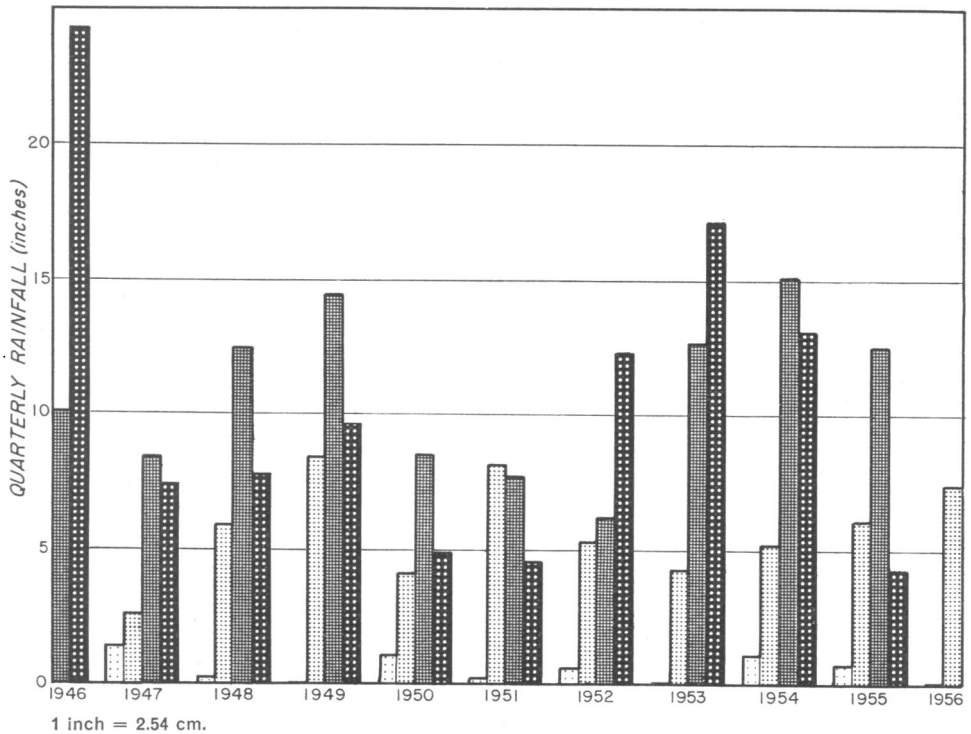
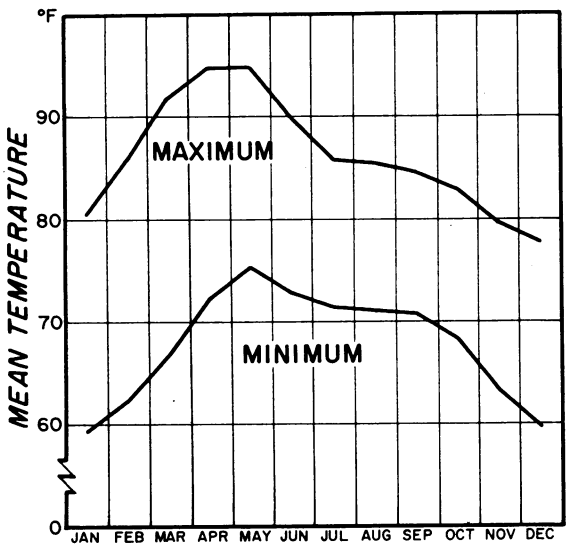


FIG. 4
AVERAGE MONTHLY MINIMUM AND MAXIMUM TEMPERATURES, 1946-55, RECORDED AT AROGYAVARAM



wake of the rains. In dry seasons very few cases occur, but after heavy monsoons the incidence of malaria can be very high. During the winter of 1953-54 a serious malaria epidemic occurred, which also hit the villages in the present study area; very few families were unaffected. Hookworm and other types of helminthiasis are very common. The infant mortality is probably as high as elsewhere in India.

The population is served by a small government hospital in Madanapalle, a mission hospital and some private clinics, besides a government dispensary in Vayalpad. In Madanapalle there are only three private general practitioners trained in Western medicine but many who practise the Ayurvedic and Unanic systems of medicine.

Education

The general level of education is low. The degree of illiteracy in India is estimated to be about 85 per cent, and this would appear to correspond to what is found among the villagers in the study area. There are schools in most villages but they are not very well attended.

The low educational standard raises many obstacles in the conduct of the survey. The fact that most people are illiterate prevents the use of name, birth year or birth date as a means of exact identification. Most people do not know their age, which must therefore be estimated. The error is considerable; as the age is usually assessed in multiples of five, the age-distribution is uneven and shows gross accumulations at round figures.

As it is not customary for a person to be known by more than one individual name, and certain names are more popular than others, identification during repeated surveys becomes a real problem. In order to ensure correct identification at repeated surveys it is necessary to include detailed notes about the guardian of each family, his name, occupation and position within the family, and also to make inquiries about other known members of the family, so that there can be little doubt that the person in question is the same as the one examined on an earlier occasion.

III. FIELD FACILITIES

Owing to its remoteness from other centres of research or medical institutions, the present investigation has had to depend upon its own resources in most respects. The work has been administered from the UMT Sanatorium at Arogyavaram.

THE UMT SANATORIUM

The Sanatorium was founded in 1915. It has now 369 beds, including 134 general ward beds, 24 post-operative and 75 children's beds. It is equipped for and capable of undertaking all diagnostic and therapeutic procedures normally done in large sanatoria in western countries. The laboratory has done tubercle bacilli culture as a matter of routine since 1939; in recent years drug sensitivity tests have also become part of the routine work. A well-stocked animal-house was built in 1951. The X-ray department has two plants for large X-rays. The statistical department is equipped with a sorting and counting machine handling 65-column cards, the punching and verifying machines being manually operated. Most of the staff live on the Sanatorium premises.

THE HEALTH CENTRE

The Madanapalle Health Centre was opened in 1948, when the BCG vaccination programme began, and has functioned as the main centre for the field staff. On its premises is kept a complete house roster, or population register, developed by the field staff. This register was found necessary as no permanent population register existed. It is maintained and checked by special clerical staff assisted by two female health visitors, who visit the homes at Madanapalle at intervals of every two or three months to see if any movement of the families has taken place. This extra work was found necessary since no system exists under which people must report change of address to the post office or other public department. An ordinary nation-wide census is taken every ten years only, the last being in 1951.

THE ISOLATION HOSPITAL

The cases detected by the X-ray survey or patients from the survey area who were bona fide residents have been accommodated in a new special isolation hospital erected during 1950 in the outskirts of Madanapalle on a site placed at the disposal of the project by the Government of Madras (since 1953, the Government of Andhra). The hospital has 75 beds, 60 of which are housed in converted Nissen huts. It has been named the " Rajkumari Amrit Kaur Tuberculosis Hospital " in honour of the Minister for Health of the Government of India at that time, who has taken a keen interest in the research project from its very inception.

MOBILE X-RAY UNIT

A mobile X-ray unit was acquired by WHO for the project. It consists of two vehicles (Fig. 5). One is an Austin truck on which is housed a Schönander mass miniature X-ray apparatus with a mirror camera for 70-mm films, served by a Siemens Monophos X-ray unit with a Dynamix X-ray tube with rotating anode. This set is fitted permanently into a cabin (originally belonging to a United States Army X-ray van). The cabin has only one room, with a door on either side. People enter the truck from the left side, have their photographs taken and leave through the door on the right side. The cabin can be closed completely by light-proof doors and

FIG. 5
THE MOBILE MASS MINIATURE X-RAY UNIT AT WORK IN A VILLAGE

window shutters if the camera or casettes need to be opened in an emergency. The second vehicle is a Willys universal jeep fitted with a power take-off. In the back is fixed a single-phased generator producing 220 volts AC and run by the jeep engine. The whole unit was designed to be so light and manoeuvrable that it could be taken out on very poor roads and through narrow lanes. All processing of the films is done at the UMT Sanatorium.

STAFF

From 1950 three doctors were employed full time on the field project. Each doctor headed a tuberculin testing team, being trained to give and read the tests himself and also to give BCG vaccinations. However, from time to time the tests were given by a senior nurse. The doctors also shared duties at the Rajkumari Amrit Kaur Tuberculosis Hospital in addition to supervising the work at the Health Centre at Madanapalle. Each testing team consisted of a doctor, two clerks, a peon (bearer) and sometimes a nurse. Usually two teams would work in the villages while one would work in the town.

The X-ray team consisted of an X-ray technician, a female attendant for positioning the persons to be photographed, two or three clerks, a bearer and two drivers. All large X-ray films were taken at the Sanatorium.

At the Health Centre four to six clerks and two female health visitors were employed; the staff at the isolation hospital included five nurses and a number of female and male ward-aides. An extra laboratory technician and an X-ray orderly were engaged at the Sanatorium. The statistical department had a staff of one statistician and three statistical clercks.

The senior members of the UMT Sanatorium permanent staff lent their services to the project whenever need arose.

IV. GENERAL FEATURES OF THE WORK

PROPAGANDA AND PROMOTION WORK

The first survey, which was started in Madanapalle in 1948 in connexion with the pilot study of BCG vaccination, was preceded by an intensive campaign to educate the public and enlist their co-operation. A committee was formed comprising the leading citizens of the town and through its assistance and a number of public meetings throughout the town the general public was informed of the purpose of the tuberculin testing and the vaccinations. Further, during visits to the homes personal contacts were made and the whole programme was explained in full. Similarly, when the survey was extended to the villages in the vicinity, an approach was always made first to the village headman and senior and leading personalities. When their co-operation was obtained the rest of the people would usually respond favourably. Since no compulsion was possible, much time was spent in explanation and persuasion. To begin with, curiosity drew many people to the X-ray unit; later on, loudspeakers were used for general talks or for playing Indian music.

WORKING HOURS

The work had to be adapted to the local conditions. The teams started before 7 a.m. and carried on till 1-2 p.m. In the evening, usually twice or three times a week, the testing and X-ray teams would go out to examine the people who had been working in the fields during the day.

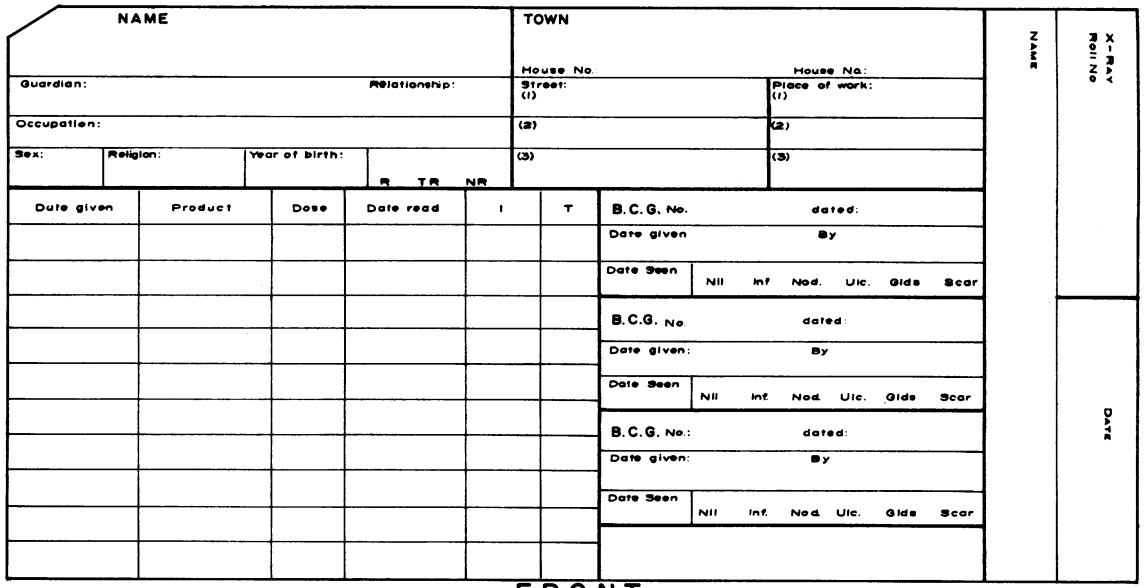
The examinations, especially the tuberculin testing, were done on the spot, where people could be found. The men were seen in their shops or offices, the women and the small children in the homes and the older children at school. As for the X-ray unit, it was located at convenient places in the towns or in the villages, sometimes just outside the village so that people could get there easily. Occasionally the villagers would have to walk some distance to reach the X-ray unit. In all cases a good deal of coaxing had to be done, so one or two clerks would serve as ushers, persuading people to go over to the X-ray unit. When tuberculin tests had to be read it was necessary for the teams to go from house to house to find the people concerned. Although people were always told the time and date of reading the tests, few would remember, so the staff had to search for them.

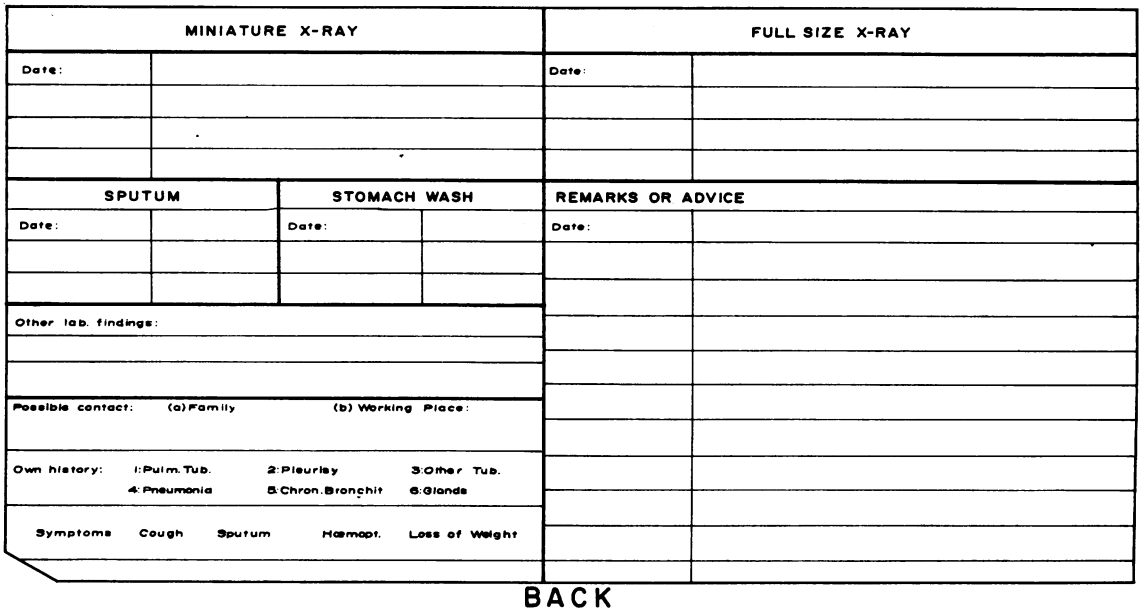
Attention had to be paid to local habits and customs; many persons could not be approached at certain hours of the day, when meals were being prepared or baths being taken. Much tact and patience had to be exercised by the staff. Other difficulties were created by the climate and the terrain. In the hot season it was difficult to operate the X-ray unit between 11 a.m. and 3 p.m. unless shelter could be found underneath large trees. During the monsoons the rains were sometimes so heavy that work had to be suspended. In order to reach remote and inaccessible villages it was often necessary to bridge ditches, remove large boulders or cut branches of trees.

CENSUS TAKING AND POPULATION INDEX

At the beginning a census of the whole study population had to be taken. This was done by one or two clerks going from house to house a day or two before the tuberculin testing teams arrived at a village. Specially prepared forms or household registers to note down all the inmates in each family household were used. A household has been defined as all those who share one cooking place. No attempt was made to record in detail the social status of the families. Though such information would have been valuable, it was decided to refrain from collecting it in order not to delay the main work unduly, but in each case the occupation and position in the family were noted. Distinction was made between residents, temporary residents, and non-residents. Visitors were normally excluded, but if examined a note was made that they were non-residents. All those who had lived most of their life in the area or had moved in recently in order to take up regular work were regarded as residents. Persons suspected of having moved in only in order to seek treatment for a tuberculous disease were excluded as non-residents. On the other hand, anyone who developed tuberculosis shortly after settling down in the area, or who had not realized he was ill at the time of his arrival, was regarded as a resident. Sometimes it was difficult to decide whether a person was resident or not—for instance, if a daughter who had been married outside the area for a number of years returned to her parental home just because she had contracted tuberculosis. If it could be definitely established that she be-

FIG. 6
FACSIMILE (REDUCED) OF INDIVIDUAL INDEX CARD





longed to a family with permanent residence, she was also be regarded as a resident.[1]

[1] For the purpose of the analysis given in this report, all temporary residents and non-residents were excluded.

When the tuberculin testing team or the X-ray team arrived in a village they would bring with them the census files already prepared by the census teams. The lists would be checked carefully daily

to see who were absentees, and much effort would be spent on persuading the defaulters to attend. For each person either tested or X-rayed an individual card was made out. These cards fitted into the slot of the X-ray machine, thus permitting the X-ray serial number and the name of the patient to be photographed on to the individual film. The individual cards were filed according to addresses.

RECORDS

Individual index card (Fig. 6)

On the front several tuberculin tests can be entered. " Product " stands for the antigen used. " I " = transverse diameter of induration measured in millimetres, " T " = type of induration. The three sections for BCG vaccination derive from the time of the first survey in Madanapalle Town when revaccinations were carried out. After 1950 only one vaccination was given to each individual. " BCG No. " refers to the production batch. Under BCG is given a description of the local lesion, such as infiltration, nodules, ulcerations, gland, scar. " R ", " TR " and " NR " after year of birth indicate resident, temporary resident and non-resident. The persons who gave the tuberculin tests and read them are indicated by different colours of ink. On the back of the card space is provided for a short description of X-ray findings. If pulmonary tuberculosis was detected or the case admitted for observation, a full case chart was prepared giving detailed information about the X-ray findings and the results of our investigation.

Household index card (Fig. 7)

These cards or sheets are typewritten copies of the entries from the household census sheets prepared by the census staff when visiting the homes in the towns or the villages. The cards are arranged in looseleaf ledgers according to streets and house numbers, and form a complete register of the total study population.

At the bottom of the card is entered the guardian's name. Under " Tuberculin Test ", " BCG " and " Miniature X-ray " the date of the last examination or injection is entered in pencil. This permits

FIG. 7

FACSIMILE (REDUCED) OF HOUSEHOLD INDEX CARD USED IN THE POPULATION REGISTER MAINTAINED AT MADANAPALLE BY THE TUBERCULOSIS FIELD RESEARCH STATION

Kalamazoo Madras G.M. 2108/59

SERIAL No.	NAME	SEX	YEAR OF BIRTH (APPROX.)	OCCUPATION OR SCHOOL	TUBERCULIN TEST				B.C.G.			MINIATURE X-RAY			REMARKS
					DT.	M.	YR.	RESULT	DT.	M.	YR.	DT.	M.	YR.	

STREET	HOUSE No.	GUARDIAN'S NAME	1	2	3	4	5	6	7	8

new dates to be entered after erasing the previous entry. The permanent entries are always found on the individual index cards. The numbers to the right at the bottom of the sheet indicate the position of tags of different colours: a red tag stands for proved bacillary tuberculosis, a blue for an observation case, a black indicates death of a case with pulmonary tuberculosis, and green indicates deaths from other causes. Great efforts have been made to keep the census up to date so that at any time it could indicate the current position in the population.

Other records

Small identification cards with name and serial numbers are given to persons requiring follow-up in order to facilitate the finding of their index cards when they return for further examination.

X-ray token cards are given by the ushers in the homes to persons due for miniature X-ray. At the mobile X-ray unit these cards are used to find the persons in the census file.

Discharge cards are filled in on discharge of patients from the isolation hospital and sent to the health centre so that an entry relating to the discharge can be made on the original cards.

Advice cards are prepared each time a person is referred from the health centre to the sanatorium either for X-ray or for laboratory examination. At the sanatorium the result of the examination is entered on the advice card and returned with instruction and advice to the health centre staff.

Special registers are kept of all cases with pulmonary tuberculosis as well as of observation cases.

STATISTICAL PROCESSING

All information of scientific value is transcribed on punch cards according to carefully prepared codes. These cards (Powers-Samas) have 65 columns with 12 positions in each. For the patients treated either in the isolation hospital or in the sanatorium additional punch cards are prepared giving details of the condition on admission and discharge as well as of the treatment; these cards are analysed separately from the other cards.

The creation and maintenance of a census and complete population index has required much work and supervision. Matching of cards was often carried out to ensure that nobody appeared as two different persons or that two persons did not appear as one. Care was also taken to see that losses due to inadequate follow-up were kept at a minimum. Nevertheless, owing to the difficulties in dealing with a population consisting largely of illiterates, inaccuracies and lapses probably occurred more often than in similar undertakings in western countries.

The population register made it possible to ascertain if a person claiming to belong to the study population was really a bona fide resident. It also made it possible to calculate the proportion of people examined or not examined by either tuberculin testing or X-ray or both.

V. SIZE AND GROWTH OF THE STUDY POPULATION

The rate of tuberculin reactors and the prevalence of tuberculosis as determined by mass miniature radiography of the population of Madanapalle have been reported earlier (Frimodt-Møller, 1949) and briefly reviewed in the introductory chapter. Since the methods of tuberculin testing and mass-miniature X-ray surveys in the villages were different from those used in Madanapalle Town, the present report deals only with the results of tuberculin testing and mass miniature X-ray examination carried out on the village population since 1950. The follow-up surveys of the Madanapalle Town population will form a separate report.

THE VILLAGE POPULATION

Between 1950 and 1955 the village population was enumerated five times (cf. Table 8, p. 79). According to the first census, which began in May 1950, the village population comprised 34 844 persons, but this figure is probably too low. Counts at subsequent surveys suggest that the first enumeration was not accurate enough. The last census was taken in 1955 at the time of the fifth survey, and the population was found to number 39 170 (disregarding villages added to the study population since 1950). At the end of the fourth round the number of persons examined—i.e., tested and/or X-rayed at least once—had risen to 42 508, or considerably more than the existing population at any given time.

SAMPLING OF STUDY POPULATION

In order to find out from where this large number of persons had come, it was decided in 1956 to carry out a careful analysis of the population movements

in random samples of the study population. For this purpose twenty villages were chosen at random from the villages comprising the study population, and one-fifth of the houses in Vayalpad, the second largest town in the area, were similarly chosen at random. The analysis in the sample villages included every house, while in Vayalpad it covered one-fifth of all houses existing at any time during the period of observation. A very careful scrutiny was made of all census files and individual index cards from the five rounds of examinations, special new tabulation forms having been designed and printed, and the observations regarding each person together with data concerning every tuberculin test and X-ray photograph taken during the whole period were transcribed to a new set of punch cards. If the sample populations could be regarded as truly representative of the whole study population much light could be thrown on problems which had often caused worry and speculation. For example, it was sometimes feared that persons appearing as new cases at the repeat surveys were actually cases discovered at an earlier round, but not recognized as such. However, continuous matchings of cards and census files and the results of the study of population movements suggest that this probability is negligible.

ADEQUACY OF THE SAMPLE POPULATIONS

The twenty villages were drawn at random from the 186 villages under survey in 1955, disregarding the eight villages taken up since the first survey in 1950-51 (Table 1), by consulting a table of random numbers. Their situation in relation to the other villages under investigation is shown on the map (Fig. 1) ; they are scattered well over the whole study area. According to size of population in 1950-51, they are distributed as follows:

Number of inhabitants	*Number of villages*
Below 100	5
100–	5
200–	6
300–	2
400–	1
500–	1

In 1950-51 the population of the 20 villages was 4198, and by 1955 it had risen to 4516. As the parent population of all the villages (excepting Vayalpad) was 33 625 (1955), the twenty sample villages constitute a sample of 14.8%.

The sample population drawn from Vayalpad Town was 1095 in 1950-51 and 1119 in 1955; as the whole population in 1955 was 5545, the sample corresponds to 20.2% of the population.

In order to test the adequacy of the two sample populations, the total number of persons examined—i.e., tested and/or X-rayed during the first four rounds of survey—has been analysed with respect to sex and birth year and compared with the corresponding expected numbers in the sample populations from the villages and from Vayalpad respectively. The results are given in Appendix Table 1. The distributions in both samples as tested by the X^2 test conform very well to what would be expected: the over-all differences are not significant at the 5% level, though within each sample there are one or two age-groups which show significant deviations from the expected values; in the village sample there is a significant deficit of males in the group born 1920-29 and an excess of men born before 1890, while in the Vayalpad sample there is a significant but small surplus of males born 1900-09.

In view of this test it is considered that the samples drawn from the village populations and from Vayalpad are sufficiently representative to permit their use for drawing conclusions with respect to the parent populations.

POPULATION MOVEMENTS

The analysis covers the period between the first census, taken in 1950-51, and the fifth, taken in 1955, equivalent to an average of 4.71 years (cf. Table 8, page 79). Considerable changes have taken place in the population during this relatively short time. Before undertaking the survey it was thought that a village population, and especially one living so isolated and remote from large cities as the present one, would show very little movement, and yet we find from Table 2 that during barely five years one-third of the village population and nearly one-half of the population in Vayalpad have changed address.

Another unexpected observation has been the rapid increase in the number of people eligible for survey; in Vayalpad the number has increased by 43%, in the villages by 28%. This increase is due to births and new arrivals. At the same time, of course, there have been losses due to deaths and departures, besides considerable moving about within the study area. Ordinarily, these movements should not cause any lapses, but the many shiftings within the study

TABLE 2

POPULATION MOVEMENTS IN 20 SAMPLE VILLAGES AND IN 20% OF HOUSES IN VAYALPAD TOWN BETWEEN ROUNDS I AND V (1950-55) *

	Observations			Rates per 1000 per year		
	Males	Females	Both sexes	Males	Females	Both sexes
(a) *20 sample villages*						
Present 1950	2173	2024	4197	1000	1000	1000
Born	265	264	529	25.9	27.7	26.8
Died	159	174	333	15.5	18.3	16.8
Arrivals	303	346	649	29.6	36.3	32.8
Departures	323	304	627	31.5	31.9	31.7
Moved between villages within study area:						
In	149	164	313	14.6	17.2	15.8
Out	96	117	213	9.4	12.3	10.8
Present 1955	2312	2203	4515	+13.6 [a]	+18.8 [a]	+16.1 [a]
Permanent residents [b]	1478	1333	2811	68.0 % [c]	65.9 % [c]	67.0 % [c]
Total eligible [d]	2741	2634	5375	124.1 % [c]	130.1 % [c]	128.1 % [c]
(b) *Vayalpad Town* (20 % sample)						
Present 1950	585	510	1095	1000	1000	1000
Born	54	53	107	19.6	22.1	20.7
Died	31	30	61	11.3	12.5	11.8
Arrivals	194	175	369	70.4	72.8	71.5
Departures	224	188	412	81.3	78.3	79.9
Moved within study area:						
In	243	198	441	88.2	82.4	85.5
Out	234	186	420	84.9	77.4	81.4
Present 1955	587	532	1119	+0.7 [a]	+9.2 [a]	+4.7 [a]
Permanent residents [b]	311	267	578	53.2 % [c]	52.4 % [a]	52.8 % [a]
Total eligible [d]	833	738	1571	142.4 % [c]	144.7 % [a]	143.5 % [a]

* Average period of observation: 4.71 years.
[a] Changes in one year.
[b] Persons occupying same house throughout 1950-55.
[c] Percentage of 1950 figures.
[d] 1950 population + Born + Arrivals.

area, even within the same village and town, have made the follow-up and identification of persons more difficult, and some may have been missed. As there was no compulsion whatever for people to report changes of address, and since only a few are literate, there is not much help to be gained by consulting the postal authorities.

The rate of migrations to and from the study area

was about 32 per 1000 per year in the villages, but in Vayalpad it was 72-80, or more than twice as high. The reason for the higher rate in the town may be sought in the frequent transfers of government and railway officials, and a quicker turnover of children of school age.

The birth and death rates are slightly higher in the villages than in Vayalpad, but the fact that Vayalpad has a larger proportion of children and young people, especially males, than the villages, might explain the differences. The death rates in the study population are discussed at length in section XVII. Special consideration is given below to the birth rates.

BIRTH RATES

In Table 2, the birth rate for the 20 sample villages, based on the 1950 population figure, is given as 26.8 per 1000. Taking 4356 as the mid-period population figure, the rate becomes 25.8 (Table 3). For Vayalpad the corresponding figures are 20.7 and 20.4, there being no noticeable change in the size of the general population during the period of observation.

In order to check our own census figures, the numbers of births and deaths for the 20 sample villages and for the whole of Vayalpad Town have also been obtained from the official registration records. There is compulsory notification of births and deaths and the records are maintained by special officers, a function which is performed in the villages by the village headmen. The data from the official registers cover the six calendar years 1950-55, whereas our own data cover an average observation period of 4.7 years; both sets of figures are given in Table 3.

The estimate of births made by our own census staff is clearly below that obtained from the official registers. In the case of the 20 sample villages the difference is 5.3 per 1000, suggesting that we have missed 17.1 % of the births in our enumeration. For Vayalpad the difference is 6.7 per 1000, corresponding to an underestimate of 24.7 %. This can very well be explained. As the purpose of our census was to enumerate only the *existing* number of persons eligible for tuberculin testing and X-ray examination, our staff paid no attention to the children born and dying between each census; they were concerned only with the children who had made their appearance since the previous enumeration. So it is clear that the birth rates based upon our own census do not take account of infant mortality, which is largely responsible for the differences between these rates and the rates calculated on the basis of the official registers.

According to the last all-India census, which took place in 1951, the infant mortality for Madras (the undivided Madras State) for the decade 1941-50 was 153.6 per 1000 births. There will, of course, be some variation within the state, so a higher infant mortality in the present study population cannot be ruled out; yet the difference between the estimate of the birth rate based upon our own census and that based upon the official registers seems too great to be wholly explained by our failure to note the children who were born and died between our own census takings, so we may also have missed some of the living children. On the other hand, although our birth rate estimate is very low, so is the one based upon the official registrations. Even apart from Vayalpad, where the rate of 27.1 may be artificially low owing to our staff having included, in the total population, a number of schoolchildren

TABLE 3
NUMBER AND RATES OF BIRTHS IN SAMPLE POPULATIONS

Samples	Mid-period population	Births			
		Own observations [a]		Official registration [b]	
		Number	Per 1000	Number	Per 1000
Twenty villages	4 356	529	25.8	814	31.1
Vayalpad Town	5 505	107 [c]	20.4	897	27.1

[a] Observation period: 4.7 years.
[b] Observation period: 6 years.
[c] In a sample of 20.2 %.

who strictly speaking should have been referred to their homes in neighbouring villages outside our study area, the rate of 31.1 per 1000 is distinctly lower than 35-36, which is the official estimate of the birth rate for Madras State for the last inter-census decade. The official registers may therefore also be incorrect. It is a common observation that the official registrations show under-registration in varying degree. In some parts of India it can be surprisingly high but in Madras it is generally about 15% only. By increasing the village birth rate of 31.1 per 1000 (Table 3) by 15%, we get a rate of 35.8 per 1000, which seems quite reasonable. If we accept 35 as the true birth rate in our study population, and 15.4 per 100 live births as the infant mortality rate, our own estimate of live children in the sample villages should have been 607, instead of the 529 observed during the period of observation of 4.7 years. This would mean that our census staff had missed 13% of the living children.

DEATH RATES

Just as the birth rates are affected by the omission to note children born and dying between the times of census taking, and by possible under-registration, the death rates given in Table 2 are minimal rates and should be raised by at least 25%. According to the Census of India Report for 1951 deaths of babies under one year in Madras State in 1950 amounted to 20.4% of all deaths that year. The crude death rate for the villages may therefore be 21 per 1000 rather than 16.8 as given in the table, and this is in keeping with the mean decennial death rate of 20.6 for Madras for the period 1941-50. (For further discussion of mortality, see section XVII.)

EFFECT OF SEX AND AGE ON POPULATION MOVEMENTS

It will be seen from Table 4 that, relatively as well as absolutely, the children and young people below 20 years of age account for the majority of population movements in the villages. Most conspicuous is the high migration rate for females between 11-20 years; this group includes the girls of marriageable age, and it is the practice that, after marriage, the girls move to the homes of their husbands or parents-in-law. During the last inter-census decade ending 1950, about 82% of all females

TABLE 4
POPULATION IN 20 SAMPLE VILLAGES DISTRIBUTED ACCORDING TO AGE AND SEX DURING THE PERIOD BETWEEN ROUND I AND ROUND V *

Age	Present in 1950		Died		Arrivals		Depar-tures		Moved between villages			
									In		Out	
	M	F	M	F	M	F	M	F	M	F	M	F
(a) *Observations :*												
10 and under	713	665	60	75	144	111	107	107	63	69	38	39
11-20	408	396	10	17	49	114	55	81	19	43	12	29
21-50	809	798	36	40	79	92	131	97	50	38	31	33
51 and over	212	143	52	41	14	15	19	13	3	3	4	6
Not recorded	31	23	1	1	17	14	11	7	13	11	10	10
Total	2 173	2 025	159	174	303	346	323	305	148	164	95	117
(b) *Rates per 1000 per year:*												
10 and under	—	—	17.9	23.9	42.9	35.4	31.9	34.2	18.8	22.0	11.8	12.4
11-20	—	—	5.2	9.1	25.5	61.1	28.6	43.4	9.9	23.1	6.2	15.5
21-50	—	—	9.4	10.6	20.7	24.5	34.4	25.8	13.1	10.1	8.1	8.8
51 and over	—	—	52.1	60.9	14.0	22.3	19.0	19.3	3.0	4.5	4.0	8.9
All ages	—	—	15.5	18.3	29.6	36.3	31.5	31.9	14.6	17.2	9.4	12.3

* Average period of observation: 4.71 years.

in the age-group 15-24 years were married in the districts of Madras included in our area. The elderly people show the least tendency to move about, but then, of course, the death rates are the highest in this group.

SIZE OF THE TOTAL STUDY POPULATION

On the assumption that the sample populations drawn from the villages as well as from Vayalpad Town are truly representative of their parent populations, the rates of movements have been applied to the whole population. The last available census data—i.e., those obtained during the fifth round of census in 1955—have been used as a starting point in estimating the 1950 population. Table 5 shows that the total study population in 1955 amounted to 39 170 (Madanapalle excluded), of whom 33 625 lived in the villages and 5545 in Vayalpad. Applying the growth rates shown in Table 2 in reverse, we obtain for 1950 a population of 36 683, of whom 31 257 lived in the villages and 5426 in Vayalpad, This figure of 36 683 is larger by 4326, or 12.4%, than the original census figure of 34 844 obtained directly in 1950. The discrepancy applies to that part of the population which was not tuberculin tested or X-rayed. The absentees were entered in our original census lists but their cards were not punched and counted till after the second census had been taken. During the second census use was made of the lists from the first census and corrections or additions were made on to these, so there is some doubt as to when exactly some of the non-contacted people were enumerated. This doubt does not apply to the persons either tested or X-rayed (or both) for whom individual index cards are available. Having sifted the evidence very carefully we believe the new figure of 36 683 is nearer the truth.

Table 5 shows that up till the time of the fifth round the number of people eligible for examination had risen to 47 814, an increase of 30% since 1950. That the total number of people contacted during four rounds of examinations could have risen to 42 508 is therefore not so surprising as was first thought. After the subtraction of cases belonging to the new villages added since 1950, and of children examined in Vayalpad as day scholars but living outside the study area, the number of persons examined is 40 392, giving a coverage of 84% of all eligible persons.

TABLE 5

ESTIMATE OF THE 1950 POPULATION AND ALL BIRTHS, DEATHS, MIGRATIONS AND MOVEMENTS BETWEEN 1950 AND 1955 IN THE WHOLE STUDY POPULATION CALCULATED ON BASIS OF OBSERVATIONS IN SAMPLE POPULATIONS AND THE 1955 ENUMERATION

	Villages	Vayalpad	Whole population	
			Number	Rates per 1000 per year
Present 1950	31 256.7	5 426.1	36 682.8	1 000
Born	3 939.6	530.2	4 469.8	25.9
Died	2 479.9	302.3	2 782.2	16.1
Arrivals	4 833.2	1 828.5	6 661.7	38.6
Departures	4 669.4	2 041.6	6 711.0	38.8
Moved within study area:				
(a) Within village or town:				
In	5 781.4	1 982.1	7 763.5	45.0
Out	5 781.4	1 749.2	7 530.6	43.6
(b) Between villages:				
In	2 331.1	203.2	2 534.3	14.7
Out	1 586.3	332.0	1 918.3	11.1
Present 1955	33 625	5 545	39 170	+14.6
Permanent residents [a]	20 935.7	2 864.4	23 800.1	—
Total eligible	40 029.6	7 784.8	47 814.4	—

[a] Persons occupying same house 1950-55.

SEX AND AGE DISTRIBUTION

In order to see whether the present study population could be considered typical of other populations in this part of the country, the distributions of males and females according to age per 10 000 in the two sample populations have been compared with the rural populations in (1) Chittoor District, which includes our area, and (2) the neighbouring district of Ananthapur, just north of Madanapalle Taluk (Table 6).

By comparing the population of Vayalpad Town with the sample population of 20 villages, it can be seen, in Table 6, that there are more males in the town in the age-groups 5-14 and 15-34 than in the villages; this indicates that boys and young men come

TABLE 6
AGE AND SEX DISTRIBUTION OF SAMPLE POPULATIONS OF 20 VILLAGES AND VAYALPAD TOWN AND OF RURAL POPULATIONS IN CHITOOR AND ANANTHAPUR DISTRICTS *

Age-group	Madanapalle Rural				Chittoor Rural per 10 000		Ananthapur Rural per 10 000	
	Villages per 10 000		Vayalpad per 10 000					
	M	F	M	F	M	F	M	F
Below 1	185	183	103	150	166	157	149	162
1-4	585	532	458	505	408	430	469	485
5-14	1352	1243	1441	1235	1134	1104	1315	1226
15-24	1426	1629	1796	1618	1615	1660	1651	1475
35-54	1133	915	1020	748	1185	1053	1160	1019
55 +	489	328	505	421	611	477	433	455
Total	5170	4830	5323	4677	5119	4881	5177	4822

* Quoted from the *Census of India, 1951*, Vol. 3, Part I (Madras 1953).

to the town for education and employment; at the same time there are relatively fewer small children and females in the town than in the villages.

Since the total population of Vayalpad forms only one-seventh of the total study population, the village distribution can very well be considered representative of the total study population for comparison with the age-sex distributions of the rural populations of Chittoor and Ananthapur districts; these figures refer to the decade 1941-50 and are given in the Census of India Report for 1951. Our study population resembles more closely the population of Ananthapur district than that of Chittoor, although even in the latter case the difference is not very marked. Compared with Ananthapur the Madanapalle village population shows a slightly higher proportion of boys and girls up to the age of 14, more women from 15 to 34 years of age, and relatively fewer males between 15 and 54 and females of 15 years and above, but in the main there appears to be a very good correlation between the two populations. It seems, therefore, that our study population does not differ materially from the neighbouring populations.

The age structure of the study population is remarkably close to that of the population of India as a whole (Table 7) with the exception that the proportion of children below 15 years of age at Madanapalle is a little higher than in the country in general. Compared with a Western country such as the USA there is a striking difference, since in the USA there are relatively much fewer children and many more middle-aged and elderly people than in India. This is not only of academic interest but of much practical significance in relation to tuberculosis, which may affect certain age-groups in particular. If, for instance, it were a question of

TABLE 7
COMPARISON OF AGE STRUCTURE OF THE STUDY POPULATION AT MADANAPALLE, AND THE POPULATIONS OF INDIA AND THE UNITED STATES OF AMERICA *

Age-groups	Madanapalle %	All India %	USA %
0-4	14.5	13.5	10.8
5-14	26.1	24.8	16.3
15-34	31.0	33.0	30.4
35-54	20.1	20.4	25.6
55 and over	8.3	8.3	16.9
Total	100.0	100.0	100.0

* Data for India and the USA quoted from the *Census of India. 1951*, Vol. 1, Part I-A.

using BCG vaccination for the children, the task would be relatively much greater in India than in a Western country with an age structure similar to that of the USA; but if it were a question of detecting cases by mass miniature radiography among adults especially, the task would be relatively smaller in India, as the adult population here is proportionately much smaller than in a Western country.

VI. COVERAGE

Originally it was the plan to test with tuberculin and X-ray, by the mobile mass miniature radiographic unit, every person in the village population once a year from 1950 onwards, but this was soon found to be quite unfeasible. First, it took a much longer time to contact all households in the nearly two hundred villages than had been anticipated, mainly because it was found that the field staff had to go to the people rather than that the people came to them. The slow and tardy response gave much extra work. The tuberculin testing, which began in May 1950, was completed in August 1951, and the X-ray photographing, which began in September 1950, was finished in November of the next year. The effort involved in trying to round up any further absentees seemed to entail a disproportionately heavy expense of time and labour. Further, it was thought that most of these absentees would be contacted the following year at the next village survey.

TIME-TABLE FOLLOWED

Between the village surveys, the X-ray unit worked in Madanapalle. The tuberculin testing in the town was carried out simultaneously with that in the villages, one team working in the town and two in the villages. The present report deals with the results in the village population only, the Madanapalle work being excluded for reasons already stated. In the villages four rounds of testing and X-ray photographings had been completed and the fifth commenced when the present analysis was undertaken. We have therefore for review the results of four full rounds. The fifth round is excluded so far as testings and X-rayings are concerned but, as described in the previous section, use has been made of the fifth census for studying the movements in the population from 1950 to 1955 over an observation period of 4.7 years. The timings of the five rounds are shown in Table 8.

The relatively long time taken to cover the whole study population once and the unequal times spent on each round have posed various statistical and analytical problems. First, there has been an interval of some months between the testing and photographing which could allow for certain developments in either tuberculin sensitivity or X-ray pathology that would be impossible to determine; secondly, an accurate assessment of the length of observation periods would be extremely complicated, and, thirdly, the route and pace of the testing and X-ray teams were not exactly the same for each round. Nevertheless, an average period of observation has been worked out on the assumption that any deviations in route or time taken have been equalized at random around the midpoint in time of each

TABLE 8

TIME-TABLE FOR THE VILLAGE WORK

Round	Tuberculin testing	X-ray examinations
I	1 May 1950 – 20 Aug. 1951	1 Sept. 1950 – 25 Nov. 1951
II	8 Oct. 1951 – 26 Dec. 1952	26 Nov. 1951 – 17 Feb. 1953
III	27 Jan. 1953 – 31 March 1954	27 Aug. 1953 – 8 July 1954
IV	1 April 1954 – 23 Jan. 1955	8 July 1954 – 15 Feb. 1955
V	9 Feb. 1955 – September 1955	15 June 1955 – September 1955

round, and that the visits to the villages were carried out in the same order during each round.

ATTENDANCE RATES

Round I

The attendance rates varied from round to round. Considering Round I, of a population of about 37 000 the total coverage for tuberculin testing was 23 158, or 62.3%, while that for X-raying was 20 993, or 56.5%. Considering that some were tested but not X-rayed and some were X-rayed but not tested, the total number of people tested and/or X-rayed was 26 960, or 72.6%. The distribution of persons tested or X-rayed or both is shown in Fig. 8. Among the children the response was very much the same for boys as for girls. In the young and middle age-groups the women attended a little better than the men, but among elderly people, particularly after the age of 60, the men responded better than the women, and this applies to testings as well as to X-ray examinations. Considering those who were both tested and X-rayed, women responded better than men in the age-groups 20-49 years, the latter consenting to be X-rayed but having no time or interest for tuberculin tests.

Rounds II-IV

The attendance at later rounds followed in general the same pattern as that of Round I, but at each subsequent round it became more difficult to persuade people to respond; the total number of persons examined at least once either by tests or X-ray increased cumulatively at each subsequent round. The effect on the analysis of the limited coverage and the production of a great many groups of unequal composition with regard to number of tests and X-rays will be discussed later when the X-ray findings are reported. Much difficulty was caused by the frequent change of residence either within the study area or by migration to and from other areas.

EFFECT OF POPULATION MOVEMENT ON THE COVERAGE

The effect of movements within the study population on the coverage obtained during the four rounds is set out in Table 9. It is noteworthy that the best coverage was obtained among persons occupying the same house throughout the whole observation period; 88%-94% of these had at least

FIG. 8

ATTENDANCE RATES AS PERCENTAGE OF PERSONS TUBERCULIN TESTED AND/OR X-RAYED IN 1950-51 (ROUND I)

TABLE 9
EFFECT OF POPULATION MOVEMENT ON SURVEY COVERAGE SHOWING PERCENTAGE OF PERSONS EXAMINED (TUBERCULIN TESTED AND/OR X-RAYED) ONCE OR MORE DURING FOUR ROUNDS OF INVESTIGATION

	Villages						Vayalpad					
	Males			Females			Males			Females		
	Total	Examined		Total	Examined		Total	Examined		Total	Examined	
		No.	%		No.	%		No.	%		No.	%
Present 1950	2173	1949	89.7	2024	1817	89.9	585	476	81.4	510	419	82.2
Born	189	111	58.7	181	97	53.6	45	26	57.8	46	22	47.8
Died	120	63	50.3	122	72	59.0	26	9	34.6	21	8	38.1
Arrivals	258	182	70.5	286	226	79.0	151	99	65.6	148	104	70.3
Departures	229	146	63.8	220	158	71.8	172	103	59.9	157	89	56.7
Moved within study area:												
(a) Within unit												
In	239	219	91.6	237	218	92.0	172	153	89.0	134	113	84.3
Out	239	219	91.6	237	218	92.0	156	123	78.9	126	112	88.9
(b) Between units												
In	112	86	76.8	127	97	76.4	20	13	65.0	19	11	57.9
Out	72	56	77.8	84	64	76.2	22	14	63.6	21	13	61.9
Present 1954	2311	2063	89.3	2192	1943	88.8	597	518	86.8	532	447	84.0
Permanent residents [a]	1846	1732	93.8	1696	1580	93.2	341	312	91.5	290	256	88.2
Total eligible	2620	2242	85.6	2491	2140	85.9	781	601	77.0	704	545	77.4

[a] Persons who occupied the same residence throughout the whole observation period.

one Mantoux test or one X-ray photo. Almost the same coverage was obtained among the group which moved about within the same village or town, although the percentages indicate that it was easier to trace the people in the smaller units—i.e., the villages—than in the town. When people moved between villages but within the study area, it became a little more difficult to contact them, about 76%-77% being covered in the villages, and 58%-65% in the town. Those who were born or who died within the observation period showed a lower rate of coverage, but this is reasonable as they were not present for more than a part of the observation period. Even though our attendance rates are not so high as those obtained in recent mass miniature X-ray surveys in the West (Cochrane, Cox & Jarman, 1955) or by ourselves in recent prevalence sample surveys in Andhra, Madras and Mysore States, (Benjamin, 1956) it would seem quite satisfactory that, of all eligible persons, it was possible either to test or to X-ray 86% at least once in the villages, and 77% in Vayalpad Town, where the proportion of migrating and shifting persons was the highest. How much this failure to achieve full coverage has affected the attempt to control the disease will be discussed in sections XVIII and XIX.

VII. TUBERCULIN ALLERGY

INTRODUCTION

The examination of the village population outside Madanapalle began in 1950; during the months of March and April the staff doctors had an opportunity to work together with Dr. LeRoy E. Bates from the TRO. While Dr Bates and his colleagues carried out a tuberculin testing programme among schoolchildren in the North and South Arcot districts, Madras State, each staff doctor from

Madanapalle had 14 days of intensive training in how to give and how to read tuberculin tests so that the results could be compared with testings done elsewhere by other TRO teams.

TUBERCULIN

The tuberculin was the same as that used by the TRO in Denmark and elsewhere. Fresh stock solutions of PPD batch RT XIX, XX, XXI were sent every three months by air to Madanapalle and stored under refrigeration. Buffer solutions were sent out by ship. The tuberculin syringes and platinum needles were similar to those used by the TRO in other places. The PPD was given in quantities of 0.1 ml intradermally on the volar aspect of the left arm by means of a 1-ml glass syringe equipped with a platinum needle, gauge 25-26. The needle was inserted just under the epidermis and pushed in far enough to ensure that the liquid would not leak out when the needle was withdrawn.

DOSES OF TUBERCULIN

During the tuberculosis survey of Madanapalle Town 1948-49, Mantoux tests were done by using 1 TU PPD for the first test, followed by 100 TU for those having reactions of 2 mm or less of induration and 10 TU for those who had doubtfully positive reactions—i.e., reactions of 3 or 4 mm of induration. Persons showing reactions of 4 mm or less to 10 TU were given 100 TU. Reactions of 5 mm or more were considered positive reactions at each level of tuberculin. The fact that the 10 TU dose was interspersed between the 1 and the 100 TU doses in a somewhat irregular manner made the interpretation of the pattern of allergy rather complicated. However, by using 1 and 100 TU, and 10 TU only in the doubtfully positive cases, it was nearly always possible to manage with no more than two injections. When the investigation was extended in 1950 to the villages surrounding Madanapalle it was decided to use 10 TU as a second dose for all those whose reactions to 1 TU were 5 mm or less, followed by 100 TU for those with similar reactions to 10 TU. In October 1950, when the International Tuberculosis Campaign in India had decided to use 5 TU for the first test, the 1, 10 and 100 TU schedule was discontinued and only two dilutions were used—the 5 TU followed by the 100 TU. The larger dose was given to persons producing reactions of 4 mm or less to 5 TU.

The present material therefore falls into two parts: one group which received 1, 10 and 100 TU and another which was given 5 and 100 TU. During subsequent rounds the same pattern of tuberculin doses was followed as that which had been adopted during Round I. From Round IV the 1, 10 and 100 TU tests were discontinued altogether and only the 5 TU tests were used. The tests were normally read after 48 or 72 hours, but since many people were absent, some were read at 96 hours or later.

MATERIAL

It was the intention to test with tuberculin the whole village population, but only 62% submitted to the testings during Round I and the attendance was lower during the subsequent rounds of investigation. During all four rounds altogether 39 496 persons were given an initial Mantoux test, and 25 092 of these were retested once or more; in all,

TABLE 10
NUMBERS OF PERSONS TUBERCULIN TESTED AT EACH OF FOUR SUCCESSIVE ROUNDS OF EXAMINATIONS

Round I	Round II	Round III	Round IV
23 159	13 940	8899	5527
			(3372)
		(5041)	1725
			(3316)
	(9219)	2999	1440
			(1559)
		(6220)	918
			(5302)
	7383	3528	1958
			(1570)
		(3855)	817
			(3038)
		6120	2890
			(3230)
			2834
Total tested 23 159	21 323	21 546	18 109

Note : Figures in brackets indicate persons not tested.

TABLE 11

TUBERCULIN TESTING DURING THE FIRST VILLAGE SURVEY 1950-51 (ROUND I)

Dose of tuberculin	Persons eligible	Persons tested		Tests read							
				Total		2-4 days		5+ days		Not recorded	
		No.	%	No.	%	No.	%	No.	%	No.	%
(a) 1-10-100 TU group:											
1 TU	14 489	9 349	64.5	8 644	92.5	6 843	73.2	1 742	18.6	59	0.6
10 TU	6 431	6 125	95.2	5 629	89.6	4 428	70.5	1 181	18.8	20	0.3
		154[a]									
		6 279									
100 TU	3 748	3 068	81.6	2 910	94.9	2 414	78.7	443	14.4	53	1.7
(b) 5-100 TU group:											
5 TU	22 660	13 656	60.2	11 775	86.2	9 152	67.0	2 623	19.2	..	
100 TU	6 244	5 436	87.1	4 638	85.3	3 760	69.2	852	15.7	26	0.5

[a] 10 TU given initially.

84 137 tests were given, or a little over two tests per person. The attendance rates according to sex and age during Round I were discussed in the previous section (see Fig. 8).

The effect of the incomplete coverage in producing a high number of incongruent groups can be seen from Table 10, which gives the number of persons tested initially, and retested, in each round. The present section deals only with the results of the initial testings done in Round I, while the following section deals with the results of retests done in later rounds.

The extent of the data available from Round I (1950-51) is given in Table 11. During the first part of the round 9349 persons were tested with 1 TU under the 1-10-100 TU scheme, and 13 656 with 5 TU under the 5-100 TU scheme during the second part. The percentage of initial tests read ranged from 86% to 92%. As most of the tests had to be read in the homes, this must be considered a high coverage; however, in order to achieve this, numerous visits had to be paid to each village, many valuable days being lost in the search for absentees, and about one-fifth of the tests were read on the fifth day or later.

As it was found that indurations wane after the third or fourth day, all tests read after the fourth day have been excluded from the present analysis. The results should therefore be comparable to tuberculin testing done elsewhere and read at 72 hours.

RESULTS

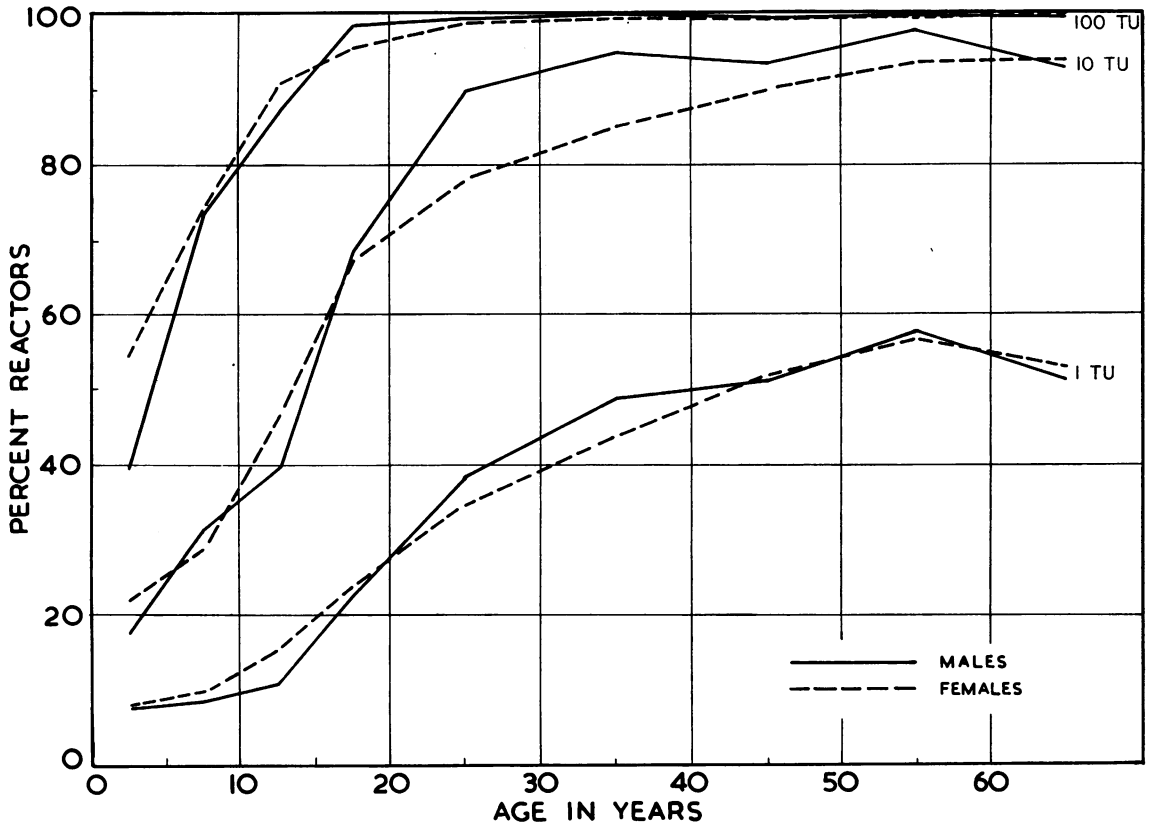
1-10-100 TU

Considering reactions to 1-10-100 TU of 6 mm or more as positive and those of 5 mm or less as negative, the rates of reactors according to sex and age are given in Fig. 9. It will be noted that nearly all react to 100 TU from 10 years of age and upwards. Studying the 1-10-100 TU pattern, the first and most striking observation is the very high proportion of persons who react to tuberculin, if not to 1 or 10 TU then to 100 TU. Conversely, it is remarkable how few persons, even children, are negative. At 10 years about 80% react, and going down the age-scale we find that even under 5 years about 40% of boys and 54% of girls react to 100 TU. Disregarding 100 TU and noting the course of the 10 TU curve it is seen that at 10 years of age about 35%, and at 15-19 years 70%, react to this dose, After 20 years of age there is a clear difference between males and females, as the former reach the 95% level at about 30 years of age, while the latter reach this level around age 50. The difference becomes smaller after 50 years.

The persons with the strongest allergy are those who react to 1 TU. Below 20 years of age there are very few of them; up to 15 years of age they number less than 20%. From 20 to 50 years of age the

FIG. 9

PERCENTAGE OF PERSONS WITH REACTIONS OF 6 mm OR MORE TO MANTOUX TESTS WITH 1, 10 AND 100 TU, ACCORDING TO SEX AND AGE, MADANAPALLE, 1950-51 (ROUND I)



curves for the two sexes run parallel towards a maximum at the age of 55 years, the males being slightly more numerous than the females. Towards the end of life both curves decline, indicating that old people show some waning of allergy.

5-100 TU

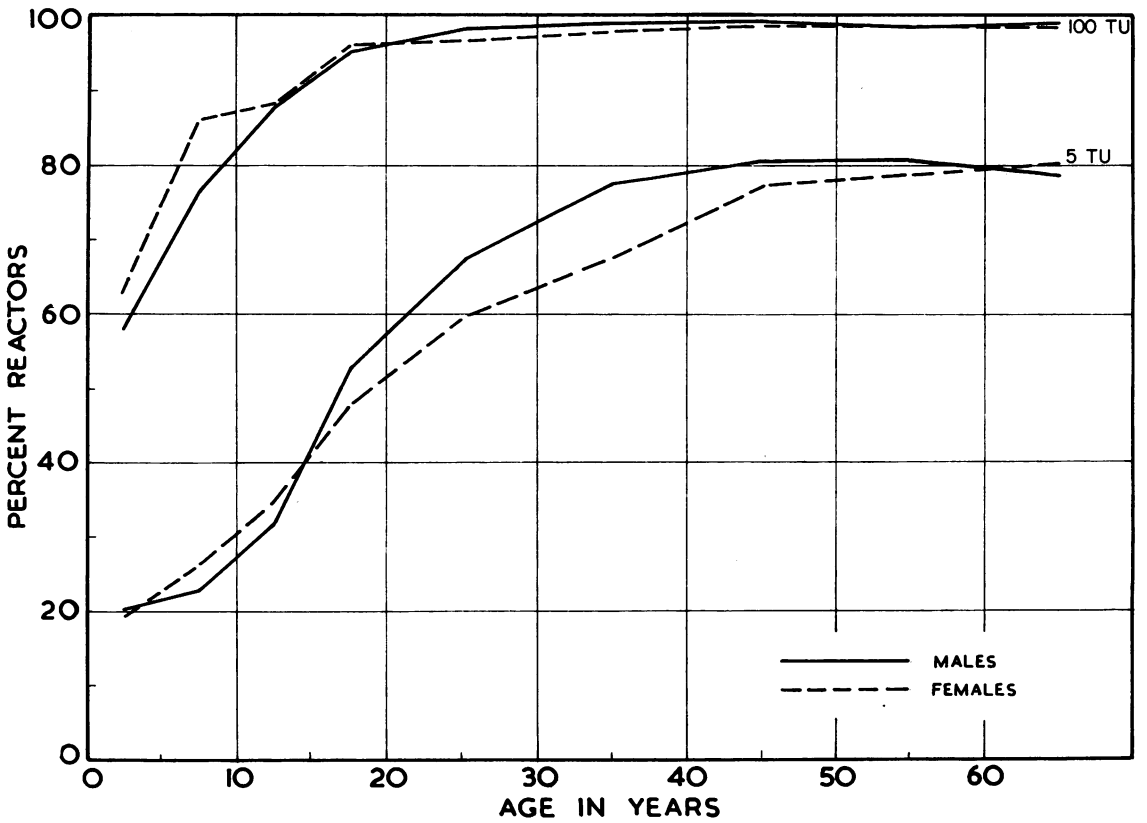
The findings shown in Fig. 10 are very similar to those described in Fig. 9. The level of the percentage of 100 TU reactors is almost identical with that following the two doses of 1 and 10 TU. For the small children, the 5 TU curve starts at the same level as the 10 TU curve in the former material, but for those above 15 years of age it assumes a position midway between the curves for the 1 and 10 TU tests. The disproportion of strong reactors to weak reactors in the age-group 10-15 years is very striking as there are nearly twice as many children reacting to 100 TU than to 5 TU, and again very few who do not react at all.

DISCUSSION

The results correspond very well to those obtained in tuberculin surveys carried out in South India before the war (Benjamin, 1938; Benjamin et al., 1939). In fact, we have material based upon tests with Old Tuberculin carried out in Vayalpad Town in the years 1939-40—i.e., in the same population with which we are concerned now. The percentage of reactors in the age-groups up to 20 years corresponds almost exactly to our present findings with 1 and 10 TU. In young adults and the middle aged there is some difference, as the number of reactors to Old Tuberculin was a little lower than was found with 10 TU, yet the total impression gained was that

FIG. 10

PERCENTAGE OF PERSONS WITH REACTIONS OF 5 mm AND MORE TO MANTOUX TESTS WITH 5 AND 100 TU, ACCORDING TO SEX AND AGE, MADANAPALLE, 1950-51 (ROUND I)



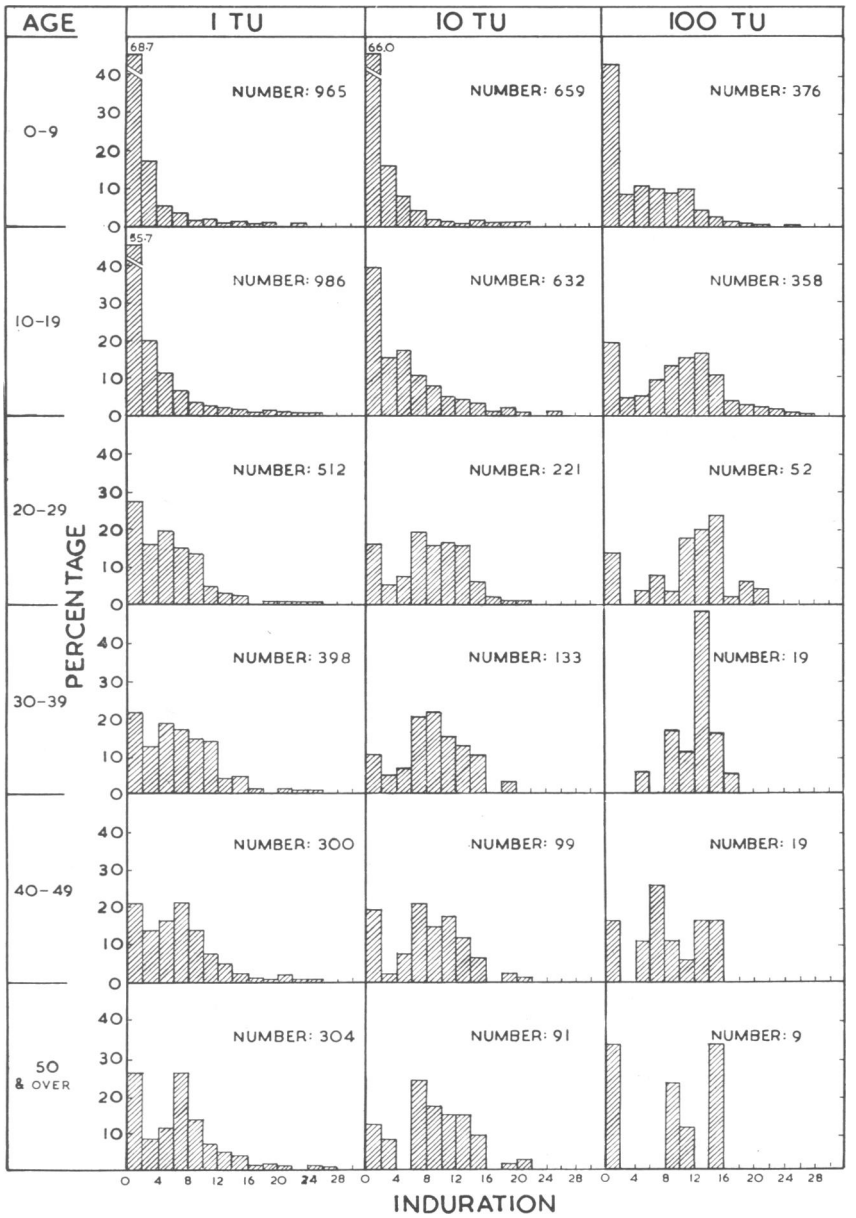
the number of reactors to tuberculin was high (Benjamin, 1957).

As for the interpretation of the present findings, it is clear that very much depends upon the definition of a reactor. If this is assumed to be every person who reacts to a tuberculin test with any of the conventional doses of tuberculin—i.e., including a dose of 100 TU—the conclusion must be that the infection rate with tubercle bacilli is very high. On the other hand, if it were possible to disregard persons who exhibit only a very low degree of sensitivity—e.g., those who react only to the 100 TU and perhaps also those whose reactions to the 10 TU test are small—the infection rate will be much lower.

The question also arises whether it is reasonable to regard all those who show reactions of 6 mm or more—or greater than some other arbitrary limit—as positive reactors, and to consider these to be previously infected with tubercle bacilli, while those with reactions of 5 mm or less are considered to be negative and non-infected. In order to examine this question histograms are reproduced in Fig. 11-14 which show frequency distributions as a percentage of reactions according to sex and age-groups as well as pattern of tuberculin tests. Fig. 11 and 12 show that among males and females who were given the initial 1 TU test there are in all age-groups relatively few persons with large reactions measuring more than 10-12 mm. From the age-group 20-29 upwards the majority of the reactions seem to gather around a mode of 7-8 mm. A somewhat similar pattern is found among the reactions to 10 TU, indicating that those who produced 5 mm or less to 1 TU also possessed a certain degree of sensitivity. The same picture is repeated with regard to the 100 TU reactions, so

FIG. 11

FREQUENCY DISTRIBUTIONS OF DIAMETER OF MANTOUX REACTIONS TO 1, 10 AND 100 TU AMONG MALES, MADANAPALLE, 1950-51 (ROUND I)

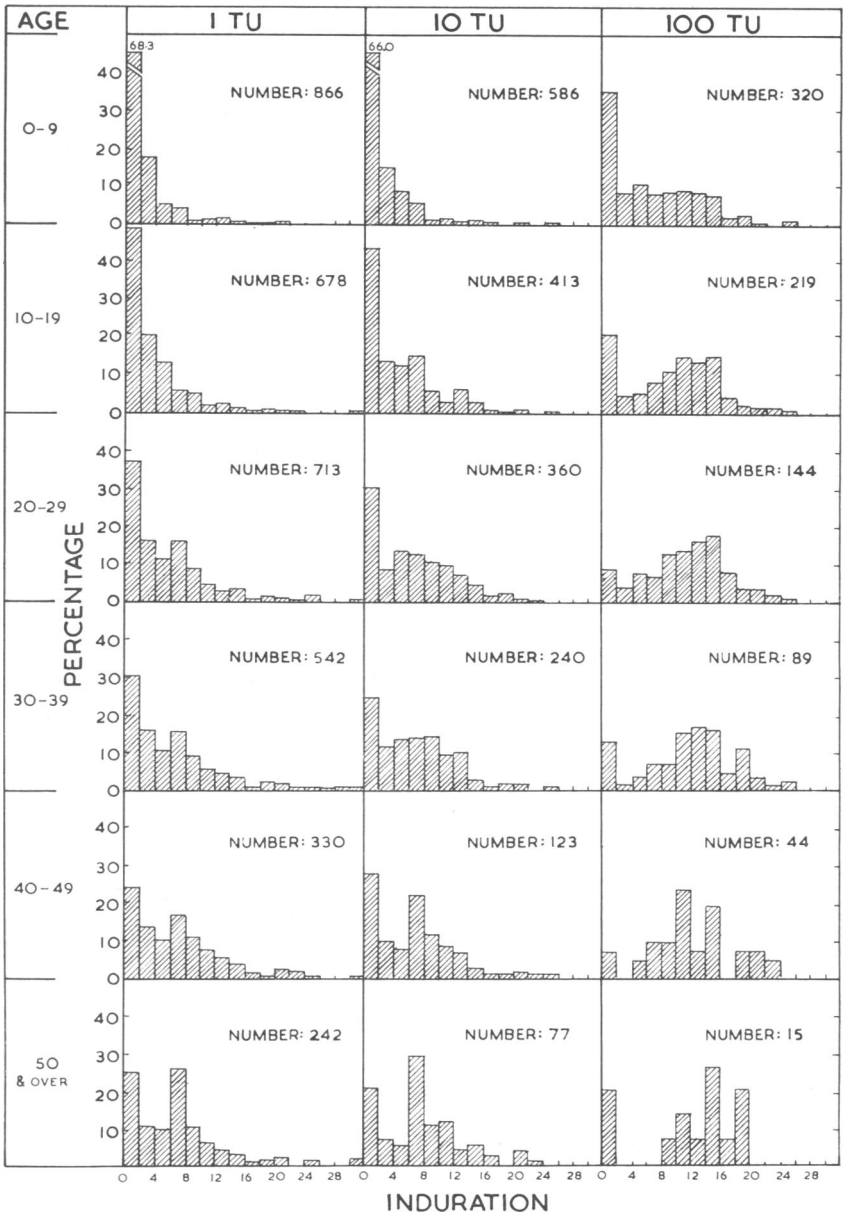


here too we find that those who showed only small reactions to 10 TU were still able to produce quite strong reactions to 100 TU. This applies even to the children below 10 years of age.

Turning now to the distributions among males and females who had 5 TU for the first test followed by 100 TU (Fig. 13 and 14), all groups show a higher proportion of larger reactions than was seen after

FIG. 12

FREQUENCY DISTRIBUTIONS OF DIAMETER OF MANTOUX REACTIONS TO 1, 10 AND 100 TU AMONG FEMALES, MADANAPALLE, 1950-51 (ROUND I)



1 TU; there is also a higher proportion of reactions measuring more than 20 mm in diameter. It can be seen from the distributions among the age-groups 0-9 and 10-19 that the great majority of reactions lie to the left of the scale—i.e., their diameters measure less than 7-8 mm—while a minority of larger reactions form a longish tail stretching from diameters of 8-9 mm right up to those of 28-32 mm,

FIG. 13

FREQUENCY DISTRIBUTIONS OF DIAMETER OF MANTOUX REACTIONS TO 5 AND 100 TU AMONG MALES, MADANAPALLE, 1950-51 (ROUND I)

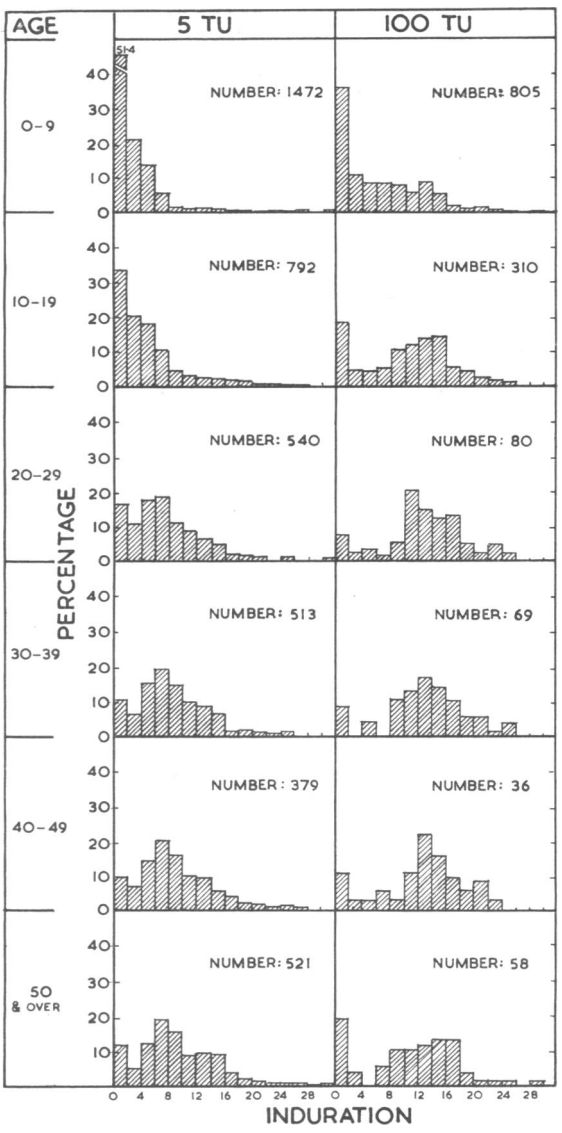
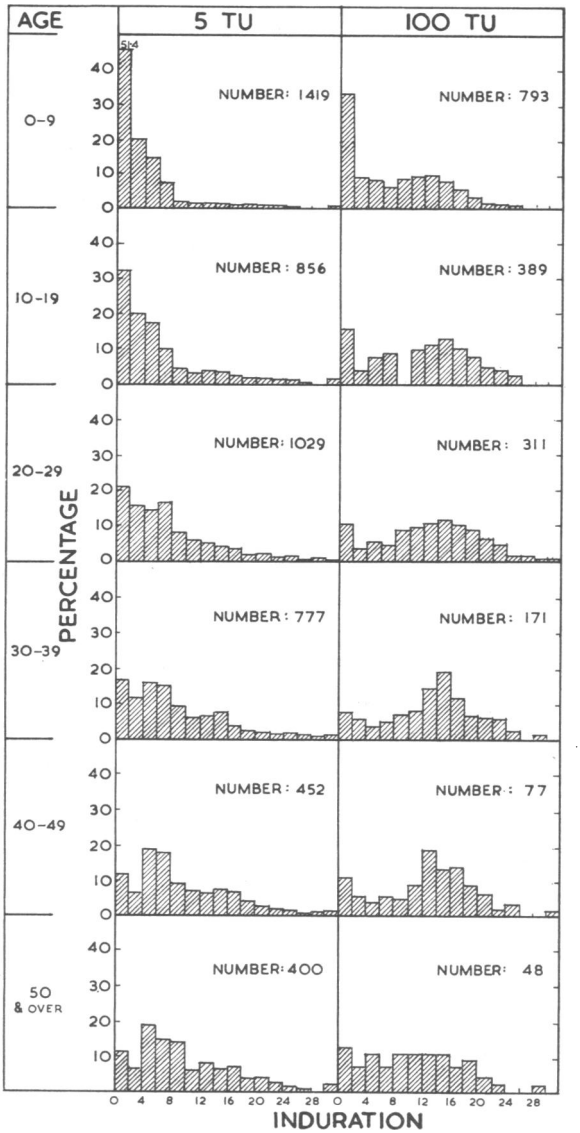


FIG. 14

FREQUENCY DISTRIBUTIONS OF DIAMETER OF MANTOUX REACTIONS TO 5 AND 100 TU AMONG FEMALES, MADANAPALLE, 1950-51 (ROUND I)



each column being very low indeed, corresponding to only a few per cent with strong reactions. In the older age-groups, from 20 to 29 and upwards, there is an increase in the frequencies to the right of the scale and a decrease in those to the left, the whole material being shifted from left to right, corresponding to an ever-increasing proportion of people showing strong reactions as the groups advance in age. Those who received 100 TU show distributions quite typical of the normal curve with a mode around 14-16 mm, indicating that the persons who showed no reactions or only very small

reactions to 5 TU still possessed some sensitivity which could be demonstrated with the 100 TU test.

It would indeed be difficult to suggest any reason for these peculiar distributions unless it were possible to compare results of similar testings in other countries. Already in 1953 Palmer and his associates (Edwards & Palmer, 1953; Edwards, Palmer & Magnus, 1953) put forward the theory that distributions like the present ones could be explained by two different types of infection operating in the same population, the one causing a low degree of tuberculin allergy and the other a high degree. While tuberculin testing with 10 TU among schoolchildren in Denmark and Mexico produced groups of strong reactors with reactions ranging from 8 to 28 mm, all the remainder having no reactions at all or only tiny indurations measuring 2-4 mm, it was possible in Egypt to demonstrate quite clearly a distinct distribution of small and intermediate-sized reactions ranging from 2 to 10 mm—i.e., occupying almost exactly the interval on the abscissa that in Denmark and Mexico showed none or at the most a few observations. Considering reactions among children in the present investigation at Madanapalle, Edwards & Palmer (1953) suggest that the findings in India can be explained—as can those in Egypt—as being composed of essentially two distributions, the one showing only small and intermediate-sized reactions to 5 TU and the other showing large reactions. The two kinds of sensitivity were designated low-grade and high-grade sensitivity. It was suggested that the latter was caused by the classic tubercle bacillus discovered by Koch, which is pathogenic for man, while the former may represent infection with an organism related to the tubercle bacillus but of a hitherto unknown origin. Tuberculin surveys by TRO teams in India and other parts of Asia as well as in Africa and the Americas have brought forth further evidence supporting this hypothesis (WHO Tuberculosis Research Office, 1955a, 1955b).

Having now before us material showing the results of tuberculin testing in all age-groups at Madanapalle and having a fair estimate of the prevalence and incidence of tuberculosis in the same population (which, as stated later in this report, are low) it may be asked: How does the above hypothesis fit into the picture here at Madanapalle ? One thing is certain, the number of persons presenting a low degree of sensitivity is unusually high. That such a finding is not merely due to technical error, such as inconsistency in measuring and interpreting the indurations, is borne out by the fact that the majority of the persons with small reactions to 5 TU show strong reactions to 100 TU, an observation which is quite unusual in some Western countries—Denmark, for example, where it is extremely rare to find strong reactions to 100 TU among those who show reactions to 5 or 10 TU measuring just a few millimetres in diameter (Edwards et al., 1953).

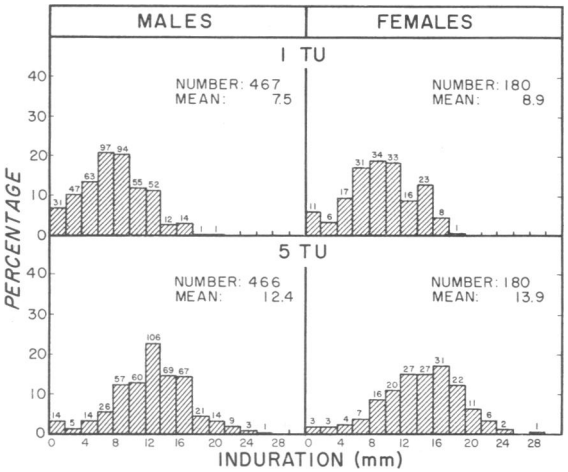
The real difficulty is to determine whether this very common low-grade sensitivity could be caused by the same type of tubercle bacilli which in Western countries produces only a high-grade sensitivity, or whether it could be due to a non-specific infection by some organism or perhaps by a mixture of both types. Scrutiny of the 5 TU distributions in the age-groups 0-9 and 10-19 years (Fig. 13 and 14) suggests that is may be possible to divide them into two normal distributions, one of which (to the right on the graphs) forms a very flat distribution, owing to the relatively small number of persons, with a mode around 14 mm, and the other (to the left) with a much lower mean containing the great majority of children. The former would represent the specific reactions and would correspond in the 0-9 year age-group to 6%-8% and in the 10-19 years age-group to 18% of those tested. With the higher age-groups, however, it becomes more difficult, if not impossible, to divide the material into two distributions. The two distributions would merge into one large distribution ranging all across the scale from small reactions to very large reactions.

TUBERCULIN SENSITIVITY IN INDIAN PATIENTS

We may now consider the type of allergy found in Indian patients treated in the UMT Sanatorium. The results of simultaneous testing with 1 and 5 TU in 647 patients (180 females and 467 males), who either had bacilli in the sputum or had previously been known to excrete tubercle bacilli, are shown in Fig. 15. Both doses of tuberculin give typical normal distributions, having a mean of 8-9 mm with 1 TU and 13-14 mm with 5 TU. The position of these distributions on the horizontal scale of millimetre indurations corresponds very closely to the position of the right-hand distributions after 1 and 5 TU tests, respectively, in the two first 10-year age-groups of the general population. From a comparison with the allergy seen in tuberculous patients in other parts of the world (WHO Tuberculosis Research Office, 1955b), it would appear that

FIG. 15

FREQUENCY DISTRIBUTIONS OF DIAMETER OF MANTOUX REACTIONS TO 1 TU AND 5 TU GIVEN SIMULTANEOUSLY TO PATIENTS WITH BACILLARY PULMONARY TUBERCULOSIS IN THE UMT SANATORIUM, 1950-51



The number above each block indicates the number examined

the allergy of patients in Madanapalle appears to be not quite so strong as that seen in Western countries. The reason for this difference is not clear. Part of it may be due to readers' differences, but it could also be due to a real difference caused by special local conditions in South India. Although every endeavour was made here to keep the stock solutions of tuberculin received from Denmark as fresh as possible, a certain deterioration or weakening of the tuberculin might have taken place. It is possible that an actual difference exists, unrelated to this factor, and that the patients in South India show an allergy not quite so high as patients examined in other countries. If the theory is accepted that there is a widespread low-grade sensitivity caused by an unknown organism that is so widespread that even small children are easily affected, the possibility cannot be excluded that this widespread non-specific allergy could produce some sort of desensitization if a superinfection with virulent tubercle bacilli took place later on; this suggestion has also been made by other investigators (WHO Tuberculosis Research Office, 1955a).

CONCLUSION

It seems very difficult to believe that all the sensitivity demonstrated in the present material could have been caused by Koch's tubercle bacillus alone. The interpretation given in the first part of the present chapter, which followed the traditional interpretation that all degrees of allergy, even those demonstrated with 100 TU alone, represent infection with the classical tubercle bacilli, would indicate an extremely high infection rate by which even small children, well under 5 years of age, were infected with tubercle bacilli. Against this stands our observation (see sections XII and XIV) that fresh tuberculosis during childhood is very rare and that the number of active infectious cases in the community is very low. It would therefore seem a very plausible suggestion that some other non-virulent organism causes the widespread low degree of sensitivity. The relative proportion of persons infected with the two types of organism would vary according to age-group. In the early part of life the non-specific infection would be very common indeed and the specific very uncommon, but after 20-30 years of age the two types of allergy would blend, making it very difficult to guess how much there would be of each kind.

The whole conception of a non-specific agent that can produce an allergy very closely resembling a true tuberculin allergy has a very serious consequence for the use of the tuberculin test as a diagnostic procedure. It should be obvious from what has been said that a reaction to 5 TU measuring anything from a few millimetres up to 8-12 mm might as easily have been caused by a non-specific agent as by the true tubercle bacillus. Only if the reaction is very strong—i.e., well over 12-15 mm in diameter—does infection with tubercle bacilli seem certain.

If the presence of a non-specific allergy is accepted, the argument must apply as well to the use of the ordinary tuberculin test for distinguishing between persons eligible and not eligible for BCG vaccination. With material such as the present, it becomes quite impossible to determine who should be given the vaccine and who should not and which size of reaction should form the dividing line between the two groups. On the one hand, one would wish to raise the limit as high as possible in order to vaccinate all those who have not been infected with the classical tubercle bacillus but perhaps with the non-specific agent; on the other hand, one would wish to lower the limit to avoid vaccinating anyone already infected with the classical tubercle bacillus. As the two distributions would appear to overlap, a clear solution does not readily present itself.

VIII. ANNUAL RETESTS

By repeating the tuberculin testing each year it was hoped that it would be possible to detect persons who had received a primary infection in the interval between the tests by finding persons who had been non-reactors the first time and later showed a definite reaction. The intention was also to study fluctuations of the allergy. It was therefore decided to test every individual in the study population each round irrespective of what their reaction had been earlier.

PROCEDURE

The procedure was to repeat the same pattern of tuberculin testing as was used before, either 1-10-100 or 5-100 TU. The analysis of the persons retested according to 1-10-100 TU is very complicated owing to the three levels of tuberculin used. The analysis has therefore been confined to the results of retests with 5 TU.

When studying the correlation tables of duplicate reactions in persons tested in two different rounds, it was found that the difference in the time interval between giving and reading the tests was partly responsible for some of the variation observed. Persons whose first test was read at five days or later and whose second test was read at a shorter interval tended to fall into the group having larger reactions at the retest, while, conversely, persons whose initial test was read at two, three or four days and whose retest was read at five days or later tended to fall into the group with smaller retest reactions. These observations were statistically significant and suggested that indurations reach a maximum size before the fifth day of reading and that tests read at five days or later do not show the full size of induration obtained. Consequently, it was decided to omit from the present analysis all reactions read at five days or later.

Although the material includes retesting results among persons tested initially in Rounds II and III, these data are not presented here. The present analysis is confined to retest results among persons who had their initial test during Round I.

MATERIAL

During Round I, 11 775 persons had Mantoux 5 TU tests given and read (Table 11). From November 1950 it was decided to vaccinate only every other non-reactor to 5 TU, in order to set up a BCG control trial (cf. section IX): of the 11 775 persons tested 2925 were done before the trial began and 8850 from the beginning of the trial to the end of Round I. Of the latter group 4363 had reactions measuring 4 mm or less to 5 TU and were allocated to the control trial, 2086 being vaccinated and 2477 remaining unvaccinated, while 4287 showed reactions of 5 mm or more. The present analysis shows the correlation between results of initial tests in Round I and retests done during Rounds II, III and IV.

In order to present retest results in a complete population the results of retests among unvaccinated persons with reactions of 4 mm or less to 5 TU in Round I have been multiplied by two to compensate for those excluded because of BCG vaccination and added to the results among the reactors. The correlation table for Rounds I-II has thus been worked out as follows: of the 4287 persons with reactions of 5 mm or more in Round I, 3451 were read at two, three or four days, and 836 at five days or later. The latter group had been excluded as the indurations had started to wane, leaving 3451 persons read at two, three or four days. Of these, 1441 were not retested in Round II, and 524 have been excluded as they were read at five days or later in the Round II retest, leaving a balance of 1486 persons read at two, three of four days in both rounds. Among the unvaccinated "controls" the corresponding number of persons was 817; by doubling this number and adding it to 1486 there are 3120 persons in all who were tested in Round I and retested in Round II, as shown in Table 12. The material for Tables 13 and 14 was built up in the same way and shows the correlation between reaction size in Round I and Round III, and Round I and Round IV respectively.

RESULTS

From the correlations shown in Tables 12, 13 and 14, it is evident that there is a positive correlation between the two readings. The correlation, however, is not nearly as close as had been expected beforehand. There is very great variation. Although most workers with some experience in reading

TABLE 12

COMPARISON OF TUBERCULIN SENSITIVITY AT ROUNDS I AND II, SHOWING CORRELATIONS BETWEEN INDURATIONS AFTER MANTOUX TESTS WITH 5 TU, READ AT 2, 3 OR 4 DAYS

Reactions at initial test in Round I: Induration in mm	Reactions at retest in Round II: 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31+	Total
0	140	—	208	106	40	178	142	78	26	18	12	8	8	4	4	4	—	2	—	—	—	—	—	—	—	2	—	—	—	—	—	—	980
1	2	—	—	—	2	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	6
2	18	—	46	14	10	30	20	16	6	—	4	—	2	2	—	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	170
3	22	—	64	24	10	68	44	20	6	6	6	4	6	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	282
4	6	—	34	24	16	36	34	16	14	2	2	4	2	—	2	4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	196
5	11	—	34	26	17	63	60	34	12	7	10	1	6	2	3	3	1	2	1	—	—	—	—	—	—	—	—	—	—	—	—	—	293
6	11	—	22	14	8	50	37	22	7	9	6	5	6	3	3	5	1	—	—	—	—	—	1	—	—	1	—	—	—	—	—	—	211
7	7	—	14	9	10	32	25	24	13	4	10	3	8	3	—	6	2	3	2	—	1	—	—	—	—	—	—	—	—	—	—	—	176
8	1	—	12	5	3	10	12	15	2	2	7	3	4	4	3	1	1	3	1	1	5	—	—	—	—	—	1	1	—	—	—	—	97
9	3	—	3	4	4	11	13	9	7	5	6	5	8	2	4	5	5	2	1	2	4	—	1	—	—	—	1	—	—	1	—	—	106
10	2	—	1	—	1	6	13	9	2	3	9	4	9	7	2	4	4	3	3	—	—	2	—	—	—	1	—	—	—	—	—	—	85
11	1	—	—	1	1	6	5	8	3	3	2	2	8	4	1	1	1	4	2	—	2	1	—	—	—	—	—	—	—	1	1	—	58
12	1	—	1	2	—	13	9	8	4	5	7	2	8	—	2	10	3	1	1	—	—	1	1	—	—	—	—	—	—	—	—	—	79
13	—	—	3	—	1	6	4	4	—	2	7	2	7	2	1	5	3	2	—	—	3	1	1	1	—	—	—	—	—	—	—	—	55
14	—	—	—	—	1	3	10	5	7	6	6	—	3	2	1	9	1	2	1	—	2	—	1	1	1	—	—	—	—	—	1	—	63
15	—	—	1	1	—	1	7	4	2	4	5	2	7	1	1	6	1	2	2	—	5	—	2	—	—	1	—	—	—	—	—	—	55
16	—	—	—	—	—	4	1	2	2	2	5	2	7	3	2	4	1	1	—	—	3	1	3	—	1	1	—	—	—	—	—	—	45
17	—	—	—	—	1	—	—	—	1	3	1	—	8	—	—	3	—	2	1	—	1	2	—	—	—	—	—	—	—	—	—	—	23
18	—	—	—	—	—	2	1	2	2	1	—	1	4	3	2	4	—	5	—	—	3	1	—	—	—	—	1	—	—	—	—	—	32
19	—	—	—	—	—	—	2	2	—	1	—	1	—	—	—	—	1	1	—	—	1	—	—	—	—	1	—	—	—	—	—	—	10
20	—	—	—	—	—	1	—	1	2	—	3	1	3	4	1	4	1	1	1	—	—	—	2	1	—	—	—	—	—	—	—	—	26
21	—	—	—	—	—	1	—	—	1	—	1	—	1	—	1	—	—	—	1	—	—	—	1	—	—	—	—	—	—	—	—	—	7
22	—	—	1	—	—	1	1	—	1	—	—	1	—	1	1	1	1	1	—	—	3	—	—	—	1	—	—	—	—	—	—	—	14
23	—	—	—	—	—	—	1	—	1	—	—	—	—	2	1	4	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	10
24	—	—	—	—	—	1	—	—	—	—	—	—	1	—	—	—	—	1	2	—	—	—	—	—	—	—	—	—	—	—	—	—	5
25	—	—	1	—	—	—	—	1	—	1	1	—	2	1	—	—	—	—	1	—	1	—	—	—	—	1	—	—	—	—	—	1	11
26	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2
27	—	—	—	—	—	—	—	—	1	—	—	1	—	—	—	—	1	—	1	—	—	—	1	—	—	1	—	—	—	—	—	—	6
28	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	2	—	1	—	—	—	—	—	—	—	—	1	—	—	—	—	—	5
29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	1	1	—	—	—	1	—	—	—	—	1	—	—	—	—	—	1	6
31+	—	—	—	—	—	—	—	1	—	—	—	—	1	—	—	2	—	—	—	—	2	—	—	—	—	—	—	—	—	—	—	—	6
Total	225	—	445	230	125	525	441	282	122	84	110	52	121	52	35	89	31	39	21	3	37	9	14	3	4	10	4	1	—	2	2	2	3120

TABLE 13

COMPARISON OF TUBERCULIN SENSITIVITY AT ROUNDS I AND III, SHOWING CORRELATIONS BETWEEN INDURATIONS AFTER MANTOUX TESTS WITH 5 TU, READ AT 2, 3 OR 4 DAYS

Reactions at initial test in Round I: Induration in mm	Reactions at retest in Round III: 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31+	Total
0	160	—	200	110	56	64	74	60	22	10	8	8	6	2	2	10	6	—	4	—	8	2	2	—	—	4	—	—	—	—	—	—	818
1	—	—	2	—	—	—	2	—	—	—	—	—	—	—	—	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	6
2	18	—	40	18	12	18	20	6	6	2	4	2	2	2	—	2	—	—	—	—	—	—	—	2	—	—	—	—	—	—	—	—	154
3	24	—	68	36	20	18	28	14	8	6	2	—	4	4	—	—	2	—	—	—	2	—	2	—	—	—	—	—	—	—	—	—	238
4	16	—	30	12	8	16	24	16	10	2	8	—	—	—	—	2	4	—	4	—	—	—	—	—	—	—	—	—	—	—	—	—	152
5	24	—	37	23	10	16	33	25	14	7	6	7	7	7	—	5	3	3	1	—	4	—	1	1	—	—	—	—	—	—	—	1	235
6	15	—	18	6	11	21	23	13	12	3	4	4	7	3	2	6	3	1	1	—	—	1	1	—	—	—	—	—	—	—	—	—	155
7	9	—	24	8	7	11	21	15	8	2	2	4	5	9	3	12	3	2	3	1	5	1	1	—	—	—	—	—	—	—	—	—	156
8	4	—	6	4	1	4	9	9	6	4	6	6	4	6	3	3	2	3	3	—	3	—	—	1	—	—	—	—	—	—	—	—	87
9	1	—	4	6	1	2	9	10	3	1	8	5	6	2	2	4	7	2	3	2	4	1	—	—	—	—	—	—	—	—	—	—	83
10	2	—	3	3	1	5	3	4	5	5	2	2	5	2	4	7	6	—	2	—	6	—	1	—	2	1	—	—	—	—	—	—	71
11	1	—	3	—	1	3	2	3	5	1	7	4	2	1	2	6	4	1	—	1	2	1	—	1	—	—	—	—	—	—	—	—	51
12	—	—	2	2	1	8	6	4	3	2	4	5	9	3	3	7	2	3	4	—	8	—	—	1	—	1	—	1	—	—	—	—	79
13	2	—	1	—	—	—	1	2	4	6	3	—	7	2	2	4	—	—	2	—	3	—	3	1	—	—	—	1	—	—	—	—	43
14	2	—	3	1	—	3	1	1	2	3	3	4	3	2	2	9	2	4	—	—	1	—	2	2	—	1	—	1	—	—	—	—	52
15	—	—	2	—	1	—	1	—	4	—	4	3	4	1	2	10	2	4	3	1	1	—	1	1	—	4	—	1	—	—	—	—	50
16	—	—	—	—	—	1	—	2	2	1	5	3	4	—	—	2	7	—	2	—	4	1	2	3	—	1	—	—	—	—	—	—	40
17	—	—	—	—	—	2	—	—	—	4	1	—	4	1	—	1	1	1	—	1	3	1	2	1	—	3	—	—	—	—	—	—	26
18	—	—	—	1	—	—	1	3	2	—	1	—	1	3	1	4	7	3	—	—	1	—	3	—	—	—	—	—	—	—	—	1	32
19	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	2	2	1	—	—	3	—	—	—	—	—	—	—	1	—	—	—	10
20	—	—	—	—	—	—	—	2	1	—	3	—	—	1	1	2	2	1	2	—	4	—	2	—	—	1	1	—	—	—	—	—	23
21	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	1	3	—	1	—	—	—	—	—	—	6
22	—	—	—	—	—	—	1	2	1	—	—	—	2	—	—	3	1	1	1	—	3	—	2	—	—	—	—	—	—	—	—	—	17
23	—	—	1	—	—	—	—	1	—	—	1	—	—	—	—	—	—	—	2	—	1	—	1	—	—	1	—	—	—	—	—	—	8
24	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2
25	—	—	—	—	—	—	—	—	—	—	—	1	1	1	—	1	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	6
26	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	2
27	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	1	—	—	—	—	—	—	2
28	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	1
29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	1	—	—	—	—	1	3
31+	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Total	277	—	444	230	130	193	259	192	118	59	82	58	84	53	30	104	68	30	38	6	68	9	28	18	2	19	2	3	2	—	—	3	2609

TABLE 14

COMPARISON OF TUBERCULIN SENSITIVITY AT ROUNDS I AND IV, SHOWING CORRELATIONS BETWEEN INDURATIONS AFTER MANTOUX TESTS WITH 5 TU, READ AT 2, 3 OR 4 DAYS

Reactions at initial test in Round I: Induration in mm	Reactions at retest in Round IV: 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31+	Total
0	72	—	154	134	88	82	30	28	18	10	10	14	2	6	8	2	—	2	6	2	4	—	—	2	2	2	—	—	—	—	—	—	678
1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2	10	—	30	24	22	8	4	12	6	4	2	—	2	—	4	—	2	2	—	—	—	—	—	—	—	—	—	—	2	—	—	—	134
3	10	—	40	24	26	30	12	28	8	2	6	4	2	—	2	2	—	4	—	2	2	—	—	—	—	—	—	—	—	—	—	—	204
4	6	—	18	10	20	26	18	16	—	8	2	2	4	—	4	—	—	—	2	—	—	—	—	2	—	—	—	—	—	—	—	—	138
5	11	—	25	16	17	24	13	18	12	11	6	5	2	5	1	3	3	—	5	3	1	—	—	1	2	—	1	—	—	—	—	—	185
6	9	—	13	12	10	12	20	13	15	4	6	2	7	5	8	3	—	6	4	2	—	3	1	1	—	1	—	1	—	—	—	—	158
7	3	—	11	7	8	9	15	18	6	6	6	3	6	4	6	2	2	3	1	—	1	—	2	—	—	—	1	1	—	—	—	—	121
8	—	—	5	4	7	1	4	3	4	3	6	6	6	5	2	3	—	4	1	2	2	—	3	1	2	—	—	—	—	—	—	—	74
9	2	—	3	4	3	1	6	5	7	2	5	5	1	6	2	5	4	2	2	—	1	1	—	1	—	1	1	—	—	—	—	—	70
10	—	—	2	2	3	2	4	3	4	3	2	—	4	3	1	1	7	3	2	2	2	2	1	1	1	—	—	—	—	—	—	—	55
11	2	—	—	—	1	1	1	1	2	—	2	3	4	1	1	1	1	3	3	1	2	1	—	—	—	—	—	1	—	—	1	—	33
12	1	—	—	2	1	1	5	2	1	2	5	2	10	6	1	3	1	1	2	2	—	2	3	—	—	—	—	—	—	—	—	—	53
13	—	—	1	1	—	1	—	2	1	1	—	—	2	4	3	4	1	2	3	1	2	—	1	1	1	—	—	—	—	—	—	—	32
14	1	—	2	1	1	1	1	1	4	6	3	1	2	3	3	5	4	3	4	2	5	1	1	—	1	—	—	—	—	—	1	—	57
15	1	—	—	1	1	1	1	3	2	—	1	1	2	—	4	5	2	3	6	4	2	2	—	—	1	—	1	1	—	—	—	—	45
16	—	—	—	1	1	—	1	1	2	3	1	1	2	2	2	1	2	1	3	1	2	—	1	2	3	2	1	1	—	—	—	—	37
17	—	—	—	1	1	1	—	1	—	1	1	1	1	2	1	2	1	1	2	—	—	—	—	—	1	—	1	1	1	—	—	—	21
18	—	—	—	—	—	—	—	—	—	—	4	2	1	—	1	—	1	1	2	—	3	3	2	1	—	—	—	—	—	—	—	—	—	21
19	—	—	—	—	—	—	—	1	2	—	—	1	3	1	—	—	—	1	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	10
20	1	—	—	—	—	—	—	1	—	—	—	2	—	2	1	1	1	1	1	—	1	—	1	—	1	—	—	—	—	—	—	—	—	14
21	—	—	—	—	—	1	—	1	1	—	1	—	—	—	—	—	—	1	1	—	—	—	—	—	2	1	1	—	—	—	—	—	—	10
22	—	—	—	—	—	—	—	—	—	1	—	1	1	—	—	1	—	—	1	—	2	—	1	1	—	1	—	—	—	—	—	—	—	10
23	—	—	—	—	—	—	1	—	—	—	—	1	—	—	1	—	—	—	—	—	1	—	2	—	—	—	—	—	—	—	—	—	—	6
24	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	1	—	—	—	—	—	—	—	—	—	—	2
25	—	—	—	—	—	—	—	—	1	—	1	—	2	—	1	2	—	1	—	1	1	—	—	1	—	1	—	—	—	—	—	—	—	12
26	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
27	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	1	—	—	1	1	—	—	—	—	—	—	—	—	—	4
28	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	1	—	—	1	—	—	—	—	—	—	—	—	—	—	—	3
29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30	1	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	—	—	1	—	—	5
31+	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	1	—	—	—	—	—	—	—	—	—	—	2
Total	130	—	304	244	210	203	137	158	96	67	70	57	68	55	57	46	32	47	54	26	35	17	22	16	17	9	7	6	3	1	2	—	2195

tuberculin tests would accede that it is not possible to be consistent to the millimetre even in reading the same tests over again independently on the same day, the magnitude of variations observed here may exceed what many would consider possible. The scatter of variation of duplicate tests is so great that the second reading may cover almost the whole range of indurations. For example, indurations of 10 mm in Round I range from 0 to 25 mm when repeated in Round II.

There can be no doubt that the experimental error is very great, and there are reasons for this. The staff changed frequently. Not often would two tests have been given and read by the same reader. The quality and length of training of new staff doctors could perhaps have been better. A certain element of inaccuracy might have been introduced by errors in the identification of persons, but it is not likely that this would affect more than a very small fraction of the persons tested. Further, there may have been variations in the strength of the tuberculin dilutions due to variations in storage, age, size of bottles, etc., although fresh dilutions of the same batch of tuberculin were prepared every day.

The question may be asked whether the variation is due only to experimental errors or whether some of the changes in size of reactions could be due to genuine alterations in the individual level of allergy. From the present material it is not possible to estimate the size of the variance of the experimental error and the relative significance of the effects contributing to the composition of the variance. In a recent experiment, not yet published, the effect of testers and readers on the results of reading Mantoux tests was examined by having duplicate tests done on 75 tuberculous patients in the UMT Sanatorium by five different doctors and readings done by seven different doctors who also read independently all the reactions a second time the same morning, giving a total of 2100 observations. Analysis showed that the variance was 9.18 and the standard error was 3.03 mm for a single observation, and 4.54 and 2.13 mm respectively after separating out the variance attributable to testers and readers.

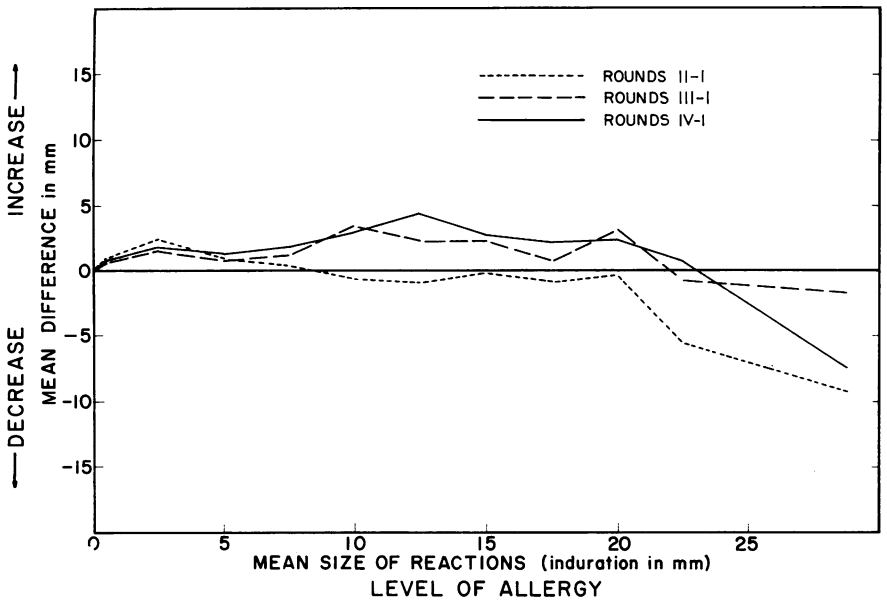
These values are not much different from estimates of the experimental error in tuberculin tests made by other workers (Guld, 1953; Nissen Meyer, Hougen & Edwards, 1951), although our estimate shows somewhat larger experimental errors, since our readers were not as highly trained as those employed by the authors mentioned. Since the experimental error of single observations will be about 2-3 mm it is obvious that two tests of the same individual may show considerably different results, and that an observed difference must be large before it can be considered significant. It seems likely that the major portion of the variations observed is simply due to experimental errors and not to real fluctuations in tuberculin allergy. Unless the changes in tuberculin sensitivity in the individual revealed by repeated tuberculin tests are very substantial, it is difficult to draw any valid conclusions as to the present state of allergy; and the same applies to the use of the tuberculin test as a diagnostic tool.

GENERAL INCREASE IN ALLERGY

Since a large proportion of the population tested includes children and young people and since it has already been shown that the general level of allergy increases with age, it should be expected that a large number of persons would show increased reactions. The greatest change should be expected among those who had small or no reactions at the initial test; they should appear in the right upper portion of the correlation table corresponding to stronger reactions at the second test. The general shift in tuberculin sensitivity has been calculated by a method of analysis described by Guld (1953), and is illustrated in Fig. 16, which shows the mean differences in size of indurations between the first test in Round I and the retests in Rounds II, III and IV respectively. No significant change was found between Rounds I and II and only a moderate increase in average size of indurations between Rounds I and II and between Rounds I and IV. In the last-mentioned case, which represents a time interval of 3.7 years on an average, the reactions have increased 2-5 mm. In all three sets of correlations persons with strong reactions above 20-25 mm in Round I show a decrease at the second test; how much of this decrease is real and how much is due to over-reading of the reactions at the initial test is not easy to determine. So, although it was difficult to determine whether genuine fluctuations took place in individuals, analysis for the whole group indicates a general increase in allergy, the greater the longer the observation period.

FIG. 16

CHANGES IN AVERAGE LEVEL OF SKIN SENSITIVITY OF PERSONS TESTED WITH 5 TU INITIALLY IN ROUND I AND RETESTED IN ROUNDS II, III, AND IV



IX. TUBERCULIN SENSITIVITY IN A BCG CONTROL TRIAL

INTRODUCTION

As mentioned in the introduction to this report, it was with a desire to try out BCG vaccination in Indian children before introducing BCG on a wider scale in the country that the Government of India requested the UMT Sanatorium to conduct a pilot study in Madanapalle Town in 1948. It was found that the vaccine produced very small local lesions and the postvaccination allergy was low as judged from the low conversion rate, which was only 69%. (Frimodt-Møller, 1949). The original criterion for vaccination in Madanapalle was a reaction of 4 mm or less to 100 TU. When the extended village survey was begun in 1950, BCG was given to non-reactors to 10 TU after a preliminary test with 1 TU; simultaneously with the BCG a test with 100 TU was also done. When 5 TU was introduced as first test dose later in 1950, followed by 100 TU to non-reactors (4 mm or less), BCG was given simultaneously with the second dose of tuberculin. Finally, in November 1950, it was decided to set up a BCG control trial by omitting BCG vaccination in every other person who showed an induration of 4 mm or less to 5 TU while giving 100 TU to every such person. All persons admitted to the trial were to be retested during the subsequent rounds of tuberculin testing and mass miniature X-ray examination. The present analysis deals only with the results among persons allocated to the control trial.

PROCEDURE

The BCG vaccine was sent up once a week by train from the BCG Laboratories, Guindy, Madras, in heat-insulated boxes packed with ice in water-tight containers; the transport took a little less than 24 hours. At the sanatorium the vaccine was kept in a refrigerator until use and was then taken to the villages in Thermos flasks filled with ice. In the field the syringes used for tuberculin and vaccine were carried in special injection boxes. The testings and vaccinations were often done in the open but in the shade, or when possible on verandahs or in

doorways. After the first reports from the TRO on the deleterious effect of direct and indirect sunshine on the vaccine (Edwards & Dragsted, 1952; Edwards & Tolderlund, 1952) special care was taken to protect the vaccine at all stages against exposure to sunlight. The vaccine was always injected by a doctor. The site of inoculation was inspected when the 100 TU reaction was read, and the nodule was measured across with a ruler marked in millimetres and the size noted. When the person was seen later, another note was made of the condition of the scar and its size. The average time interval between the four rounds was as follows: Rounds I-II, 1.4 years; Rounds II-III, 1.3 years; and Rounds III-IV, 1.0 year.

MATERIAL

In order to obtain comparable controls randomization was effected by taking a pack of blank individual index cards, marking a cross with ink on the back of half the cards and shuffling the pack. When reading the 5 TU test, the reader would not know until the size of the induration had been noted whether the card was marked on the back or not. Only persons with marked cards were then vaccinated, but both vaccinated and unvaccinated were given a 100 TU test.

As will be seen presently the system of randomization worked well up to a certain extent. It failed in certain cases where the child or parent resented any further injections. Thus some cases eligible for BCG did not get their vaccination or their 100 TU test, and the number of unvaccinated cases therefore exceeded that of vaccinated cases; in Round I the two groups were about equal, in later rounds the gap between vaccinated and unvaccinated became larger.

In the following analysis all persons tested whose reactions were read later than the fourth day have been excluded in order not to introduce a number of reactions where the indurations had started to wane. The number of persons retested and read at two, three or four days forms about 50% of those included in the BCG control trial in Round I.

RESULTS

The frequency distributions relating to the tests done in each round are given in Appendix Tables 2a, b and c, and the mean indurations are shown in Table 15. Retest results in Rounds II-IV among persons in the BCG control trial population initially reacting with 5 mm or more to the 5 TU test (at Round I) have been discussed in section VIII (Tables 12-14).

TABLE 15

RESULT OF RETESTS IN VACCINATED AND CONTROLS IN THE BCG CONTROL TRIAL (MANTOUX 5 TU, READ AT 2, 3 OR 4 DAYS) *

	Round I		Round II		Round III		Round IV	
	No.	Mean	No.	Mean	No.	Mean	No.	Mean
BCG	1 555	1.24 [a]	716	5.53	553	6.15	480	6.46
Controls	1 817	1.20	817	4.37	684	4.34	577	4.80
Difference				1.16		1.81		1.66
BCG			646	2.04 [a]	241	6.42	216	6.97
Controls			786	2.08	293	3.47	233	4.18
Difference						2.95		2.79
BCG					1 136	1.66 [a]	471	5.85
Controls					1 497	1.83	582	3.54
Difference								2.31

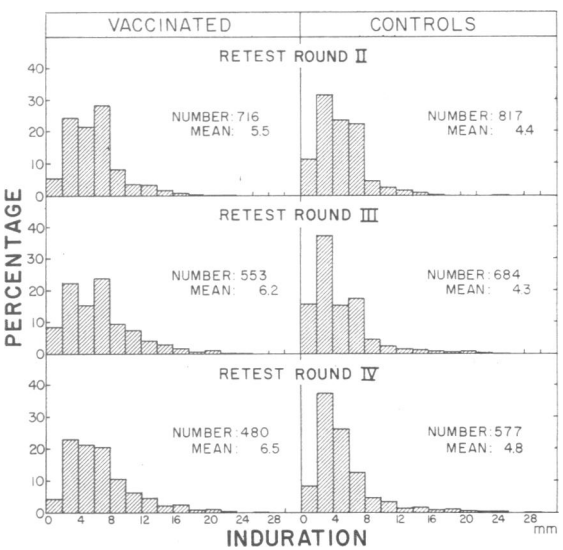
* For basic data, see Appendix Table 2c.

[a] Prevaccination tests.

The prevaccination indurations in Rounds I, II and III for vaccinated and unvaccinated range in mean size from 1.2 to 2.1 mm. The postvaccination retests for those vaccinated in Round I showed at Rounds II, III and IV indurations with a mean size of 5.5, 6.2 and 6.5 mm respectively (Fig. 17). Compared with the size of postvaccination indurations obtained by the TRO in their vaccination studies in Denmark (Edwards, Palmer & Magnus, 1953) also after one or two years, these results are poor indeed. Considering those vaccinated in Rounds II and III, when the adverse effect of sunshine had been realized and precautions for the protection of the vaccine issued, the retest results are not much different: for those vaccinated in Round II, the mean postvaccination indurations in the Rounds III and IV were 6.4 and 7.0 mm respectively, and for those vaccinated in Round III and retested in Round IV the mean size was 5.8 mm. It seems, therefore, that the results are quite uniform and consistent throughout the whole period of investigation. Either it is not the effect of sunlight on the vaccine which is the cause of the poor postvaccination results, or the precautions taken to protect the vaccine against light have been quite ineffective.

FIG. 17

FREQUENCY DISTRIBUTIONS OF DIAMETER OF MANTOUX REACTIONS TO 5 TU AT RETESTS IN ROUNDS II, III AND IV OF PERSONS ALLOCATED TO THE BCG CONTROL TRIAL IN ROUND I



COMPARISON WITH RETESTS IN CONTROLS

The mean sizes of indurations obtained by retests in the unvaccinated corresponding to those mentioned above for the vaccinated are also shown in Table 15 and Fig. 17. They are persistently and significantly lower than the mean sizes of indurations in the vaccinated. This is as it should be, but the remarkable and critical observation is the fact that the differences, though statistically significant, are very small—namely, only 1.2-2.9 mm. This means that the part played by the BCG vaccination in setting up an allergy which is reflected in the size of indurations measured at the postvaccination retest described above is even more modest than at first thought.

DISCUSSION

The low postvaccination allergy observed at Madanapalle is very disturbing. TRO teams have obtained reactions (to 10 TU) of 16-17 mm in mean size after 6-12 weeks among Danish schoolchildren (Edwards, Palmer & Magnus, 1953). In India special teams, also from the TRO, retesting in 1954 persons vaccinated in the mass BCG vaccination programme in different parts of India between 1950 and 1953, using the same lots of vaccine as were used at Madanapalle, obtained mean post-vaccination indurations ranging from 7 to 15 mm (WHO Tuberculosis Research Office, 1955 b); in 1955 the average size obtained was 9.9-12.5 mm, while groups vaccinated by the assessment team with Copenhagen vaccine showed reactions of which the mean size varied between 12.5 and 15.5 mm (WHO Tuberculosis Research Office, 1957). All this points to an unusually low allergy-producing effect of the vaccine at Madanapalle. Taking into consideration the results of retests in the unvaccinated controls in Madanapalle, the effect of the vaccine is very modest indeed.

It is difficult to explain why the vaccine has given such poor results. Many factors could have played a part, such as possible damage to the vaccine in transit between Madras and Madanapalle or when being handled in the field, variations in the tuberculin dilutions, differences in reading techniques, and factors relating to the vaccinated persons themselves. Of these possibilities, it is not likely that variations in the vaccination techniques and in the preparation and/or handling of the tuberculin dilutions could

account for much of the differences. The readings of the reactions could have introduced an experimental error larger than that observed in readings carried out by specially trained personnel such as those employed by the TRO assessment teams, the readers at Madanapalle having changed from time to time; a certain bias operating in favour of either large reactions or the opposite cannot be excluded, but it is difficult to trace. As for individual factors in the vaccinated persons there is no reason to suspect fundamental differences between persons examined at Madanapalle and persons vaccinated in other parts of India; whether there could be a difference in response between Indians and Europeans is not so easy to say, but special investigations designed and carried out by the TRO to examine this question do not indicate that such differences exist, at least not to any very marked extent. One such investigation may be briefly reviewed.

In February 1951 Indian children in schools at Punganur and Chittoor, 20 and 60 miles (32 and 96 km) from Madanapalle, respectively, and Danish children in Denmark were vaccinated on the same day with both Danish and Indian vaccines prepared simultaneously in Copenhagen and Madras. Special precautions were taken to protect the vaccine: it was brought up to Madanapalle by special messenger, packed in ice in Thermos flasks. The vaccinations were given indoors; and retests were done after six weeks. The results are shown in reports by Edwards et al. (1953) and by Frimodt-Møller (1953). The postvaccination tests showed indurations of 14.8 mm with the Danish vaccine and 14.0 mm with the Indian vaccine in the Indian children, and 18.5 and 16.4 mm with the two vaccines, respectively, in the Danish children. The reactions in the Indian children were thus a little smaller than in the Danish, but how much of this difference could be ascribed to reader's differences is not possible to know. As the Indian vaccine contained a smaller dose of BCG than the Danish vaccine, it is reasonable that some difference in the reaction-sizes was observed.

For the purpose of the present discussion it will be noted that the Indian children produced reactions (to 10 TU at 6 weeks) which were much larger and stronger than those shown by the children and adults vaccinated by the same personnel in the villages near Madanapalle. As any fundamental difference between the groups vaccinated in the special investigation and those living near Madanapalle can be ruled out, an explanation of the great difference between the postvaccination allergy observed in the Punganur-Chittoor investigation and that observed by us in the field must be sought elsewhere. Although the differences in tuberculin dilutions (10 TU against 5 TU) and time of retests (6 weeks against 1-3 years) in the two sets of investigations are quite formidable, the differences in size of reactions are so great that these variations may not be sufficient to account for them all. The fact that the vaccine used for the special investigation was sent up to Madanapalle from Madras without undergoing the hazards of a train journey with possible exposure to high day temperatures, and that it was used entirely indoors, should not be overlooked. Despite our efforts to bring the vaccine used in the routine work up safely from Madras and to protect it against direct or indirect exposure to sunlight, it is possible that the major reason for the diminished effect of the vaccine when given in the field could be due to the vaccine having suffered significantly in viability. The postvaccination allergy observed is comparable to what is seen if vaccinations are done with heat- or light-killed BCG.

It may not be possible to say exactly which is the factor, or factors, responsible for the failure of the vaccine to induce a good skin sensitivity. It is discouraging that vaccinations given over a period of several years should produce such persistently poor results. The question arises whether in spite of the low tuberculin allergy measured by the skin tests, the vaccinations could have produced sufficient immunity to protect the persons vaccinated against developing tuberculosis. This point is discussed in section XVI, which gives the incidence of fresh cases observed in the vaccinated and unvaccinated groups of the present BCG control trial.

As the unvaccinated group shows increased allergy at the first retest, which is not likely to be due merely to experimental errors, and as they show a steady increase in mean size of indurations from retest to retest, it seems likely that superinfection takes place all the time. As will be discussed in the next chapter much of this superinfection might be caused by a non-specific but not yet identified organism (or organisms), so the BCG vaccine may be competing with another agent. How this process affects the BCG allergy is difficult to assess.

X. RATE OF INFECTION

INTRODUCTION

The common method of estimating the infection rate is to note the number of persons who develop tuberculin sensitivity during a certain period from a state of no sensitivity, as demonstrated by repeated tuberculin tests. This is a fairly simple and accurate method when used in populations where tuberculin tests produce either strong indurations or no reactions at all or only small vague infiltrations in the skin attributable to the trauma or impurities in the solutions containing the tuberculin. The method is not very applicable in populations like the present study population, which show a large range of degrees of tuberculin sensitivity in nearly all age-groups. When at the same time the reactions are often ill defined owing to poorly developed indurations, the error in measuring the diameters becomes quite formidable (2-3 mm for a single test, as mentioned earlier), and the interpretation becomes difficult and ambiguous.

INFECTION RATES ESTIMATED FROM PREVALENCE CURVES OF REACTORS

Assuming that the general infection rate in a community is constant over one year, a rough estimate of the infection rate at various ages can be calculated from data or curves which show the percentage of reactors at each age. Noting the increase in the percentage of reactors from a certain age to another and noting the percentage of non-reactors at the lower age, the rate of new reactors in the time period corresponding to the difference between the two ages can easily be computed. The steeper the slope of the curve of reactors the higher is the infection rate.

Table 16 and Figure 18 show the average rate per year per 1000 males whose indurations to the tuberculin test increase over a certain size. In the case of reactors to 1 TU and 100 TU the rates indicate a change from indurations of 5 mm or less to indurations of 6 mm or more in diameter. With regard to 5 TU reactors the rates have been calculated on the basis of (*a*) indurations changing in size from 4 mm or less to 5 mm or more (as shown in Fig. 18), and (*b*) from 9 mm or less to 10 mm or more.

TABLE 16

AVERAGE CONVERSION RATE PER 1000 PER YEAR IN MALES ACCORDING TO AGE AND DOSE OF TUBERCULIN *

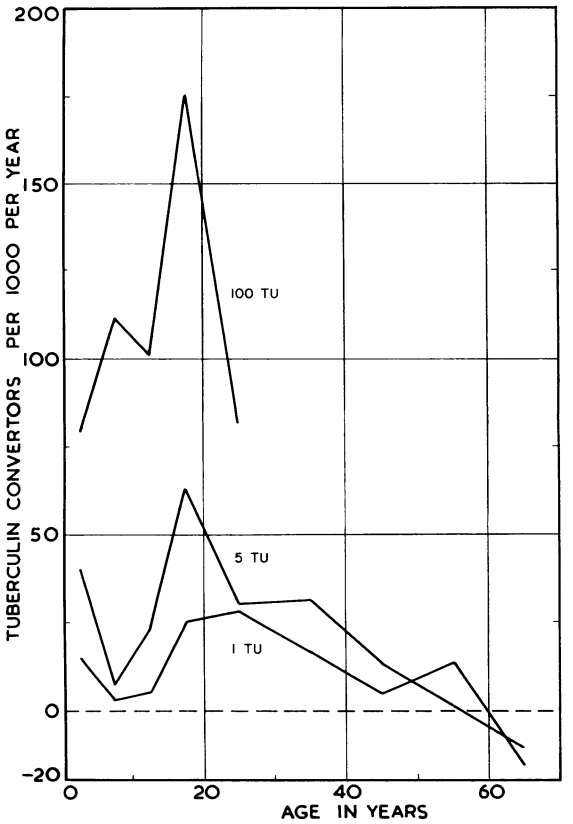
Age	1 TU	5 TU		100 TU [a]
		(*a*)	(*b*)	
0–	14.8	40.0	9.4	78.4
5–	2.8	7.0	3.6	111.4
10–	4.8	23.4	10.3	100.8
15–	25.6	62.4	17.6	175.6
20–	20.8	30.1	4.1	81.4
30–	16.6	31.7	13.1	—
40–	4.5	13.8	2.2	—
50–	13.9	1.0	2.3	—
60+ [b]	-16.1	-10.5	-13.1	—
Average	9.1	18.9	4.2	104.8 [c]

* *Reactors* to 1 TU = indurations 6 mm or more in diameter.
Reactors to 5 TU (*a*) = indurations 5 mm or more in diameter.
Reactors to 5 TU (*b*) = indurations 10 mm or more in diameter.
Reactors to 100 TU = indurations 6 mm or more in diameter.
[a] Following after 1 and 10 TU.
[b] Calculated as 60-69 only.
[c] For first 30 years only.

The question now is: Which set of conversion rates should be accepted as the best estimate of the infection rate in tuberculosis? Obviously, the 100 TU curve is not suitable unless the hypothesis of non-specific allergy is rejected; the 100 TU estimate would give an infection rate in this village population as heavy as that seen in hospital personnel in Western countries. (Ferguson (1955) found an annual infection rate of 147 among hospital nurses in Saskatchewan and Winnipeg.) The choice may be between the 1 TU and 5 TU estimates. As regards the latter, only the rate (*a*) based upon indurations of 5 mm or more is shown in Fig. 18. A peak of 62 per 1000 is found in the age-group 15-19 years which appears to be closely related to a peak at the same age in the 100 TU curve, suggesting that the cause of the peak in the two curves is the same, by which it is implied that the 5 TU curve probably includes

FIG. 13

RATES PER 1000 OF MALES WHOSE MANTOUX REACTIONS TO 1 TU AND 100 TU CHANGE FROM INDURATIONS OF 5 mm AND LESS TO 6 mm AND MORE, OR WHOSE REACTIONS TO 5 TU CHANGE FROM INDURATIONS OF 4 mm AND LESS TO 5 mm AND MORE, DURING ONE YEAR



Estimated on basis of percentages shown in Fig. 9 and 10 respectively.

some non-specific reactors also. Cutting the 5 TU distributions at 10 mm, we get the rates for converters shown under (*b*) in Table 16. According to this the rates are very low. Finally, there is the estimate based upon the curve of 1 TU reactors. The rates fall between the two estimates based upon 5 TU reactors. Here too there is a maximum between 15 and 20 years but the rates in the higher age-groups fall only slowly to a minimum at 50 years and more. Perhaps the 1 TU estimates are on the low side, and those based upon 5 TU a little too high, but this is merely a surmise. Between the ages of 15 and 39 the infection rate may be between 20 and 40 per 1000 per year.

THE INFECTION RATE BASED UPON RETESTS IN " CONTROLS " OF THE BCG CONTROL GROUP

Procedure

For the purpose of estimating the infection rate directly by observing the number of " converters " in persons with no initial sensitivity, it is fortunate that the BCG control study was set up by the end of 1950. Without that we should have proceeded with the vaccination of all so-called negative reactors. An examination of the material presented in Appendix Tables 2a, b and c will show a number of cases with large reactions in all groups of retested persons in the " control " group. Taking arbitrarily reactions of 10 mm or more as indicative of presence of allergy caused by the classical tubercle bacillus, rates of infection have been worked out for all three intervals between the four rounds of tuberculin/X-ray surveys (Table 17). The material consists of three groups: one observed from Round I to Rounds II, III or IV; one group started in Round II and

TABLE 17

ESTIMATES OF ANNUAL INFECTION RATE PER 1000 BASED ON OBSERVATIONS OF CHANGES IN SIZE OF INDURATIONS FROM 4 MM AND LESS AT INITIAL MANTOUX TEST (5 TU) TO 10 mm AND MORE AT RETESTS IN UNVACCINATED CONTROLS IN THE BCG CONTROL TRIAL

Round interval	Number retested	Persons with indurations of ⩾ 10 mm	Theoretical distribution of persons with reactions ⩾ 10 mm in size according to round interval [a]		
			I-II	II-III	III-IV
(a) *Observations*:					
I- II	817	43	43	—	—
I-III	684	56	36.00	20.00	—
I-IV	577	58	30.37	16.87	10.76
II-III	293	14	—	14	—
II-IV	233	17	—	11.1	5.9
III-IV	582	30	—	—	30
(b) *Rates per 1000 per year*:					
I-IV	577	58	37.8	23.9	20.5
II-IV	233	17	—	37.0	26.9
III-IV	582	30	—	—	52.2

[a] Round intervals I- II = 1.39 years
II-III = 1.29 ,,
III-IV = 0.99 ,,

retested in Rounds III and IV; and one group started in Round III and retested in Round IV. The number of " converted " cases arising in each interval has been calculated by applying the experience gained during the first interval to the next. For example, of the 56 cases found in the group tested in Round I and again in Round III, it can be calculated on the experience of the 817 retested in Round II that 36 arose in the interval I-II, leaving 20 arising in the interval II-III. From the average length of the intervals the rates per 1000 per year can easily be computed.

Results

From the material obtained from testing in Round I we get rates of 37.8, 23.9 and 20.5 per 1000 for the three intervals respectively. It would be tempting to conclude that we have here an indication of the result of an intensive tuberculosis control programme—the annual infection rate has been brought down by nearly 50% in less than four years ! But to our disappointment we find a rate of 37.0 in the group initially tested in Round II and 52.0 in that tested for the first time in Round III. There is no reason to think that the general infection rate should not apply equally to all the groups examined within the same time period. The average rate of infection calculated on the first interval after initial test (whether in Round I, II or III) is 41.6 per 1000 per year.

The drop in the infection rate in the group first tested in Round I is not easy to explain, but since a similar drop is seen in the group first tested in Round II, it seems that it cannot be due to mere chance. As the groups observed for more than one interval—e.g., the one tested first in Round I and retested in Round IV—contain persons tested in the intervening rounds as well, there is a possibility that persons with strong reactions refused to be retested again at later retests because they feared that they would again have strong reactions. Such an eventuality could easily introduce a bias which would reduce the infection rate from round to round. However, an examination of the present material, as well as the much more extensive material comprising persons with reactions of 5 mm or more in Round I, reveals no such tendency. We may therefore look for another explanation.

It was noted in the discussion of postvaccination allergy in the previous section that there is a sharp, though not large, increase in the mean size of the indurations of the control group at their first retest. This could partly be due to a number of non-reactors having been under-read at the first test and showing larger reactions at the next, even though their allergy may not have changed. It seems unlikely, however, that this is the whole explanation. There are only a small proportion which at the first retest exhibit such strong reactions that they would be classified as genuine reactors, so that much of the sensitivity revealed by the small reactions below 10 mm, or thereabouts, may have been caused by infection with the hypothetical " non-specific " organisms. This may be another instance pointing to the high infectivity of such organisms.

It is also possible that the apparent reduction in the rate of infection with tubercle bacilli, which seems more pronounced the longer the interval between the first test and the retest, could have something to do with the development of " non-specific " allergy. Since the chances of being infected with the unknown organisms responsible for the " non-specific " allergy are much greater than being infected with tubercle bacilli, it can be assumed that the later the infection with tubercle bacilli takes place the greater is the probability that the persons would already have acquired the " non-specific " allergy. If this is so, it seems very likely that a certain degree of immunity would also have been acquired which may then interfere with the multiplication of the tubercle bacilli, and therefore also with the setting up of high-grade, " specific " allergy. A process of this kind would lead to fewer persons showing fresh large reactions.

Another explanation could be that the constant superinfection with the unknown organisms produces desensitization of the " specific " allergy due to the tubercle bacillus.

CONCLUSIONS

Apart from the theoretical considerations of the relation of " non-specific " to " specific " allergy, which are rather speculative but perhaps nearer the truth than might be supposed by workers adhering to a more orthodox view sustained by their experience in circumstances less complicated than they are in India, it may be concluded that evidence has been produced to suggest that the infection rate with tubercle bacilli may be about 40 per 1000 per year. Even though the absolute figure is debatable, based as it is upon several assumptions, yet it seems fairly certain that the cause of high-grade tuberculin sensitivity is not very common in the present study population.

XI. EXAMINATION OF THE VILLAGE POPULATION BY MASS MINIATURE X-RAY

INTRODUCTION

Whereas the tuberculin testing began in May 1950, the X-ray photographing started only in September of the same year. The X-ray equipment was sent out from Europe and arrived in India in July. The X-ray apparatus had to be assembled in Madras and installed in a new X-ray cabin and fixed on the new truck. All this inevitably took some time. There was therefore an initial gap of four months between the testing and the X-raying of the villagers. Moreover, during the subsequent rounds of X-ray examinations there was a delay of two to three months between the tuberculin testing and the X-ray examination. In spite of the fact that three testing teams were operating in the field, it was found that the one X-ray team worked faster, so if the X-ray examination had had to be simultaneous with the testing it would have meant a slow-down of the X-ray survey. There would naturally be some disadvantages in separating the X-ray examination from the tuberculin testing, mainly that some people tested might be absent when the X-ray unit arrived and *vice versa*, and that the conditions reflected by the tuberculin reactions could have changed before the X-ray picture was taken.

GENERAL PROCEDURE

The 70-mm miniature X-ray films were developed at the sanatorium and read by one reader, the majority by the writer, and in his absence by his associates. All abnormalities seen were noted down on the original index card, which had also been used for entering the results of the tuberculin testing. The readings were made without seeing the cards or knowing the result of the testing. A short description of the abnormalities seen was dictated and advice was noted about possible further action to be taken. All cases which suggested active or possibly active lesions were either called for large X-ray photo and bacteriological examination or advised admission directly to the isolation hospital at Madanapalle. As postal contact was found to be quite ineffective in getting the people to attend, it became necessary to send a messenger back to the villagers to ask them personally to come for further examination at the sanatorium, or a car was sent out to fetch them. Nevertheless, some cases with X-ray abnormalities refused to come for ordinary large X-ray photo and bacteriological examination when asked to do so. More surprising was it to find that even cases with definite active tuberculous lesions of advanced character would refuse to go to the hospital for the necessary treatment.

Cases with relatively small lesions which did not appear to be active were either called for check-up after two to three months or left to be picked up again during the next visit of the X-ray unit to the village. The reason was not so much to save the effort of getting them but rather to see what would happen to such cases if left to themselves for a period of a year or so.

All cases referred to the sanatorium for further examination would have a large photo taken and a sputum microscopy done; if no sputum could be produced they would have either a laryngeal swab culture or a culture after gastric lavage; in addition, all would undergo an erythrocyte sedimentation rate test. Persons admitted to the isolation hospital would be subjected to the full range of clinical examinations which are routine at the UMT Sanatorium, including culture after gastric lavage and laryngeal swab if four consecutive smears were microscopically negative. From 1951 onwards cultures would be done in every case, whether bacilli were seen or not, and if growth were obtained the cultures would be submitted to drug sensitivity tests.

At the second and subsequent X-ray rounds the films were read without knowledge of previous X-ray results. If abnormalities were found and entries from previous X-ray examinations indicated lesions or an earlier occasion, the previous films would be taken out and compared with the new film. Should the new films show nothing abnormal, however, no reference would be made to earlier readings.

CHECKING AND CLASSIFICATION OF X-RAY ABNORMALITIES

For the purpose of the present analysis all the miniature X-ray films that had been read as abnormal on the initial reading were read again and classified by the writer. In every case where more than one film had been taken, all films—both small and large—were inspected and again compared with one another. All entries on individual cards and case sheets were checked, especially with respect to

bacteriological findings, and mistakes in the identification of persons and readings of films were corrected. In several cases the re-reading of all the films in series brought to light lesions which had been missed on the first reading; previous entries were then corrected. In cases who had had one or more normal films to begin with and then developed disease, care was taken to ensure that all the films were of the same person by examining in detail the bony thoracic cage. In this way some mistakes in identification were detected and corrected. Sometimes the mistakes had occurred through the persons giving wrong names or through a mix-up between two sisters or two brothers. In some instances whole families had to be called in for large photographs, which were compared with the suspect small films, and often the correct identity could be established. In a few cases it has happened that some patients not belonging to the study area have deliberately and falsely given the name of a person belonging to the study area and already examined by the survey teams so that they might obtain admission to the isolation hospital and be treated for their disease.

Another and important purpose of reading the films was to ensure that the abnormalities were described and classified in a uniform manner. It should be remembered that the material was gathered over a period of four to five years so there would be considerable variation in the readings between different readers as well as by the senior reader, who might have changed his own opinion as to the character of certain X-ray lesions as time went on.

X-RAY CODE

For re-reading the X-ray films, an X-ray code was adopted which had been evolved in 1955 in connexion with the all-India Tuberculosis Survey conducted between 1955 and 1957 under the auspices of the Indian Council of Medical Research (ICMR) in which the Madanapalle Field Research Station had also taken part. Each abnormal X-ray photo was described under each of the four following headings:

I. Type of Pathology
II. Cavity
III. Impressions Regarding Etiology
IV. Calcifications

The sub-groups under each heading were as follows:

I. *Type of Pathology*
   1. Apparently normal
   2. Minimal parenchymal lesions
   3. Moderate „ „
   4. Extensive „ „
   5. Lobar pneumonia
   6. Atelectasis
   7. Fibrotic scar in lung
   8. Hilar adenitis
   9. Pleural scar
   10. „ effusion, small
   11. „ „ moderate or extensive
   12. Hydropneumothorax/pneumothorax
   13. Cardiovascular pathology
   14. Operated (thoracoplasty, resection, etc.)
   15. Special pathology
   16. Technical error

II. *Cavity*
   1. Not seen
   2. Doubtful
   3. Present

III. *Impressions Regarding Etiology*
   1. Probably non-tuberculous
   2. Probably tuberculous but inactive
   3. Probably tuberculous, possibly active
   4. Probably tuberculous and active
   5. Undecided

IV. *Calcifications*
   1. Absent
   2. Present

If more than one lesion was seen, the main lesion was recorded. Calcifications were noted irrespective of other lesions.

As for definitions of each group, especially " Type of Pathology " and " Impressions Regarding Etiology ", reference may be made to the preliminary report presented by Benjamin (1956) to the XIVth International Tuberculosis Conference in New Delhi, 1957. As for the extent of " parenchymal lesions " under " Type of Pathology ", these were defined as follows:

" Minimal parenchymal lesions ": lesions up to 1 cm^2 in area, or not exceeding the width of the posterior end of a rib;

" Moderate parenchymal lesions ": lesions varying in size between " Minimal " and " Extensive ";

" Extensive ": lesions occupying an area corresponding to at least two-thirds of one lobe, attention being paid to the density of the lesions.

The sub-groups under heading III— " Impressions Regarding Etiology "—allow the reader to express an opinion as to the quality of the lesions, mainly with regard to the likelihood of demonstrating tubercle bacilli.

This code is open to criticism like any other code dealing with the interpretation of X-ray findings; it could be criticized as being too ambitious and demanding more of the reader than is really possible. It is generally agreed that it is not possible to interpret X-ray films wholly accurately; there will always remain a certain degree of uncertainty, and even the same reader may not be consistent with himself when asked to read the same series of films over again independently of his first reading. Nevertheless, the present code, however incomplete and ambiguous it may seem to be, has proved its value by enabling cases detected by mass miniature radiography to be separated into different groups according to the ease with which tubercle bacilli could be demonstrated on subsequent bacteriological examinations.

Bacteriological results obtained in material consisting of 1322 cases with X-ray abnormalities drawn from a series of 48 600 persons X-rayed in connexion with a sample survey of various population strata in Andhra, Mysore and Madras States, carried out by the Madanapalle Field Research Station in 1955-57 under the National Survey mentioned above, will illustrate the value of the X-ray code. Each case was examined by a bacteriological team within two to three weeks after the X-ray had been taken and the following had been carried out in the field: (*a*) two laryngeal swab cultures, and—when sputum was available—(*b*) two direct smears for microscopy, (*c*) two sputum swab cultures, and (*d*) collection of sputum to be taken back to the UMT Sanatorium for culture after homogenization. The bacteriological results in relation to the X-ray readings are given in Appendix Table 3 and are summarized in Table 18.

The figures bear out quite clearly the merits as well as the demerits of the classifications; on one side there is an obvious association between the demonstration of tubercle bacilli and the extent of parenchymal lesions, presence of cavities or estimate of activity; on the other side, the finding of bacilli among persons with little suspect pathology indicates the difficulty in estimating the nature of the lesions from an X-ray film alone. Going one step further and studying the results by combining groups, as is done in Appendix Table 3, a percentage of positive bacteriological findings as high as 86 could be obtained in cases with extensive lesions, cavities present and probably active tuberculosis, in spite of the fact that only one specimen was collected. The failure to find tubercle bacilli in the remaining 14% may just be due to the fact that specimens were collected only once, or that the patients might have been under antibiotic treatment, or that the diagnosis of tuberculosis was not correct. In any case, by working out the chances of finding tubercle bacilli among persons classified under each heading, or combinations of headings, the value of the code has been established so that even if bacteriological examinations should not be available, it might be possible to estimate the incidence of bacillary cases, granted, of course, that the photographic technique, the reading and other aspects of the survey are conducted in the same manner.

TABLE 18
BACTERIOLOGICAL RESULTS RELATED TO THE X-RAY CODE IN MATERIAL FROM A SAMPLE SURVEY OUTSIDE THE MADANAPALLE STUDY AREA

	Number examined	Tubercle bacilli found	
		No.	%
I. *Type of pathology*			
Minimal parenchymal lesions	206	7	3.4
Moderate " "	753	70	9.3
Extensive " "	218	106	48.6
Others " "	145	6	4.1
II. *Cavity*			
Not seen	920	76	8.3
Doubtful	150	45	30.0
Present	107	62	57.9
III. *Impressions regarding etiology*			
1. Probably non-tuberculous	290	8	2.8
2. Probably tuberculous, inactive	278	16	5.8
3. Probably tuberculous, possibly active	332	35	10.5
4. Probably tuberculous, active	216	121	56.3
5. Undecided	206	9	4.4

Having established the usefulness of the X-ray code given above, it was decided to apply it retrospectively to the present material. This would also enable comparisons to be made between the present findings in the Madanapalle village population with those obtained from the sample survey in the surrounding areas.

One difficulty needs to be pointed out. It is not easy to define morbidity on the basis of this rather complicated code. Should Code I be used, which indicates the type of pathology only, or should it perhaps be combined with Code II relating to cavity findings? Or would it be sufficient to depend upon Code III, which indicates the type of etiology and degree of activity? The reader would himself have formed mentally an over-all picture of the character of the case while deciding on the type of "etiology", so Code III does form a sort of evaluation of his impressions. However, it is necessary for statistical purposes to reduce the multiplicity of sub-groups into half-a-dozen simple categories, each one with a distinct meaning, so they can form the basis for an estimate of prevalence, incidence, mortality and so forth.

In order to ensure that all the sub-groups in the code would contribute to the final classification, the readings of each abnormal film have been transcribed by the statistical staff to one of six categories. The categories have been decided upon empirically by carefully examining the value of the combined readings shown in Appendix Table 3. The various groups have been ranked according to the chances of finding tubercle bacilli. Thus the group consisting of extensive cavitary cases and classified as active tuberculosis which yielded bacilli in 86% has been taken as the category with the greatest activity and designated "*A1*". Then follows *A2*, *A3*, *B* and *C* in order of decreasing probability of finding bacilli, and *D*, proved non-tuberculous conditions. The conversion table used for punching from the detailed X-ray code to the new simplified form is given in Appendix Table 4. Applying this to the material summarized in Appendix Table 3, the bacteriological findings according to the new categories are given in Table 19.

It would seem justified to regard all cases in the three categories *A1*, *A2* and *A3* as representing more or less active forms of tuberculosis that would normally require treatment or, after close observation, would soon lead to the start of treatment, while category *B* would correspond to what are generally regarded as "observation cases" and category *C* to cases considered clinically insignificant, comprising persons with either healed inactive lesions, or small inactive lesions, perhaps in some cases of non-tuberculous nature. To these are added one more group, category *D*, which contains cases proved to be non-tuberculous by subsequent examination.

TABLE 19

BACTERIOLOGICAL RESULTS ACCORDING TO NEW CLASSIFICATION OF X-RAY READINGS IN 1322 X-RAY ABNORMAL CASES DETECTED AND EXAMINED BACTERIOLOGICALLY IN CONNEXION WITH A SAMPLE SURVEY IN ANDHRA, MYSORE AND MADRAS STATES OUTSIDE THE MADANAPALLE STUDY AREA

Category	Number examined	Tubercle bacilli found	
		No.	%
A. Clinically highly significant:			
A1. Most probably active with tubercle bacilli present	59	51	86.4
A2. Probably active and bacilli probably present	97	55	56.7
A3. Probably active, bacilli possibly present	121	24	19.8
B. Clinically significant:			
Observation cases, bacilli probably absent	647	48	7.4
C. Clinically insignificant:			
Minimal lesions or fibrotic changes, presence of bacilli not likely	398	11	2.8
D. Proved non-tuberculous conditions	—	—	—

The system of X-ray categories adopted, which is given in Table 19, has the advantage of having a gradation within the "active" group which permits a case to move from one to the other category owing either to an improvement of the condition or to an aggravation; similarly, cases moving from either *A1*, *A2* or *A3* to *B* or *C*—or to "Nil abnormalities found"—would indicate significant improvement, again permitting various degrees of improvement to be noted.

In applying the ICMR code to the X-ray positive cases in our present study material, all cases which have been admitted to hospital or otherwise been diagnosed as suffering from definite non-tuberculous conditions have been grouped under category *D*. When all the abnormal mass miniature X-ray films were checked, attention was given to all information

derived from earlier or later X-ray films of each case but as far as possible without any consideration of bacteriological results; for example, cases might be classified under the ICMR code under headings which would lead the case to be punched under category *B*—" observation case "—even though bacilli may have been demonstrated. So apart from the exclusion of cases proved free from tuberculosis, the classification of the miniature films was purposely done as if no knowledge of bacteriology and prognosis were available. This may seem ambiguous, and might very well be so, but by following this principle as closely as possibly, it was hoped to give the same value or weight to an X-ray lesion whether the case had been examined bacteriologically or not. This was important, as a fairly high percentage of cases were not examined for bacilli. To ignore or exclude from analysis cases not examined bacteriologically was not possible, as too much valuable material would have been lost.

STAGES

All cases were, if possible, classified according to X-ray findings (as well as to bacteriology) at three points in time: (*a*) when the first X-ray abnormality was detected, either on first reading or retrospectively; (*b*) when active disease was recognized either radiologically or bacteriologically; and (*c*) at the last available X-ray film. Each " stage " was then referred to the appropriate round of X-ray survey so that it would be possible to estimate the observation period.

THE MATERIAL

When the investigation was started in 1950, it was hoped that it would be possible to X-ray the whole population once a year. It was thought that 50 000 people would be no more than could be handled by one mobile unit and that everybody could be X-rayed once during 12 months. The X-ray examination would be carried out not merely to ascertain the prevalence of the disease but as a means of discovering and hospitalizing bacillary cases. However, the plan was too optimistic. During the calendar year 1951, 29 681 miniature films were taken in Madanapalle town and the surrounding villages, but in the following years the number was less. Time was lost by annual holidays and repairs to the X-ray unit. Excluding from the present analysis the X-ray examinations done in the town the material comprises 31 889 persons X-rayed at least once during four visits of the X-ray unit to the villages between September 1950 and February 1955. During this period another 31 372 repeat X-rays were taken, giving a total of 63 261 photos in all, or nearly two X-rays per individual. The numbers of films taken at each round were as follows:

Round	*Period*	*Initial photos*	*Repeat photos*	*Total*	*Number of photos taken per month*
I	1/ 9/50 - 25/11/51	20 993	—	20 993	1 418
II	26/11/51 - 17/ 2/53 [a]	4 997	11 097	16 094	1 348
III	27/ 8/53 - 8/ 7/54	3 970	10 975	14 945	1 437
IV	8/ 7/54 - 15/ 2/55	1 929	9 300	11 229	1 553
	Total	31 889	31 372	63 261	1 425

[a] X-ray out of order 83 days during May, June and August 1952

COVERAGE

During Round I, 56.5% of the entire population had an X-ray taken; excluding children below five years, who were not considered eligible for X-ray examination, the attendance rate was 66%. The influence of sex and age on attendance at examinations has already been discussed in section VI (see Fig. 8, p. 80). At each subsequent round it became increasingly difficult to get people to attend. The novelty had worn off, and people were not too much interested. Few could understand the purpose of repeated examinations, although they should have known how patients had been detected and given treatment. During Round II, the coverage among those eligible for X-ray was 51%, including repeat photos; at Round III, 46%, and at Round IV, only 34%. The attendance rate was better among those already X-rayed than among newcomers or persons who had refused to be X-rayed on previous occasions. Table 20 gives an estimate of the total population at each round, the number eligible for X-ray, those X-rayed before as well as those not previously X-rayed, and those actually X-rayed of each group within each round. Of people not

TABLE 20

ESTIMATE OF NUMBER OF PERSONS ELIGIBLE FOR X-RAY EXAMINATION AT EACH ROUND, AND THE NUMBER AND PERCENTAGE X-RAYED

	Round I	Round II	Round III	Round IV
Total population	37 150	37 334	38 181	38 575
Children below 5 years	5 297	5 544	5 670	5 728
Eligible for X-ray	31 853	31 790	32 511	32 847
(*a*) Not X-rayed before	31 853	12 225	10 073	7 474
(i) X-rayed				
Number	20 993	4 997	3 970	1 929
Percentage	65.9 %	40.9 %	39.7 %	25.8 %
(*b*) Previously X-rayed	Nil	19 571	22 444	25 374
(ii) Re-X-rayed				
Number	—	11 097	10 975	9 300
Percentage	—	56.7 %	48.9 %	36.7 %
(*c*) Total X-rayed per round				
Number	20 993	16 094	14 945	11 229
Percentage	65.9 %	50.6 %	46.0 %	34.2 %
Number X-rayed at least once	20993	24 568	26 414	27 303
Percentage	65.9 %	77.3 %	81.2 %	83.1 %

previously X-rayed the coverage during Rounds II, III and IV was 41%, 40% and 26% respectively, and of people previously X-rayed it was 58%, 49% and 37%. By picking up at each round more people among those not previously X-rayed the total number of people who had had at least one X-ray rose from 66% in Round I through 77% in Round II and 81% in Round III, to 83% in Round IV (excluding children below five years of age).

Repeated X-ray examinations

Of 31 889 persons X-rayed at least once, 18 711, or 59%, had one or more repeat X-rays, as shown below:

Number of miniature X-ray photographs per individual	*Persons photographed* Number	%
1	13 178	41.3
2	9 374	29.4
3	6 013	18.9
4	3 324	10.4
Total	31 889	100.0

It was not possible to ensure that people had a film taken at each visit of the X-ray unit to their village, so some of those X-rayed in Round I had their second X-ray in either Round II, Round III, or Round IV, while those X-rayed for the first time in Round II might have had their second

TABLE 21

NUMBER OF PERSONS PHOTOGRAPHED AT EACH OF FOUR SUCCESSIVE ROUNDS OF X-RAY EXAMINATIONS

Round I	Round II	Round III	Round IV
20 993	11 097	6 180	3 324
			(2 856)
		(4 917)	1 193
			(3 724)
	(9 896)	2 703	978
			(1 725)
		(7 193)	862
			(6 331)
	4 997	2 092	986
			(1 106)
		(2 905)	486
			(2 419)
		3 970	1 471
			(2 499)
			1 929
Total X-rayed 20 993	16 094	14 945	11 229

Note: Figures in brackets indicate persons not X-rayed.

X-ray either in Round III or in Round IV, and so on. The number of different groups available for analysis and the number of persons in each are shown in Table 21.

As will be seen from Table 21, there are 15 groups at Round IV who had at least one miniature X-ray but who differ from each other with respect to the number of repeat photos they had and the time at which these were taken. Taking into consideration as well the persons who were not X-rayed at any round of X-ray examinations, there are altogether 30 different groups of persons available for analysis. The analysis has therefore been rather complicated and laborious.

XII. PREVALENCE OF TUBERCULOSIS

THE MATERIAL

During the first village survey with the mobile X-ray unit, which took place from September 1950 to November 1951, 20 993 persons were photographed in a population of 37 150. Among these 618, or 2.95%, showed abnormal findings according to the last revision of the films. They were distributed as follows:

	Cases	
	No.	*%*
A. Far advanced to moderately advanced, active or probably active tuberculosis	79	12.8
B. Probably tuberculous, observation cases	218	35.3
C. Clinically insignificant	204	33.0
D. Non-tuberculous pulmonary pathology[a]	53	8.6
E. Non-pulmonary chest pathology[a] . .	64	10.3
Total	618	100.0

[a] For details, see Appendix Table 8.

The following cases were examined bacteriologically:

Category	*Cases examined*	*Tubercle bacilli found*	
		No.	*%*
A1	12	11	91.7
A2	10	8	80.0
A3	28	7	25.0
B	74	11	14.9
C	31	0	0

" SPONTANEOUS " CASES

Besides the cases detected by the mass miniature radiography, another 18 patients came to the Sanatorium on their own initiative for diagnosis and treatment, on account of clinical symptoms. They belonged to the same village population but arrived before the X-ray unit had reached their villages.

The question arises as to how these " spontaneous " cases affect calculation of the prevalence. Obviously, it would not be correct to ignore these 18 patients, 16 of whom belonged to category A and two to category B, as at least some of them would have been detected by the X-ray unit had they not already come to the Sanatorium. On the other hand, it cannot be taken for granted that all 18 would have been X-rayed, as some would have refused or been absent. A high percentage of the total population refrained from attending the X-ray, and the reasons for their abstaining might have applied just as well to these 18 cases. It is not possible to ascertain why normal, healthy individuals or persons with potential or actual disease refuse to be X-rayed. We have seen cases who, according to their miniature X-ray, most certainly were suffering from advanced tuberculosis flatly refuse hospitalization and even large X-ray photo and sputum examination, and this in spite of many requests to come for further investigation. Some died of their disease without ever coming to the Sanatorium, and many in the observation group came only when they were moribund. There can therefore be no doubt that among the group not X-rayed there are also cases who, from sheer fear of being found to have tuberculosis, will stay away from X-ray examinations and dare not come for hospitalization. Conversely, it has also been our experience that many people have been anxious to be examined because they thought they were suffering from some disease, so there is also a risk of exaggerating the estimate of the prevalence by potential or actual cases deliberately seeking examination. How these two trends, which affect the results in opposite directions, are balanced cannot be ascertained. In the absence of such knowledge it has been assumed that the factors which govern the healthy population with regard to accepting an X-ray photo also govern the sick people.

The 18 cases who turned up because of symptoms before they could be X-rayed have been regarded as being drawn from the total population. For the purpose of estimating the prevalence, they have been allotted to those X-rayed in the same propor-

TABLE 22

CASES WITH CHEST PATHOLOGY DETECTED IN 1950-51 AT THE FIRST X-RAY SURVEY OF THE RURAL POPULATION AT MADANAPALLE, AND PREVALENCE RATES ACCORDING TO SEX AND AGE

I. Observations

Sex	Age	Number X-rayed	X-ray categories [a]						
			A1	A2	A3	B	C	D	E
Males	0- 9	2 009	—	—	1	3	4	2	4
	10-19	2 859	0.70	—	—	6	9	3	7
	20-29	1 956	2.68	4.68	3.68	13.68	11	6	3
	30-49	2 910	12.55	3	10.63	58	53	8	5
	50+	1 566	2.50	6	14	63	49	10	7
	All males	11 300 [b]	18.43	13.68	29.31	143.68	126	29	26
Females	0- 9	1 862	—	—	1	7	4	3	2
	10-19	2 081	1	—	2	6	7	3	7
	20-29	2 165	2	—	—	16.6	9	3	6
	30-49	2 697	4.43	2	5	24	30	8	11
	50+	870	1	3	6	22	28	7	12
	All females	9 675 [b]	8.43	5	14	75.64	78	24	38
Males and females		20 975 [b]	26.86	18.68	43.31	219.32	204	53	64

II. Prevalence rates per 1000

Sex	Age	A1	A2	A3	Whole A group	B	C	D	E	All types
Males	0- 9	—	—	0.5	0.5	1.5	2.0	1.0	2.0	7.0
	10-19	0.2	—	—	0.2	2.1	3.2	1.1	2.5	9.0
	20-29	1.4	2.4	1.9	5.6	7.0	5.6	3.1	1.5	22.9
	30-49	4.3	1.0	3.6	9.0	19.9	18.2	2.8	1.7	51.6
	50+	1.6	3.8	8.9	14.4	40.2	31.3	6.4	4.5	96.7
	All males	1.6	1.2	2.6	5.4	12.7	11.2	2.6	2.3	34.2
Females	0- 9	—	—	0.5	0.5	3.8	2.2	1.6	1.1	9.1
	10-19	0.5	—	1.0	1.4	2.9	3.4	1.4	3.4	12.5
	20-29	0.9	—	—	0.9	7.7	4.2	1.4	2.8	16.9
	30-49	1.6	0.7	1.9	4.2	8.9	11.1	3.0	4.0	31.1
	50+	1.1	3.5	6.9	11.5	25.3	32.2	8.1	13.7	90.8
	All females	0.9	0.5	1.5	2.8	7.8	8.1	2.5	3.9	25.1
Males and females		1.28	0.89	2.06	4.23	10.46	9.73	2.53	3.05	30.00

[a] A1-A2-A3: Far advanced to moderately advanced, active or probably active pulmonary tuberculosis.
B : Probably inactive lesions — observation cases. D : Non-tuberculous pulmonary pathology.
C : Clinically insignificant, inactive cases. E : Non-pulmonary chest pathology.
(For further explanation of classifications, see section XI; for cases under D and E, see Appendix Table 8.)

[b] Excluded: 13 males and 5 females with age not recorded.

tion as their respective sex and age-groups have been covered by the mass miniature X-ray examination.

RESULTS

The number of " spontaneous " cases found and the number detected by mass miniature X-ray, as well as their respective base populations according sex and age, are shown in Appendix Table 5, while a summary of these observations as well as the prevalence rates per 1000 persons are shown in Table 22.

Radiological signs of active or probably active tuberculosis were found in 4.23 per 1000; another 10.46 per 1000 were classified as observation cases, giving a total of nearly 15 per 1000 clinically significant cases.

SEX AND AGE

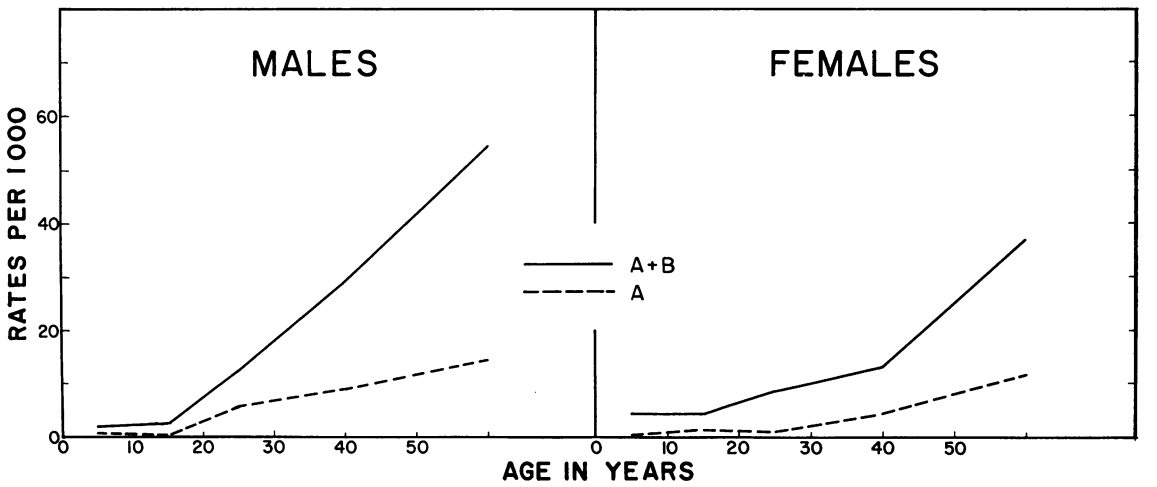
The prevalence rates for active cases (group A) and observations cases (group B) were twice as high for males as for females (Fig. 19 and Table 22), and elderly people in particular, both men and women, were affected. There was a steady rise in the prevalence rates with age. Taking category A alone—i.e., the cases which are most likely to be advanced and active—there was a steady increase among males from 0.2 per 1000 in the 10-19 year age-group to 14.4 per 1000 among elderly men above 50 years. Among females there was a similar trend, except that young women between 10 and 19 years showed a slightly higher rate than the men—1.4 against 0.2 per 1000—although the observations are too few to render the difference statistically significant. Prevalence of pathology classified as B and C (observation and inactive cases) also increases with age. As all the rates given are based upon radiological appearance only, apart from the exclusion of proved non-tuberculous cases (category D), they may include some cases, especially among the older people, wrongly classified as tuberculous. Even though there may be such an error, there can be no doubt that tuberculous lesions are increasing in frequency with age.

BACTERIOLOGICAL RESULTS

Unfortunately, the coverage by bacteriological examination has not been as complete as could be desired. As mentioned already, many persons called for futher examinations refused to come despite energetic and repeated requests to do so. Cases with small inactive lesions were often left undisturbed to be picked up by the next X-ray survey. In a few of these cases, if they had been examined, it might perhaps have been possible to demonstrate bacilli, but the number would have been small.

FIG. 19

PREVALENCE RATES PER 1000 OF TUBERCULOUS CASES DETECTED IN THE VILLAGE POPULATION AT MADANAPALLE, 1950-51 (ROUND I)



A = active or probably active pulmonary tuberculosis.
B = observation cases.

TABLE 23

NUMBER OF CASES DETECTED DURING FIRST MASS MINIATURE X-RAY SURVEY (a), NUMBER EXAMINED BACTERIOLOGICALLY (b) AND NUMBER WITH TUBERCLE BACILLI DEMONSTRATED (c), AND PREVALENCE OF BACILLARY CASES ACCORDING TO AGE AND SEX

Sex and age	Spontaneous cases									Cases detected by X-ray									Rate of bacillary cases per 1000 [b]	
	A [a]			B [a]			C [a]			A [a]			B [a]			C [a]			(i) [c]	(ii) [d]
	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c		
Males																				
0-9	—	—	—	—	—	—	—	—	—	—	—	—	3	2	0	4	—	—	—	—
10-19	1	1	1	—	—	—	—	—	—	1	1	0	1	1	0	6	2	0	0.2	0.2
20-29	3	3	3	1	1	1	—	—	—	9	6	3	13	8	2	11	5	0	4.0	5.4
30-49	5	5	5	—	—	—	—	—	—	23	18	13	58	19	7	53	9	0	8.0	14.2
50+	4	4	4	—	—	—	—	—	—	20	15	6	63	16	0	49	4	0	5.4	6.7
All	13	13	13	1	1	1	—	—	—	53	40	22	143	47	9	126	19	0	3.5	5.6
Females																				
0-9	—	—	—	—	—	—	—	—	—	1	—	—	7	5	0	4	3	0	—	—
10-19	—	—	—	—	—	—	—	—	—	3	1	0	6	3	0	7	—	—	—	—
20-29	2	2	2	1	1	1	—	—	—	2	1	1	16	3	2	9	2	0	1.7	6.7
30-49	—	—	—	—	—	—	—	—	—	10	4	2	24	19	0	30	3	0	1.3	1.8
50+	—	—	—	—	—	—	—	—	—	10	4	1	22	7	0	28	4	0	1.2	2.9
All	2	2	2	1	1	1	—	—	—	26	10	4	75	37	2	78	12	0	0.8	2.3
Males and females																			2.3	4.1

[a] For X-ray categories, see footnote [a] to Table 22.

[b] For base populations, see Table 22 (A) and Appendix Table 5.

[c] Rates are calculated on basis of bacillary cases in relation to number X-rayed.

[d] Rates are calculated on the assumption that if all detected cases had been examined bacteriologically they would have shown the same proportion of bacillary cases as those actually examined.

In working out the prevalence of bacillary cases there are two ways to proceed. The one is to calculate on the basis of bacillary cases actually found, which will give a minimum figure: of 20975[1] persons X-rayed, 48.18[2] had bacilli demonstrated, giving a prevalence rate of 2.3 per 1000; for males it was 3.5 and for females 0.8 per 1000. These are certainly minimum rates, as it is known that several of the advanced cases were not examined, as they died of their disease before they could be called for bacteriological examination. The other way is to assume that the cases actually examined represent a random sample of all cases with X-ray pathology in their respective categories whether examined or not, and then to calculate the rate of bacillary cases as if all had been examined. This method is certainly not correct either, especially with regard to group B. Nevertheless, according to this method the rate of bacillary cases is 4.1 per 1000; for males 5.6 per 1000 and for females 2.3 per 1000 (Table 23). Summarizing, the incidence of existing bacillary cases is likely to be between 2.3 and 4.1 per 1000.

[1] Excluding 18 persons whose age was not recorded.

[2] The fraction indicates an adjustment for " spontaneous " cases according to X-ray coverage.

PREVALENCE RATES AT ROUNDS II, III AND IV

While persons examined for the first time in Round I provide an adequate basis for calculating

prevalence rates, persons examined for the first time in subsequent rounds become increasingly less representative of the whole population for each round done. They include very young children reaching the age when they become eligible for X-ray examination, previous " refusers " and fresh arrivals among the study population.

Estimates of prevalence at each round must be based on the results of *all* persons X-rayed, not only those examined for the first time. The prevalence at Round IV has been estimated thus and is reported in section XVIII.

DISCUSSION

Two factors may affect the prevalence rates presented here. One relates to the technique, the other to geographical considerations. First, the films were originally read by one reader only and not by two independent readers. This procedure has undoubtedly led to some cases being missed. Dual readings made experimentally by the writer on a large sample of miniature films showed that he has probably missed about 10% of significant cases, even bacillary cases. Some of these may have been recovered in the retrospective revision of all abnormal X-ray films, so the error may be a little less. However, even if an error of 10% is accepted as being the most likely, it would not materially affect the prevalence rates given, as instead of having found, for example, 4.2 per 1000 active cases (category A) the corrected figure would be 4.6 only, and if the prevalence of bacillary cases were 3.5, a second independent reading might have increased the rate to only 3.9.

The second factor which needs consideration is the fact that the study population consists of nearly 200 villages surrounding a large tuberculosis sanatorium, which had been in existence for 35 years before the present investigation took place. Would it be possible that the disease could have been spread into the surrounding village population either by patients who had boarded themselves into the homes, or by the villagers having found employment in the Sanatorium through more than one generation? Regarding the first part of the question, it may be stated that from its very inception it has been the firm policy of the Sanatorium not to allow any patients either applying for admission or after discharge to settle down in the vicinity of the Sanatorium either temporarily or permanently; just for that reason, the Sanatorium has never maintained an out-patient department giving ambulatory treatment. As for the second part of the question, it is true that a large number of villagers living within a mile or two of the Sanatorium have found employment there either directly or indirectly (the Sanatorium staff living on the Sanatorium premises have been excluded from the present analysis). There are six villages with a population of about 1200 in close proximity to the Sanatorium. Table 24 shows the number of cases detected in these villages as against the rest. There were 21 cases classified in the A, B and C groups, whereas only 15.6 were expected from the distribution in the total village population; the difference is, however, not significant. Even if it were, the people living in the six villages close to the Sanatorium form such a small proportion of the whole study population that a few extra cases among them would not upset the over-all picture.

It might also be argued that the Sanatorium could have caused a reduction in the tuberculosis prevalence by having taken care of at least some of the infective cases during the many years prior to the present survey. However, the Sanatorium has never been able to admit more than a very few local patients. It may therefore be maintained that the fact that the Sanatorium is lying in the midst of the study population does not *a priori* render the study area unrepresentative of other rural populations. However, this representativeness no longer holds *after* the survey has been in progress for four to five years, because the population has been sub-

TABLE 24

CASES DETECTED AMONG VILLAGERS LIVING CLOSE TO THE SANATORIUM AND CASES DETECTED AMONG THE REST OF THE STUDY POPULATION DURING THE FIRST X-RAY SURVEY

Category of lung pathology	Villages adjacent to the Sanatorium		Other villages		Total
Population	1166		35984		37150
Persons X-rayed	655		20338		20993
	Observed	*Expected*	*Observed*	*Expected*	
A	2	2.47	77	76.53	79
B	10	6.80	208	211.20	218
C	9	6.37	195	197.63	204
Total cases	21	15.64	480	485.36	501

jected to a deliberate attempt to reduce the incidence of tuberculosis to an extent which has not been done in any other part of the country.

The finding that pulmonary tuberculosis is far more prevalent among elderly people than among the young was most unexpected. About half the active and possibly active cases (groups A and B) were found among persons more than 45 years old. Ninety-one per cent of the cases were found among persons 20 years of age or more, although persons over 20 years comprise only little over half (52%) of the study population; 9% were found among young people under 20, who comprise little less than half of the population.

The effort entailed in detecting one clinically significant case by mass miniature X-ray, according to age-group, can be appreciated from the following data:

Age-group	*Persons to be X-rayed per one case detected of A or B groups*
0 - 9	323
10 - 19	315
20 - 29	95
30 - 49	47
50+	21

It is therefore a matter for consideration, if means are scarce, whether it would not be advisable in a tuberculosis control programme based upon case-finding by mass miniature X-ray to photograph only adult persons.

The question arises whether the findings in the Madanapalle rural area have any validity for other parts of South India. Since September 1955 the Madanapalle Field Research Station has participated in a national mass miniature radiography survey, examining sample villages and towns in Mysore State, the southern half of Andhra Pradesh and the North Arcot District in Madras State; 31 village census blocks were examined and about 90% of the population, apart from small children, were covered by the X-ray examinations. The preliminary report of these findings (Benjamin, 1956), as well as those from other parts of India, gives the results according to the X-ray code described in the previous section (page 104). In order to make these results comparable to those obtained in the Madanapalle rural area, the national survey findings have been expressed in the code finally adopted in the present report and are given in Table 25. These results are the more comparable as the same techniques have been used, except that in the national survey the coverage was much better and the X-ray positive cases were examined bacteriologically in the field.

While the preponderance of tuberculosis among men appears to be a general observation, it appears that the Madanapalle village population enjoys a significantly lower rate than is found elsewhere in the surrounding states and districts, particularly so in comparison with towns in Andhra and North Arcot, where the prevalence rates of active and possibly active cases (categories A and B) for males are about three times as high, and for females two to three times as high, as in Madanapalle. Even

TABLE 25

PREVALENCE OF TUBERCULOSIS * PER 1000 AS FOUND BY THE MADANAPALLE FIELD RESEARCH STATION MOBILE X-RAY UNIT UNDER THE INDIAN COUNCIL OF MEDICAL RESEARCH NATIONAL TUBERCULOSIS SURVEY 1955-56 AS COMPARED WITH THAT OBTAINED IN THE MADANAPALLE RURAL AREA 1950-51

	Males			Females		
	A	B	C	A	B	C
VILLAGES :						
Madanapalle rural area	5.4	12.7	11.2	2.8	7.8	8.1
Andhra and N. Arcot	12.2	18.3	12.3	3.5	10.9	10.2
Mysore	10.2	16.9	16.9	3.7	12.4	15.1
TOWNS :						
Andhra and N. Arcot	16.7	38.7	18.3	7.7	24.1	16.8
Mysore	13.1	22.7	19.9	6.3	18.4	14.6

* For X-ray categories, see footnote [a] to Table 22.

the rates for the village population in Mysore, low in themselves, are higher than the Madanapalle rates. From this comparison, it follows that the prevalence rates at Madanapalle for 1950-51 are lower than elsewhere. The finding of a low prevalence is the more remarkable when the high rate of tuberculin reactors described in section VII is recalled.

XIII. FOLLOW-UP RESULTS OF X-RAY ABNORMAL CASES FOUND BY MASS MINIATURE X-RAY SURVEY

The significance of the different types of lesion detected in the mass miniature X-ray survey will be better understood when the cases are followed up. The follow-up will show whether the classification of cases into active, probably active, potentially active and so forth has any real meaning. It will also be of value to know the fate of the cases detected by a prevalence survey when trying to estimate how many active cases may develop in the future.

The rate of major changes observed from round to round has been worked out on the basis of cases who have been checked either by a repeat X-ray photo or have come by themselves because of symptoms.

PROCEDURE

For the purpose of analysis any information gathered in the intervals between rounds has been referred to the time of the subsequent round. If more than one major change took place within one interval between rounds, the most recent change was noted; for example, if an observation case detected in Round I developed advanced active disease and died before the next visit of the X-ray unit, the death would be recorded. If no information about the lung condition at a later stage was available, the patient having had only his initial X-ray film and no further examination, but it was known that he was alive and still residing in the study area, it has been assumed that his lung condition was unchanged. The more advanced the initial disease or lung condition the greater is the chance that the case has been followed up with further X-rays, while the smaller the initial lesions the greater is the chance that the case has not been investigated further. It follows, therefore, that under categories B and C there will be a fairly large proportion of cases about whom it is known only that they are alive and well, no further examinations having been made. To exclude them would not have been right, as they were still potential cases who might have turned up if they had developed clinical symptoms. Reports about aggravation of the initial lesion were likely to be better substantiated than reports about improvement, especially if the improvement had led to formation of clinically insignificant shadows (category C), or to the clearing up of all shadows. In the latter case the information has most often been obtained by the subsequent X-ray examinations. As the follow-up coverage has been incomplete, a number of previously known X-ray abnormal cases have been missed.

RESULTS

In Table 26 is shown the annual rate of major changes per 1000 according to extent of disease as seen on the first miniature X-ray. The basic data are found in Appendix Table 6. The material is based upon all the X-ray abnormal cases detected during the first three rounds and observed up to Round IV.

Since by far the largest number of cases were found during the first X-ray examination in 1950-51, and those are the cases which have been observed over the longest period, the incidence corresponds mainly to the first period of the investigation. This means that the fate of the active cases has largely been determined by the treatment available after 1950; all cases have had the possibility of getting streptomycin and PAS under hospital conditions, if they so wished, while isoniazid first became available in March 1952 and can therefore only have affected the cases detected during Rounds II and III as well as any active cases remaining from Round I who were still in need of treatment. Nevertheless, it is important to remember that the present population has had the benefit of modern antibiotics and is therefore to a large extent representative of present-day conditions. Should it appear, however, that the beneficial effect of the treatment has been modest, to put it mildly, compared with results obtained in recent drug trials

TABLE 26

FOLLOW-UP RESULTS OF CASES WITH LESIONS DETECTED BY MASS MINIATURE X-RAY EXAMPLES, GIVING THE ANNUAL INCIDENCE PER 1000*

Classification [a] of lesions observed on first X-ray photo	Number of cases	Person-years	Classification of lesions observed on subsequent X-ray photo							
			Rate per 1000 per year							
			Died	Left or untraceable	A1	A2	A3	B	C	Nil
A1	31	48.3	310.7	—	—	20.7	41.7	103.6	—	20.7
A2	28	42.2	189.6	47.4	71.1	—	118.5	94.8	23.7	23.7
A3	54	127.0	78.7	15.7	15.7	15.7	—	47.2	15.7	31.5
B	378	768.1	29.9	29.9	13.0	23.4	28.6	—	49.5	83.3
C	335	659.1	21.2	80.4	1.5	3.0	6.1	51.6	—	94.1

* Basic data are given in Appendix Table 6.

[a] For X-ray categories, see footnote [a] to Table 22.

under the best hospital conditions, it should be recalled that we are dealing here with an unselected material of fresh untreated cases who represent a cross-section of all types of patients under all sorts of regular or irregular treatment. Some would be so ill that they would die within the first month despite vigorous drug treatment, others might have refused treatment altogether and others absconded when they began to enjoy a tolerable feeling of well-being; others again are cases who have relapsed under home conditions in spite of having been treated until a satisfactory stage of improvement had been reached in hospital and with drugs. The policy has been to keep the patients in hospital until they were considered fit to resume work or to live under home conditions, but it was not the policy to continue the drug treatment after discharge from hospital. All cases, however, were told to report for check-up after discharge at regular intervals of one, two or three months or longer according to each individual case. At any sign of relapse cases were readmitted immediately.

The results as given in Table 26 should not be read as an indication of what modern drugs can achieve in Indian patients under ideal conditions but only as to how much can be achieved under the prevailing social conditions in a rural community where literacy is low; where the majority are labouring under poor economic conditions; where it is a daily struggle to earn enough to keep the family together; and where the understanding of prolonged, regular treatment and regular check-up is very limited. But it is also a population which has had a unique opportunity to receive modern treatment under hospital conditions if they so wished. It may be stressed that there has been no question of compulsion. All entreaties to people to be X-rayed or to go to hospital for treatment and remain there sufficiently long had to be based upon persuasion, education and repeated appeals to their common sense. Where such conditions prevail results such as ours may be expected.

Turning again to Table 26 it will be seen that among the most advanced cases, category A1, the mortality was high—31.1% in a year; 18% improved, and of these two-thirds shifted into the inactive or probably inactive group. With regard to the other categories, it will be seen that the mortality was less as the disease was less pronounced or less active. Yet, in A3, representing the least active group, a mortality of 79 per 1000 is well above the general death rate in the population, which is about 16 per 1000. This observation, besides the fact that another 31 per 1000 showed aggravation of their disease, does not necessarily mean a failure of the therapy as such but rather that some of the patients did not come for treatment when it was first required but waited until their condition became worse.

As for the follow-up of the large and important group designated B, which includes cases with lesions which may or may not be active and which

do not normally require treatment, 65 per 1000 developed more disease. It if is presumed that some of the cases who died would also have had aggravation of their initial condition, it may be reckoned that 70-80 per 1000 turned into active cases. At the same time 133 per 1000 showed clearing or definite reduction of their lesions. If more of the observation cases could have been examined again, this rate would probably have been higher—by how much we do not know. It has to be admitted that with lesions of this type where bacilli cannot be demonstrated or where many cases had no sputum examination at all, there may be some which could have a non-tuberculous etiology.

The last group, designated C, represents cases which appeared inactive or had only small insignificant lesions. Even so, a few—just about 10 per 1000—developed active or probably active disease, while another 52 per 1000 showed an increase of lesions which moved them into category B. It might be argued that if the lesions had increased, this observation would be a sign of "activity", and therefore the cases should be classified as A. But cases need not have been active at the actual time of the second X-ray photo; they might have been active some time during the interval and become inactive once more. By classifying such cases as B it is indicated that the likelihood of demonstrating activity by culture etc. is very small. That many cases in this group should show complete clearing of their lung fields is not surprising.

The examination of the fate of the X-ray abnormals has shown that there is a good correlation between the degree of activity judged by the first films and the subsequent incidence of either deterioration or regression and clearing of lesions. This lends support to the validity of the classification used and gives confidence in using the tables for predicting the course of events in other similar surveys, provided, of course, that the same classification is used and that the same facilities exist for detecting and treating tuberculosis.

XIV. INCIDENCE OF TUBERCULOSIS IN X-RAY NORMAL CASES

Though by now several investigations of the prevalence of tuberculosis in various parts of India have been carried out, there is no information available about the incidence of the disease in a given period of time. The present investigation permits an estimate of the attack rate per year, or the annual incidence of tuberculosis in the village population around Madanapalle. The following analysis deals only with those persons having a normal chest X-ray on one or more occasions during the four rounds of mass miniature X-ray examinations from 1950 to 1955. The follow-up of cases showing lung pathology on their first miniature X-ray film was dealt with in the previous section.

MATERIAL

During the first three rounds of the mass miniature X-ray unit a total of 29 180 persons had an initial X-ray which appeared to be quite normal; 18 282, or 62.7%, of these had a second X-ray photo, during either Round II, III or IV; some had also a third or a fourth film. The majority—i.e., 14 309 or 78%—had their first photo during Round I. Of these 10 832, or 76%, were X-rayed again in Round II--i.e., after an average interval of one year and 86 days. For the whole group the average period of observation was two years and 166 days The distribution of the material according to rounds is shown in Table 27.

The coverage for those X-rayed initially in Round I was 70%, and allowing for losses due to deaths and departures from the study area during the intervals between Rounds I and IV, it was 87%. The reason why the coverage was so much higher for this group than for the other two groups, which had their first films in Rounds II and III, is that it was covered

TABLE 27
NUMBER AND PERCENTAGE OF PERSONS WITH AN INITIAL NORMAL CHEST X-RAY WHO SUBSEQUENTLY HAD A SECOND MASS MINIATURE X-RAY PHOTO

Round of the initial X-ray	Number having an initial normal X-ray	Total number having a second X-ray	%	% after correction for deaths and departures
I	20 439	14 309	70.0	86.8
II	4 845	2 521	52.0	59.5
III	3 896	1 452	37.3	38.8
Total	29 180	18 282	62.7	74.7

by three subsequent surveys, whereas the two other groups were followed by two and one surveys, respectively; further, as already stated, the general coverage became less satisfactory at each subsequent round (cf. Table 20, page 108).

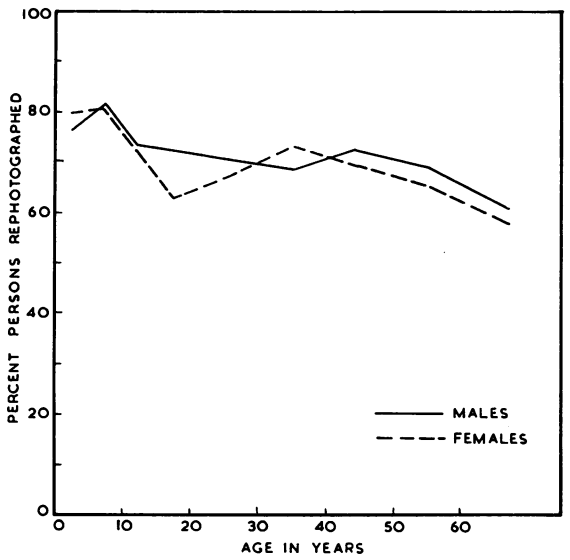
COVERAGE ACCORDING TO SEX AND AGE

The distribution of persons according to sex and age who had a normal initial chest X-ray in Round I and a second miniature X-ray later on is shown in Fig. 20. They constitute 78% of the whole material. The coverage by a second X-ray for persons examined for the first time in later rounds was very much the same.

The coverage (disregarding losses by death and departures) was about the same for males and females. Boys and girls were re-X-rayed in equal degree; about 80% of children aged 5-9 years and about 70% of schoolchildren between 10 and 14 years old were re-photographed. In the next two age-groups, 15-19 and 20-29 years, there is a better coverage among males than among females, the latter dropping to 62% in the marriageable age of 15-19 years against 70% among males. There is no doubt that the movements of the population in the young ages are largely responsible for the poor attendance. The coverage of the two sexes above the age of 30 was similar, although a little less in the case of women over the age of 40.

FIG. 20

PERCENTAGE COVERAGE OF A SECOND MASS MINIATURE X-RAY OF PERSONS X-RAYED INITIALLY IN ROUND I



PERIODS OF OBSERVATION

For the purpose of estimating the attack rate each case discovered has been related to each of the three intervals between the four visits of the mass miniature X-ray unit. It has been assumed that the villages have been visited in roughly the same order during each round, and that the speed within each round has been fairly uniform. The length of each interval has been calculated from the midpoint in time of one round to the midpoint of the next one. Cases coming to the Sanatorium for diagnosis and treatment because of symptoms have been presumed to have been distributed at random throughout the intervals between rounds. The average lengths of the periods of observation were as follows:

Round	I-II	14.8	months
,,	II-III	18.9	,,
,,	III-IV	8.6	,,
,,	I-III	33.7	,,
,,	II-IV	27.5	,,
,,	I-IV	42.3	,,

CASES OBSERVED

Apart from cases showing non-pulmonary chest abnormalities, altogether 196 X-ray abnormal cases were noted in the whole material of 18 282 persons having at least one miniature X-ray following a normal miniature X-ray film. During the same period 39 cases came on their own initiative because of clinical symptoms arising from lung pathology; these too had had a normal miniature X-ray previously. These cases had developed between the visits of the X-ray unit to their villages, and had the Sanatorium not existed with its facilities for diagnosis and treatment, they would presumably have been found in their villages at the next visit of the unit. It is therefore assumed that the attendance rate of these cases would have been the same as for the rest of the village population. If they are ignored in calculating the attack rate, a substantial portion of the active cases—probably one-third—would be missed; if they are simply added to those found by mass miniature X-ray the rates would be inflated, as it is unlikely that everyone would have been X-rayed. So following the same policy as adopted when

calculating the prevalence rates (see section XII), these " spontaneous " cases have been added to those detected by mass miniature X-ray in a proportion corresponding to the percentage of attendance of their respective sex and age-groups. The assumption has therefore been made that the factors which determine who gets a second miniature X-ray are without relevance to the state of health.

The cases detected subsequent to an initial normal miniature X-ray were distributed as shown in Table 28.

It should be noted that the cases have been classified according to the conditions as seen on the first X-ray that revealed any form of pathology, and not according to maximum disease at a later stage. The only exception to this rule has been the pulmonary cases which later proved to be definitely of a non-tuberculous etiology; it is possible that among those classified as being probably tuberculous, but who had no further investigation done, some may have been suffering from non-tuberculous lesions. The question of the reliability of the X-ray classification here adopted has already been discussed (see section IX).

The distribution of the cases in relation to their appropriate base populations is given in Appendix Table 7.

TABLE 28
DISTRIBUTION OF CASES DETECTED SUBSEQUENT TO A NORMAL CHEST X-RAY

Category	Type of pathology radiologically	" Spontaneous " cases	Cases detected by mass miniature X-ray	Total
A	Active or probably active tuberculosis	12	15	27
B	Probably inactive tuberculosis—observation cases	15	84	99
C	Clinically inactive	5	76	21
D	Non-tuberculous pulmonary disease [a]	7	21	28
	Total	39	196	235

[a] Diagnosed after further investigation.

RESULTS

Table 29 shows that the annual incidence, or attack rate, of active cases of tuberculosis arising after a normal X-ray photo is not high. For the whole population it is 0.44 per 1000, and about the same for males and females. Cases in category B having lesions, probably of a tuberculous nature and inactive, were about four times more frequent than cases in category A, having an incidence of 2.3 for males and 1.6 for females, or 2.0 per 1000 for all. It may be argued that as these lesions were known to be of a recent date, they should rightly be designated " active ", but as it is not known how fresh they were—and, according to their radiological appearance, they did not look active—the same classification has been used as was followed when studying films of persons photographed for the first time.

As for cases classified as C, " clinically inactive ", which comprise small insignificant lesions or lesions which do not at all appear to be active, they had about the same incidence as group B. Although a few of these cases may later turn into active lesions (about 1%) this group has not nearly such a poor prognosis as B cases and has therefore not been included in the general estimate of the attack rate given below and shown in Fig. 21.

Groups A and B together give a rough measure of the cases which need special attention, the former mainly from a therapeutic point of view, the latter as potential sources of new active cases. Together, they give an incidence or attack rate of 2.4 per 1000. This figure does not, however, represent the total number of fresh active cases arising in a community, but only those arising in persons with a *normal* X-ray; a relatively large number of active cases develop in persons showing lesions on their first X-ray film, but these were dealt with in the previous section and have been excluded from the present analysis. Their contribution to the total morbidity is discussed in section XVIII.

ATTACK RATE ACCORDING TO AGE AND SEX [1]

The attack rate in small children was too low to be ascertained. Among females in the 10-19 year age-group no case was detected by mass miniature X-ray, but one case turned up " spontaneously ", giving an incidence of only 0.1 per 1000. In the 20-29 year age-group the attack rate was the same for men and women. Adults above 30 years show a slight increase in active cases in both sexes as age advances, but no essential difference between sexes.

[1] Cf. Table 29 and Fig. 21.

TABLE 29

ANNUAL ATTACK RATE OR INCIDENCE PER 1000 AFTER NORMAL CHEST X-RAY

I. Observations [a]

	No. of persons	Person-years of observation	Cases with lung pathology [b]				Bacillary cases
			A	B	C	D	
(i) *Males:*							
0-9 [c]	2373	5594.0	—	4.43	3.00	1.67	—
10-19	2506	6283.6	2.92	9.59	7.00	1.81	2.92
20-29	1580	4017.4	2.17	5.26	6.26	3.00	2.17
30-49	2294	5786.5	3.71	19.83	20.00	4.50	4.50
50+	1109	2743.7	2.44	17.38	14.13	6.00	2.44
Total	9862	24425.2	11.24	56.49	50.39	16.98	12.30
(ii) *Females:*							
0-9 [c]	2142	5172.7	—	4.00	—	1.00	—
10-19	1759	4187.2	0.24	8.11	2.00	1.00	1.31
20-29	1734	4197.6	2.46	4.00	5.96	1.00	1.46
30-49	2131	5367.4	4.57	12.56	10.09	3.50	0.57
50+	652	1482.0	1.00	3.00	9.00	—	—
Total	8418	20406.9	8.27	31.67	27.05	6.50	3.34

II. Rates per 1000

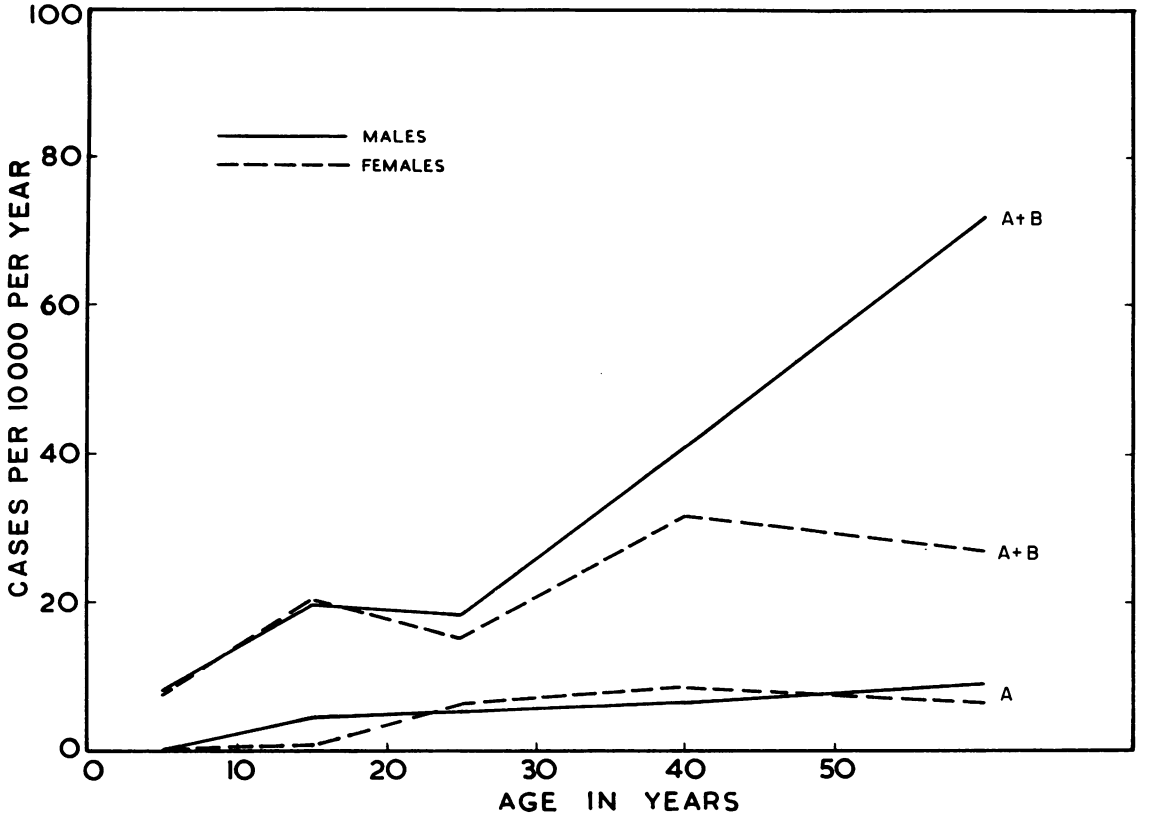
Sex	Age	A	B	C	D	Bacillary cases
Males	0-9 [c]	—	0.79	0.54	0.30	—
	10-19	0.46	1.53	1.11	0.29	0.46
	20-29	0.54	1.31	1.56	0.75	0.54
	30-49	0.64	3.45	3.46	0.78	0.78
	50+	0.89	6.33	5.15	2.19	0.89
	All ages	0.46	2.31	2.06	0.70	0.49
Females	0-9 [c]	—	0.77	—	0.19	—
	10-19	0.06	1.94	0.48	0.24	0.31
	20-29	0.59	0.95	1.42	0.24	0.35
	30-49	0.85	2.34	1.88	0.65	0.11
	50+	0.67	2.20	6.07	—	—
	All ages	0.41	1.55	1.33	0.32	0.16
Males and females		0.44	1.97	1.73	0.57	0.34

[a] For basic data, see Appendix Table 7.

[b] For X-ray categories, see footnote [a] to Table 22.

[c] Mostly children of 5-9 years of age.

FIG. 21
ANNUAL ATTACK RATE PER 10 000 PERSONS WITH NORMAL CHEST X-RAY



A = active or probably active cases
B = observation cases.

As for the " observation group " (category B), the rates for the two sexes in the two first decades of life follow each other closely, but thereafter the males, especially above 50 years of age, show a higher rate than the females.

DISCUSSION

The most striking observation is the absence, even a total absence, of a peak in the attack rate in young age-groups, whether males or females. This observation is very different from what had been expected when considering either the age-sex curves of tuberculin-reactors as found from previous surveys in India (cf. section I of this report), from the findings already described in section VII, or from the experience gained in Western countries.

Although estimates of the annual incidence rates based upon repeat X-ray surveys in the West are rare (Cochrane et al., 1955; Great Britain, Medical Research Council, 1956), it is possible to get some general idea of the conditions in the West by studying morbidity curves, which are available from many countries. Although there are differences in the nomenclature, the definition of " active tuberculosis " or simply of " tuberculosis ", and in the standards of investigation and notification, much can be learned by studying the shape of morbidity curves.

It is a very common observation that until very recently morbidity curves based upon compulsory notification of fresh pulmonary tuberculosis show a marked peak in the younger age-groups. In Norway (*Tuberkulose-Jahrbuch 1954/55*, 1957) the

annual incidence of fresh bacillary tuberculosis showed a very high and marked peak—about 63 per 10 000—at the age of 25 in the year 1927; during the following years the morbidity fell steadily but the fall was most pronounced for the younger age-groups around 25-30 years. The "youth peak" at the age of 25 was reduced to 35 in 1938, and reached a low level of only 13 per 10 000 in 1953. Although the "youth peak" has been much reduced, the curve for 1953 still shows a maximum at this age. In Denmark (Groth-Peterson, Knudsen & Wilbek, 1957) the morbidity from fresh pulmonary tuberculosis had in 1935 a maximum about the age of 25, which for men was 15 and for women 20 per 10 000. In 1954 the morbidity for men at that age was 4 only, and barely higher than at other ages, while in women the morbidity maximum was still found at the age of 25 but was now as low as 10 per 10 000. In Sweden (*Tuberkulose-Jahrbuch 1954/55*, 1957) the rate of fresh cases of tuberculosis for men at 25 years was 45 per 10 000, forming a marked peak of the curve; in 1954 the peak had been almost entirely flattened out, the morbidity for men at 25 years being only 11 per 10 000.

In a survey of the population in the mining valley at Rhondda Fach, Wales, Cochrane et al. (1955) determined the annual attack rate on the basis of a repeat survey by mass miniature X-ray of the population after an interval of 2.6 years. Their age curves show a marked peak, about 70 per 10 000, at the age of 20-25 for males (non-miners) and at the age of about 30 for females. The incidence in the higher age-groups is markedly lower.

It will therefore be clear that the findings in the rural population at Madanapalle differ considerably from what might have been expected. The absence of a pronounced youth peak is very striking. The curves for men and women resemble what is now found in some of the Western countries where the disease is on the verge of becoming extinct. It has been suggested (Cochrane et al., 1955; Groth-Petersen et al., 1957) that the disappearance in recent years of the high rate of fresh cases in early adulthood, which formerly was considered almost axiomatic for tuberculosis, is due to a marked reduction in infectivity. Few people would ascribe it to a lowering of the virulence, but most workers believe it is due to a great decrease in the prevalence of bacillary, infectious cases.

An interesting observation made here is that bacillary and radiologically advanced cases have usually been found singly and scattered throughout the study population. It had been expected that cases would often occur in groups of two or three within the same families or households. Although it is true that the cases detected did show a greater tendency to accumulate in families than could be expected by a mere chance distribution—e.g., according to Poisson's law—yet it has been surprising how often cases of proved active tuberculosis were found isolated and far from one another.

It seems reasonable to assume that the major reason for the low attack rate in Madanapalle (even if active cases arising from previously X-rayed positive cases are added) is the very low number of infectious cases existing in the population. However, other factors such as mode of living, climate, habitat, etc. may also be partly responsible. In a hot climate many people sleep outside their huts in the courtyards, perhaps under an improvised roof of mats or leaves; much of the daily work is done outdoors, not only by men working in the fields but also by women, who often do their cooking on improvised and simple fireplaces in the courtyard.

The question may be raised: When exactly do the majority of people become infected ? If the low attack rate is due to a low infectivity, it follows that primary infections will occur relatively late in life. It simply takes time before people become infected. The question is therefore pertinent whether the fresh cases in adult life are due to a flare-up of endogenous lesions acquired much earlier or are really primary cases. Before this question is answered the relationship of incidence to tuberculin allergy may be considered.

XV. ATTACK RATE RELATED TO TUBERCULIN ALLERGY

INTRODUCTION

For theoretical as well as practical reasons the problem of the relationship between infection and the development of radiological and clinical manifestations of disease must be considered one of the most important in tuberculosis epidemiology. In which age-groups are primary cases most common ? How long is the period between infection and the first manifestation of pathological lesions ? Of all fresh cases observed during a given period of time in a certain population how many have arisen after a recent infection and how many have followed an

infection which took place years ago ? These are some of the questions which need to be answered not only to understand the laws which govern the epidemiology of tuberculosis in general but also to appreciate the immediate situation in a given population. If the answer can be provided, it may be possible to take the proper steps to control the disease.

Some light may be thrown on these problems by studying the incidence of fresh cases in relation to the degree of allergy in persons examined at the beginning of an observation period. Such material is available from the follow-up results of persons who had a normal chest X-ray and a Mantoux test in Round I.

MATERIAL

During Round I, 8644 persons had a Mantoux 1 TU test given and read in the series 1-10-100 TU, and 11 775 had a Mantoux 5 TU test in the series 5-100 TU. The present analysis has been confined to persons tested with 5 TU. Of these, 8047 had a normal chest X-ray in Round I. As 2159 persons were vaccinated with BCG, they have been excluded from the analysis. Among the balance of 5888 persons, 31 developed lesions in the lungs: 8 were cases discovered because of clinical symptoms (Table 30, part I, columns (*a*)) and 23 were detected by mass miniature X-ray (Table 30, part I, columns (b)). As 70% only of the 5888 persons were X-rayed

TABLE 30

CASES OBSERVED BETWEEN ROUND I AND ROUND IV * AND ANNUAL ATTACK RATE PER 1000 FOR PERSONS HAVING A NORMAL CHEST X-RAY AND A 5 TU TUBERCULIN TEST IN ROUND I

I. Observations [a], [b]

Size of induration in mm	0-19 years					20-39 years					40+ years					All ages				
	No.	(a)		(b)		No.	(a)		(b)		No.	(a)		(b)		No.	(a)		(b)	
		A	B	A	B		A	B	A	B		A	B	A	B		A	B	A	B
0—	996	—	2	—	—	504	—	—	—	1	283	—	—	—	2	1783	—	2	—	3
5—	633	—	1	—	2	1017	—	—	—	—	719	—	2	—	9	2369	—	3	—	11
10-	187	—	1	—	—	481	—	—	—	3	342	1	—	—	1	1010	1	1	—	4
15-	125	1	—	—	—	153	—	—	—	—	180	—	—	1	3	458	1	—	1	3
20-	36	—	—	—	—	87	—	—	1	—	60	—	—	—	—	183	—	—	1	—
25+	19	—	—	—	—	40	—	—	—	—	26	—	—	—	—	85	—	—	—	—
Total	1996	1	4	—	2	2282	—	—	1	4	1610	1	2	1	15	5888	2	6	2	21

II. Number of cases after adjusting for coverage by subsequent mass miniature X-ray examinations

Indurations in mm	0-19		20-39		40+		all ages	
	A	B	A	B	A	B	A	B
0-	—	2.0	—	1.5	—	3.0	—	6.5
5-	—	3.7	—	—	—	15.6	—	19.3
10-	—	1.0	—	4.4	1.0	1.5	1.0	6.9
15-	1.0	—	—	—	1.5	4.5	2.5	4.5
20-	—	—	1.5	—	—	—	1.5	—
25+	—	—	—	—	—	—	—	—
Total	1.0	6.7	1.5	5.9	2.5	24.6	5.0	37.2

III. Annual attack rate per 1000

Indurations in mm	0-19		20-39		40+		All ages	
	A	B	A	B	A	B	A	B
0-	—	0.7	—	1.1	—	3.9	—	1.3
5-	—	2.2	—	—	—	8.5	—	3.0
10-	—	2.0	—	3.4	1.1	1.6	0.4	2.5
15-	3.0	—	—	—	3.1	9.2	2.0	3.6
20-	—	—	6.4	—	—	—	3.0	—
25+	—	—	—	—	—	—	—	—

* Average observation period: 2.71 years.

[a] (a) = " spontaneous " cases; (b) = cases detected by mass miniature X-ray examinations.

[b] A = active or probably active pulmonary tuberculosis.
B = observation cases.

in Rounds II, III and IV the latter group has been adjusted and given a weight as if all had been covered by mass miniature X-ray at least once; the sums of " spontaneous " cases and adjusted miniature X-ray cases are given in part II of Table 30.

The average observation period was 2.71 years.

RESULTS

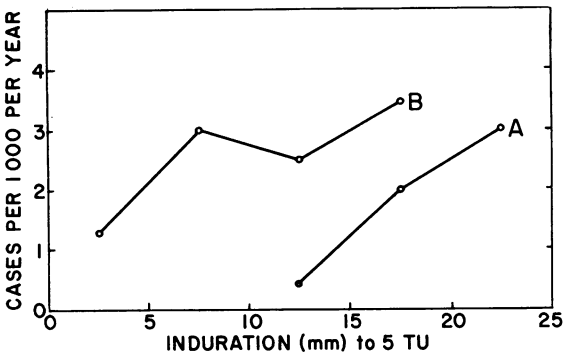
The annual attack rate, or incidence per 1000, is given in part III of Table 30 and shown in Fig. 22 for types A and B cases separately.

Although the material is small the curves in Fig. 22 clearly indicate a close association between the incidence and size of induration to 5 TU. The larger the reactions the higher is the incidence, and this observation applies to both categories of cases; however, it is noteworthy that all the advanced cases classified under A arose in persons with an initial reaction of 10 mm or more, none among persons with smaller reactions. Fresh cases classified as B—observation cases—developed over the whole range of indurations, from persons with very small reactions to persons with strong reactions 15-19 mm in diameter, and the more so the stronger the reactions. There seems to be an intermediate maximum corresponding to indurations of 5-9 mm, but as the number of cases is small it is not possible to attach much significance to this finding.

Keeping in mind the limited material, it can be said that the present observations point to the rule that most, if not all, fresh active cases (category A) develop among persons with reactions to 5 TU, larger than 10 mm, and the rate increases with size of reaction. The milder type of cases (category B), which are generally less extensive and appear less active than those in category A, develop mainly among persons with reactions measuring less than 10 mm, and they too show a close association with the size of induration.

FIG. 22

ANNUAL ATTACK RATE PER 1000 RELATED TO SIZE OF MANTOUX REACTIONS TO 5 TU IN PERSONS WITH NORMAL CHEST X-RAY AND TESTED IN ROUND I



A = active or probably active pulmonary tuberculosis.
B = observation cases.

DISCUSSION

Is it possible to identify the cases which are primary and those which are post primary ? Since there is no generally accepted definition of these terms, " primary " cases are here taken to mean persons with lung lesions developing as a result of infection with tubercle bacilli taking place after the tuberculin tests were done in Round I. In this sense all the A-type cases are ruled out as it seems very unlikely that initial reactions of 10 mm or more could have been caused by anything other than infection with pathogenic bacilli.

Turning to cases arising among persons with reactions smaller than 10 mm the answer to the query depends entirely upon what is the lower limit of a true tuberculin reaction. The lower the limit the smaller is the number of primary cases, the higher the limit the greater the number. The significance of this statement will be borne out when examining the material again after taking into consideration what the number of fresh cases would have been in the present study population if the majority of persons with reactions of 4 mm or less had not been vaccinated. On the basis of the incidence per 1000 in Table 30 the number of fresh cases (A + B) which would be expected if no one had been vaccinated has been calculated, and the result is shown below:

Indurations in mm	*Age-group 0-19*	*20-39*	*40+*	*Total*	*%*
0-4 . . .	5.1	3.0	4.4	12.5	26.0
5-9 . . .	3.7	0	15.6	19.3	40.0
10+ . . .	2.0	5.9	8.5	16.4	34.0
Total	10.8	8.9	28.5	48.2	100.0

The adjustment applies only to the group having indurations of 4 mm and less. Of the total material these form 26.0%. If, therefore, the criterion for distinguishing between persons infected with tubercle bacilli is set at 5 mm, the primary cases comprise about 26% of all the fresh cases observed. If,

however, the criterion is placed at 10 mm, the proportion of primary cases increases to 66%.

Reverting once more to the hypothesis that a large proportion of small reactions, less than 9 mm in diameter, might be due to infection with non-specific non-pathogenic bacilli different from the classical tubercle bacilli, it must be assumed that about two-thirds of the fresh cases with lung lesions demonstrable by X-ray are truly primary and caused by very recent infection with tubercle bacilli; most of these cases, if not all, belong to the B group. Many of them represent lesions which may later develop into active disease. Considering these lesions according to age-groups, 8.8, or 81%, of the 10.8 cases under 20 years of age would be considered to be primary; this is high but perhaps not unreasonably so. Of the 28.5 cases in the age-group 40+, 20.0, or 70%, were found among persons with an induration of less than 10 mm, and these too, according to the hypothesis, should be considered to be due to fresh infection. Does this seem possible ? If the limit is lowered to 5 mm, thereby restricting the number of persons likely to have been infected with the non-specific microbes to those with indurations of 4 mm and less, the primary cases in the 40+ age-group correspond to 16% only.

It will be seen that the interpretation of the nature of the tuberculin sensitivity as revealed in different sizes of reactions to 5 TU has great importance in assessing the nature and age of the fresh lesions observed later. The correct interpretation of the fresh cases with regard to the time when they were first infected has great practical consequences when planning tuberculosis control measures. Further discussion on this point will be found in the last section of this report.

The annual incidence of fresh cases (categories A + B), irrespective of sex and age, according to the findings in the previous section was 2.44 per 1000. Adopting arbitrarily 10 mm as the lower limit for persons in Round I already infected with the classical tubercle bacillus, and in conformity with the principle adopted in section X of estimating the infection rate on the basis of conversions in tuberculin reactions to a size of 10 mm or more, we should expect that 66% of the 2.44 per 1000 —i.e., 1.6 per 1000—are due to recent infections. As the infection rate was estimated to be 40 per 1000, it follows that 1:25, or 4%, of all persons infected primarily with tubercle bacilli develop lesions demonstrable by X-ray within one year. This ratio does not seem unreasonable but may be on the low side compared with the findings in Western countries.

XVI. INCIDENCE IN THE BCG CONTROL TRIAL

INTRODUCTION

An important objective in setting up the present investigation was to study the effect of BCG vaccination in an Indian population, not only by determining the degree of allergy and conversion rate induced by vaccination but also by ascertaining, if possible, the protection offered by the vaccine in preventing the development of fresh tuberculosis. While the former determination can be made relatively quickly the latter requires observation over many years. Since the first pilot trial of the effect of BCG vaccination in India was conducted in Madanapalle in 1948-49 (Frimodt-Møller, 1949), it was natural to follow up this population and to extend the study also to the village population taken up for investigation in 1950.

Already during the first two years after 1948 some cases of tuberculosis were observed among those vaccinated. This indicated that the protection given by the vaccination could not be complete, but this was as could be expected from experience elsewhere. The degree of protection could, however, be determined only by setting up a control group composed of unvaccinated persons comparable to those vaccinated. A control trial was therefore started in November 1950 by dividing at random persons with indurations of 4 mm or less to 5 TU into two groups, of which one received BCG vaccination and the other was left unvaccinated to serve as controls. The method of randomization and a description of the two groups were given in section IX. In the present section a report is given on the number of cases observed in the two groups during the period between Rounds I and IV of mass miniature X-ray examinations. The cases observed among the villagers who were tested with 1-10-100 TU and with 5 TU before the trial was established are excluded from consideration here. The present analysis is confined to the BCG control material only.

MATERIAL

Although the BCG control trial has included persons tested for the first time during all the four rounds, the present analysis has been confined to those who were allocated to the trial during Round I —i.e., between November 1950 and August 1951. These form the main bulk of the total material and include persons who have been observed longest and have had the best coverage by mass miniature X-ray examination. Since the results of post-vaccination tuberculin retests among those entering the trial in Rounds II, III or IV—i.e., up to March 1954—do not differ essentially from the results obtained among those allocated to the trial during Round I, as shown in section IX, the present material may be considered typical of the total material.

During Round I, 4768 persons were found eligible for the trial. Of these, 195 who should have had BCG refused and are excluded from the analysis. Of the remaining 4573 persons, 2082 were vaccinated and 2491 left unvaccinated. The two groups would have been of equal size had the randomization been perfect. Since the control group is larger than the vaccinated, the indication is that about 200 persons, or 9%, have slipped into the control group and cannot be separated at the present time from the true controls.

Of the 2082 vaccinated, 1727, or 82.9%, had an X-ray photo, 1338 in Round I and 389 at a later round (Table 31). Of the 1727 X-rayed, 1146, or 66.4%, were re-X-rayed once (or more than once) at a later round. Of the 2491 unvaccinated, 2033, or 81.6%, had an X-ray photo, 1593 during Round I and 440 later on. Of the 2033 X-rayed, 1314, or 64.6%, were re-X-rayed once (or more than once) during the subsequent rounds.

The X-ray films of all those taking part in the trial were read in series with the films taken of the rest of the population and without any reference to the original index cards. The reader had therefore no knowledge of any possible relationship of the persons X-rayed to the vaccination trial, so the question of bias does not arise with regard to the detection of abnormal X-ray cases. However, all the abnormal films and available records were checked in 1956 by the writer, and although no special attention was paid to trial groups, the possibility of bias cannot be excluded. Finally, in working out the results presented here, all the films and records of the cases in the BCG control trial were once more gone over by the writer and reassessed; if there has been any bias in judging the cases, it could have happened at this stage. The classification of the cases as shown in Table 31 refers to the condition as seen on the first film on which any X-ray abnormalities were noted and not to the stage of maximal disease.

None of the vaccinated cases was revaccinated so the results are based upon the effect of one BCG vaccination only.

RESULTS

Forty-eight cases with abnormal chest X-rays were found, 24 in each group. All the cases except one were detected by mass miniature X-ray examinations; the exception, a girl of three years, was vaccinated in January 1951 and brought to the Sanatorium seven months later with a lesion in the right upper lobe with a cavity (the sputum showed tubercle bacilli). Nine cases, four among the vaccinated and five among the unvaccinated, were probably of non-tuberculous origin (category D). This leaves 20 cases among the vaccinated and 19 among the unvaccinated having X-ray findings suggestive of tuberculous lesions. Eleven among the vaccinated and 12 among the unvaccinated were found by the X-ray survey in Round I; these will be discussed presently. Nine cases among the vaccinated and seven among the unvaccinated either were found on their first film during Rounds II, III or IV, not having had an X-ray photo taken during Round I, when they entered the trial (four vaccinated and four unvaccinated), or showed lesions by miniature X-ray after having previously had a normal chest film (five vaccinated and three unvaccinated). The distribution of these with regard to age-group and type of lesion (categories A, B or C) is shown in Table 31 (part II).

In calculating the incidence the groups which either had a normal chest film followed later by another miniature X-ray film, or were not X-rayed in the Round I but were detected on their first X-ray film in a subsequent round, have been merged and the results are shown in Table 31 (part III (i)). Basing the calculation upon all cases classified as either A, B or C, the incidence per year was 1.9 in the vaccinated group and 1.4 among the unvaccinated. Omitting Group C, or the clinically insignificant cases, the incidence of A- and B-type cases was 1.2 among the vaccinated and 0.6 among the unvaccinated. The difference is greater in the age-group below 20 years, where the incidence among the vaccinated was 1.4 as against 0.3 among the unvaccinated, but this difference is not statistically significant.

TABLE 31

FOLLOW-UP RESULTS BY MASS MINIATURE X-RAY IN THE BCG CONTROL TRIAL

Part I

Age-group	Vaccinated					Unvaccinated				
	Number	first X-ray in			X-rayed twice	Number	first X-ray in			X-rayed twice
		Rd. I	Later	Total			Rd. I	Later	Total	
Below 20	1 475	880	329	1 209	812	1 650	946	365	1 311	867
30-39	482	362	51	413	258	581	451	52	503	305
40 +	125	96	9	105	76	260	196	23	219	142
All ages	2 082	1 338	389	1 727	1 146	2 491	1 593	440	2 033	1 314

Part II. Number of cases detected according to age, types [a] and time of detection

Age-group	Vaccinated								Unvaccinated							
	detected by X-ray								detected by X-ray							
	1st photo						2nd photo		1st photo						2nd photo	
	Round I				Rounds II-IV		Rounds II-IV		Round I				Rounds II-IV		Rounds II-IV	
	Chronic		Recent						Chronic		Recent					
	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
Below 20	—	—	—	—	—	3	—	1	2[b]	—	—	1	—	1	2	1	—	—	1	—	—	—	1	—	—	—	—	1	—	—	—	1	—	—	—	1
20-39	—	1	1	—	—	1	2	—	—	2	—	—	1	0	1	—	—	—	1	1	—	1	—	—	—	1	2	—	1	—	—	1				
40 +	—	—	3	1	—	—	—	—	—	—	—	—	—	—	—	—	—	3	3	—	—	1	—	—	—	—	1	—	—	1	—	2				
All ages	—	1	4	1	—	4	2	1	2[b]	2	—	1	1	1	3	1	—	3	6	1	—	2	1	—	—	1	3	1	1	1	1	3				

Part III

Age-group	Vaccinated			Unvaccinated		
	Person-years	Cases observed A B C	Rate (A + B + C) 0/00	Person-years	Cases observed A B C	Rate (A + B + C) 0/00
(i) Number of cases observed at Rounds II, III and IV and annual rate per 1000 (excluding cases detected by X-ray at Round I)						
Below 20	3 174.4	2[b] 1 2	1.4	3 378.7	— — 1	0.3
20-39	878.7	1 2 1	4.6	999.2	1 1 2	4.0
40 +	233.5	— — —	..	478.8	— 1 1	4.2
All ages	4 286.6	3[b] 3 3	1.9	4 856.7	1 2 4	1.4
(ii) Annual rate if " recent " cases detected by X-ray photo at Round I are included						
Below 20	3 194.8	2[b] 4 2	2.3	3 402.4	— — 2	0.6
20-39	909.9	1 3 3	7.7	1 043.0	1 2 2	4.8
40 +	239.5	— — —	..	495.0	— 2 1	6.1
All ages	4 344.2	3[b] 7 5	3.3	4 940.4	1 4 5	2.0
(iii) Annual rate if " recent " as well as " chronic " cases detected by X-ray photo at Round I are included						
Below 20	3 194.8	2[b] 4 2	2.3	3 402.4	— — 4	1.2
20-39	909.9	1 4 4	9.9	1 043.0	1 2 3	5.7
40 +	239.5	— — 3	12.5	495.0	— 5 4	18.2
All ages	4 344.2	3[b] 8 9	4.4	4 940.4	1 7 11	3.9

[a] A, B and C indicate lesions suggestive of tuberculous origin: A: probably active, B: probably inactive, observation cases and C: inactive, clinically insignificant lesions; D: probably non-tuberculous pulmonary lesions.

[b] One " spontaneous " case was not detected by mass miniature X-ray: for the purpose of calculating the incidence, it has been given the weight of 0.3, corresponding to an attendance rate of 30 % for the particular sex-age group to which it belongs. All the rest were found by X-ray.

In the above estimate of the incidence, the cases found during the first mass miniature X-ray survey have been excluded. Since the tuberculin testing on the basis of which the persons were allotted either to the vaccinated group or to the control group was carried out in Round I, when the first X-ray survey also took place, it may be the most correct procedure to disregard the cases showing abnormal X-rays in the same round. However, certain circumstances may justify their inclusion when calculating the incidence. As was pointed out earlier, owing to the late arrival in 1950 of the new mobile X-ray unit which was used during the first round of examinations, the tuberculin testing was started in May while the X-ray examinations were begun only in September of that year. Further, it was always the policy to let the tuberculin testing teams work independently of the X-ray unit, which would examine the villagers some months after the tuberculin testing had been done. The average interval in Round I between testing and vaccination and the X-ray examination was 3 months and 18 days, or 0.3 years. This is a not inconsiderable period, and the possibility that fresh cases of tuberculosis developed in such a period cannot be altogether dismissed. The cases found by mass miniature X-ray during Round I have therefore been re-read and classified according to whether the lesions might have developed within three months or might have been older; the results of this grouping are shown in Table 31, part II, under the headings " recent " and " chronic " respectively, and in part III (ii) the incidence has been calculated including those classified as " recent ". The results are as follows: 3.3 per 1000 per year among the vaccinated and 2.0 among the unvaccinated. As for the age distribution the pattern remains the same as above, showing a preponderance of cases (2.3 per 1000) among the vaccinated below 20 years of age as compared with the unvaccinated (0.6 per 1000), but in the age-groups of 40 years and above the pattern is reversed (0 and 6.1 per 1000 among the vaccinated and unvaccinated, respectively).

As it may be argued that the separation of cases found during the mass miniature X-ray examination in Round I into recent and chronic is arbitrary and easily open to bias, the incidence has also been estimated after inclusion of all the cases discovered irrespective of the apparent age of the lesions. The incidence was 4.4 among the vaccinated and 3.9 per 1000 among the unvaccinated (Table 31, part III (iii)). The peculiar distribution noted before of more cases among the vaccinated than among the unvaccinated in the age-group below 20 years and the reverse in the age-group of 40 and above is still apparent; the differences, however, are not statistically significant.

Summing up, the present material does not indicate any lowering of the incidence among the vaccinated as compared with the unvaccinated. In view of the limited material, the small number of cases, and other factors discussed later, it is not possible to say that the BCG vaccine, as here used, does not have any protective effect, though the present results do suggest that the effect may be only of a very moderate nature. As these findings are at variance with experience based upon investigations outside India, they require further discussion and examination.

DISCUSSION

Several aspects need to be considered: (*a*) the merits and demerits of the way the present trial has been conducted; (*b*) the results with regard to incidence in relation to the results of retests (as described in section IX); (*c*) the relationship between the results of the present trial and those obtained in recent trials conducted by the British Medical Research Council and by the United States Public Health Service; and (*d*) the possibility of an interference with the action of the BCG as a result of local conditions such as pre-existing non-specific allergy, possible damage to the vaccine by exposure to sunlight, and other local factors.

Criticism of the present trial

Since the vaccinated and unvaccinated groups are not equal in size—as they should have been had the system of randomization functioned well—the objection may be raised that the two groups are not truly homogenous and comparable. Examination of the number of persons in each of the three age-groups in Table 31 (part I) indicates that in the largest group, i.e., the age-group 20 years and younger, the difference corresponds to a loss of 5.6% from the intended vaccinated who may have slipped over to the control group, and in the age-group 20-39 years the difference corresponds to a loss of 9.3% from the vaccinated with an equal addition to the controls; these differences are not very large. However, in the age-group 40 years and over, 35% of those eligible for vaccination are found in the control group, but then this age-group forms only 10.5% of the total material, and even if the persons over

40 were excluded from the analysis altogether, it would not affect the main result of the analysis.

Since the allocation of persons to the BCG control trial took place during the first survey of the villages, well before the X-ray examinations had taken place, there is no likelihood of any interference with the random selection as a result of the field staff's having known who were contacts of infectious cases and who were not. Such information was not available at that stage except for some very few cases of tuberculosis already admitted to the Sanatorium. It is, therefore, quite irrelevant factors that have caused the uneven distribution of persons in the two groups. There is no evidence that the intensity of X-ray follow-up has been significantly different in the two groups.

Another objection which may be raised against the conduct of the trial is the omission of initial dual readings of the miniature films. Since, however, the readings were done without the reader's having had any knowledge of the results of the tuberculin tests, the omission of a second reader cannot have affected the relative numbers of X-ray abnormals detected in the two groups but can only have resulted in a certain but equal proportion of cases being missed in the two groups. In the experience of the writer by either checking his own results by a second independent reading, or having another reader going over samples of films already read by him, the significant cases missed are likely to be about 10%-15%. Such losses should not affect the relative difference in incidence between the two groups. A third objection may possibly be levelled against the trial—namely, that the cases were not submitted to a neutral observer for classification a disadvantage. However, if the subgroups such as A, B and C, and even D (the non-tuberculous cases) were completely ignored and only the total number of cases considered, the main result of the analysis would not be altered; there would still be no significant difference in incidence between the two groups.

The relationship of incidence to post-vaccination allergy

It was stated above that the results with regard to incidence were quite unexpected. But need these findings really cause a surprise ? It was already shown (section IX) that the degree of post-vaccination allergy was low, and compared with the degree of allergy found in the controls, it must be characterized as being even very low. If there is a close association between the degree of allergy as reflected in the skin sensitivity and the protection afforded by the immunization set up by the BCG vaccination, it would not be reasonable to expect much in the way of reducing the incidence among the vaccinated as compared with the unvaccinated. However, it has been maintained by Calmette and associates that the effect of the immunization produced by the BCG may be operative even if no measurable degree of allergy after vaccination is demonstrated. There does not seem to exist any indisputable evidence to support this theory. On the other hand, recent experimental evidence (Tuberculosis Programme, Public Health Service, USA, 1955) supports the theory that without production of a sizable degree of allergy after vaccination, the protection offered by the vaccination will be low. The present material may confirm the close association between the degree of post-vaccination allergy and induced immunity by the poor response obtained in both respects. However, the explanation of the similarity of the incidence in the vaccinated and the controls may not be quite so simple; there are other factors that might tend to confound a real difference in incidence in a trial like the present.

Relation to British and United States trials

There is considerable difference not only in results but also in organization between the Madanapalle trial and the British Medical Research Council's trial and the two trials conducted by the United States Public Health Service in Puerto Rico and in Muscogee and Russell counties in Georgia and Alabama. Not only are the last three on a much larger scale than the first but there are differences in the criteria for allocation, vaccines used, methods of its delivery, coverage by X-ray and basis for assessing the incidence—besides, of course, the fact that the people and the environments are quite different. A study of recent reports by D'Arcy Hart, Pollock & Sutherland (1957) and Palmer, Shaw & Comstock (1958) will show the differences, but these will not be dealt with here in great detail. Attention may be drawn, however, to the different methods of finding the cases of tuberculosis. Whereas the British trial has made use of yearly postal inquiries, home visits, and a chest X-ray and tuberculin tests, in addition to notification of fresh cases from chest clinic physicians all over the country, and the United States trials have based their information regarding fresh cases entirely upon the ordinary existing facilities and regular notification of such

cases without engaging actively in a search for them, the Madanapalle trial has operated within a well-defined community within short distance of the Centre, and the detection of fresh cases has been based almost entirely upon mass miniature X-ray coverage of the community, not merely of persons admitted to the BCG control trial but of the whole population, the trial itself being only a minor part of a community-wide control programme. Since the cases detected in the Madanapalle trial are mainly persons with lesions found by mass miniature X-ray and not primarily cases with obvious clinical symptoms, the Madanapalle material will contain a higher proportion of cases with small lesions than in the American trial, which has not made use of miniature X-ray in general.

While the British trial has given an annual incidence of 1.9 per 1000 among the unvaccinated controls and 0.4 per 1000 among the vaccinated during the first 2½ years—i.e., about 80% reduction in the incidence among the vaccinated; and the American trials have shown an annual incidence of 0.43 per 1000 among the unvaccinated and 0.30 among the vaccinated in Puerto Rico, and 0.22 and 0.14 per 1000, respectively in Muscogee-Russell—i.e., reductions of 31% and 36%, respectively; the figures for the Madanapalle trial are 1.4 per 1000 for the unvaccinated and 1.9 for the vaccinated (omitting X-ray abnormals found in Round I). If the clinically insignificant cases (group C) are omitted in order to bring the types of cases at Madanapalle more in conformity with those recorded in the other two trials, the annual incidence is only 0.6 per 1000 for the unvaccinated and 1.2 for the vaccinated, showing no evidence of any reduction among the vaccinated; however, it may be stated that the number of cases is so small that despite the apparently negative results the data are not necessarily incompatible with a low degree of protection.

It is apparent that the differences in environment, methods used and results obtained are much less between the American and the Madanapalle trials than between either of these two and the British trials.

With regard to the conversion rates, a conversion of 86% to 3 TU was obtained in the British trial; 89% to 10 TU in Puerto Rico and only 54% to 5 TU in Muscogee-Russell; and 64% to 5 TU in Madanapalle. In terms of conversion rates the Madanapalle results compare well with those of the American trials but are inferior to the British. However, since the mean size of the reactions obtained at the other trials is not given, it is not possible to make valid comparisons of the degree of post-vaccination allergy produced at the trials outside India, and—even more important—the absence of information regarding results of retests in the unvaccinated in the other trials deprives the figures given for the vaccinated of much of their value. Again in terms of conversion rates, the vaccinated at Madanapalle showed 64.5% as mentioned, but the controls showed as much as 40.3% "convertors" at the same time, so the effect of the vaccination is considerably less than the figure for the vaccinated alone might suggest. It seems quite possible that in the United States trials the effect of the vaccination in setting up postvaccination allergy may be found to be considerably less when the results of retests in the controls are also considered. It may be mentioned that the same strain of Danish BCG vaccine was used in the British and the Madanapalle trials, the vaccine used in the British trial being prepared in Copenhagen in doses of 0.075 mg per 0.1 ml, the vaccine for the Indian trial being prepared in Madras in doses of 0.05 mg per 0.1 ml; both were given intradermally. In the American trial in Puerto Rico the dose was 0.1 mg per 0.1 ml, while in Muscogee-Russell an undetermined dose of BCG was administered by the multipuncture method.

In view of the findings of the TRO on the effect of variation in doses of BCG (Edwards, Palmer & Magnus, 1953), it does not seem that the differences in strains and doses alone can account for the differences in terms of protection as found between the three trials. Nevertheless, there are, it would appear, other differences.

In Great Britain the BCG trials were purposely confined to specially selected population groups—namely, school-leaving children of 14½-15 years of age living in industrial centres known for their high prevalence of tuberculosis. In the British trials great care was taken to exclude persons already infected with tubercle bacilli by admitting to the trial only children reacting negatively to 100 TU. In Muscogee-Russell presumably, and in Madanapalle definitely, no selection of special age-groups took place, all persons irrespective of age being eligible within the criteria laid down by the tuberculin tests, which in both trials were identical, while in Puerto Rico the trial included persons 1-18 years of age who were non-reactors to 10 TU and not to 5 TU, as in Muscogee-Russell and Madanapalle.

It is stated by Palmer, Shaw & Comstock (1958) that in Puerto Rico as well as in Muscogee-Russell there is a widespread low-grade sensitivity; so there is in Madanapalle. In Britain, however, there is no low-grade sensitivity, or only very little.

Conclusion

We have on the one hand, therefore, British children exposed to a high risk of infection with virulent bacilli and carefully sifted to eliminate anyone already infected, and on the other, in the American and Indian trials, persons exposed to little risk of infection with tubercle bacilli but possibly to a high risk of infection with bacilli of very little virulence, tested with a smaller dose of tuberculin that may not have excluded all persons infected with virulent bacilli. In the Madanapalle trial there has no doubt been considerable error in the division of the population into infected and uninfected. First, the experimental error in reading the 5 TU test has been high owing to circumstances already discussed (see section VIII); secondly, the unusually high proportion of persons with small reactions about 5 mm in size that could have been caused either by a non-specific infection or by the classical tubercle bacillus would have resulted in a certain proportion of persons already infected with tubercle bacilli being incorporated into the persons selected for the trial. If such persons are found among the vaccinated as well as among unvaccinated controls and followed up where the infection rate with virulent bacilli is low, and also the development of demonstrable lesions after infection is slow, it is clear that there will be much less difference in incidence of fresh cases between the vaccinated and the unvaccinated, most of the cases arising as a result of infections having taken place before allotment of the persons to the trial. These circumstances differ greatly from those pertaining to the British trial.

So even if the vaccination does confer immunity, it would be much more difficult to demonstrate this in a population such as that of Madanapalle—and perhaps also in populations such as those investigated in the two American trials—than in Great Britain. It seems, therefore, that the inability to demonstrate a reduction in the incidence of tuberculosis by BCG vaccination in Madanapalle may be due not only to a possible damage to the vaccine but also to a multiplicity of factors that are difficult to determine at present.

XVII. MORTALITY

DEATHS FROM ALL CAUSES

The general death rate, pertaining to all causes, was discussed previously in connexion with the movements in the population from year to year (see section V). It was found to be 16.1 per 1000 per year, based upon the study of population movements in two sample populations of 20 villages and one-fifth of the houses in Vayalpad Town. How reliable is this estimate, and can it be used as a basis for working out specific mortality rates according to sex and age ?

Sources of data

As a check on the reliability of the death rate estimated from the study of population movements, reference was made to the official death registers pertaining to the 20 sample villages and to the whole population in Vayalpad for the years 1950-55. Although entries are made in the official registers about the causes of death, they are not very accurate, as they are based upon statements made by the relatives of the deceased and not on any medical opinion. The accuracy with which these registers are maintained varies very much from state to state and from district to district, but in general the registration in South India is considered to be of a fairly high standard, the most common error being under-registration. According to the Census of India Report for 1951, this generally does not exceed 20%.

The deaths pertaining to the two sample populations recorded in the official registers as well as by our field staff are shown in Table 32. The two sets of data relate to the same populations but with the difference that the deaths recorded in the official registers took place over a six-year period, whereas those noted by our own staff occurred in the period between the first and fifth round of investigation —i.e., 4.7 years. With regard to Vayalpad Town, the mortality data in the official registers refer to the whole town population, whereas the deaths recorded by the field staff relate only to the 20% sample of

TABLE 32

COMPARISON OF DEATH RATES ACCORDING TO OFFICIAL REGISTRATION AND OWN CENSUS

I. Sample of 20 villages [a]

Age	Males					Females				
	Number of persons [b]	Deaths				Number of persons	Deaths			
		Official registration [c]		Own census [d]			Official registration [c]		Own census [d]	
		Number	Annually per 1000	Number	Annually per 1000		Number	Annually per 1000	Number	Annually per 1000
0-	607	100	27.9	56	19.6	570	111	32.4	70	26.1
10-	413	6	2.4	10	5.1	380	8	3.5	14	7.8
20-	307	3	1.6	7	4.8	384	11	4.8	19	10.5
30-	293	3	1.7	11	8.0	269	4	2.4	12	9.5
40-	219	9	6.9	16	15.5	185	7	6.3	5	5.7
50-	160	19	19.8	11	14.6	119	13	19.6	24	42.8
60 +	147	52	58.9	47	67.9	98	36	61.2	29	62.3
?	30	—	—	1	—	23	—	—	1	—
Total	2 176	192	14.7	159	15.5	2 028	190	15.6	174	18.2

II. Sample of Vayalpad Town

Age	Males					Females				
	Number of persons [b]	Deaths				Number of persons	Deaths			
		Official registration [e]		Own census [d]			Official registration [e]		Own census [d]	
		Number	Annually per 1000	Number	Annually per 1000		Number	Annually per 1000	Number	Annually per 1000
0-	139	68	16.3	5	7.7	134	57	14.2	17	26.9
10-	112	3	0.9	2	3.8	114	7	2.0	2	3.7
20-	118	3	0.8	1	1.8	85	9	3.5	4	10.0
30-	63	6	3.2	3	10.1	60	8	4.4	2	7.1
40-	57	7	4.1	1	3.7	47	8	5.7	0	—
50-	47	5	3.5	7	31.6	29	8	9.2	0	—
60 +	33	47	47.4	12	77.3	31	36	38.7	5	34.3
?	13	—	—	—	—	6	—	—	—	—
Total	582	139	7.95	31	11.3	506	133	8.75	30	12.6

[a] Deaths in one village (Eguvajangamvaripalle) omitted, as registration of deaths merged with another village inseparably for present purpose, the population in 1950 being only 50.

[b] 1950-51 sample population.

[c] All deaths during six calendar years (1950-55).

[d] All deaths observed between Rounds I and V (4.71 years).

[e] All deaths during six calendar years (1950-55) drawn from whole town population of which sample forms 20.05 % only.

the population. In the case of one small sample village, with a population (in 1950) of 50 only, it was not possible from the official register to identify the deaths which had occurred, as the register figures included those for another village, which was not included in our sample, and it was not possible to make out which deaths belonged to the sample village. However, the population of this village is only 1.2% of the whole sample population, so in omitting it the error is quite insignificant.

The death rates in Table 32, based upon the official registers, are considerably lower than those based upon our own observations. This applies to both sexes but especially to males, among whom death rates appear to be grossly under-registered in the age-groups 10-49 years; between 20-39 years of age the rates are only 20%-25% of those noted in our census. In Vayalpad there also appears to be considerable under-registration, but the number of deaths in our sample is so small that it is not possible to be too definite. With respect to infant mortality, however, there is definite evidence that it is grossly underestimated according to our own census; this point will be discussed presently.

The discrepancy between the two estimates of the death rates is even greater than appears from the figures. An attempt was made to match the deaths noted in our census with those recorded in the official registers. In the case of Vayalpad this was not possible, as our sample covered only one-fifth of the houses, and the addresses given in the death registers were not sufficiently detailed to permit an exact identification of individual cases. With regard to the 20 sample villages, it was found that correct matching of the deaths could be carried out in less than 50% of instances. Quite a number of persons entered in the official registers did not appear in our records despite an enumeration of the population five times; and conversely a large number of deaths noted by the field survey staff did not appear in the official registers. It is not possible to explain fully how this could happen, but some of the discrepancies could be due to persons moving into the area and dying between two enumerations. It might also have happened that persons belonging to the study area died elsewhere and were recorded by the field staff as having died, the relatives not mentioning where they died.

With these limitations it seems preferable to base the estimate of death rates upon our own data rather than upon those of the official registers. There remains the possibility, however, that not only the official registers but also our own records suffer from under-registration.

Adequacy of data

Ideally the estimate of the total mortality should be based upon observations of the total study population, and this can, in fact, be done for persons contacted during the surveys. It was not possible, however, to check information relating to non-contacted persons—i.e., persons neither tested nor X-rayed—in the total study population, and estimates of the death rates among these persons can only be got from the sample populations, where information on deaths among non-contacted persons was carefully checked.

To test the adequacy of the sample population data with respect to deaths, a comparison of the number of deaths among contacted persons in the sample populations and the total study population was made (see Table 33). The expected deaths in the sample population, according to age and sex, have been calculated on the basis of the number of deaths observed in the total population of contacted persons. The differences between the expected and the observed number of deaths are small and in general within the limits of chance distribution. The number of deaths among males is generally a little lower than expected, whereas the number of deaths among females is a little higher; the only exception occurs among females in the 50-59 year age-group, in which nearly twice as many deaths were observed than expected.

In view of the satisfactory correlation between observed and expected number of deaths among contacted persons in the sample population, it seems justified to conclude that the sample population is truly representative of the non-contacted persons as well. Estimates of deaths from all causes among contacted persons are therefore based on the total study population, and estimates for non-contacted persons on the sample population. The death rates have been worked out on the basis of the 1950 population, as it has been shown in section V that no essential changes in the structure of the study population took place during the period of observations. The annual general death rates thus estimated are given by age and sex in Table 34.

Results

The crude death rates for males and females of all ages (Table 34) are nearly the same—namely, 15.7 and 16.1 per 1000 respectively. However, in the

TABLE 33

ANALYSIS OF ADEQUACY OF SAMPLE POPULATION WITH REGARD TO REPORTING OF DEATHS

Sex	Age-groups	Whole population		Sample population				
		Number of persons [a]	Number of deaths [b] observed	Number of persons [a,c]	Number of deaths [b]		Difference	x^2
					Observed	Expected		
Males	0-4	1 369	163	182	14.7	21.7	—7.0	0.23
	5-9	2 183	87	259	6.7	10.3	—3.6	1.26
	10-14	2 118	34	254	5.0	4.1	0.9	0.20
	15-19	1 125	27	132	—	3.2	—3.2	3.20
	20-29	2 269	47	301	4.7	6.2	—1.5	0.36
	30-39	1 962	49	242	9.4	6.0	3.4	1.93
	40-49	1 425	92	192	11.7	12.4	—0.7	0.04
	50-59	1 097	122	145	13.4	16.1	—2.7	0.45
	60 +	722	168	104	30.7	24.2	6.5	1.75
	No data	21	2	6	—	—	—	—
	Total	14 291	791	1 817	96.3	104.2	—7.9	9.42 [d]
Females	0-4	1 276	186	466	25.8	24.2	1.6	0.11
	5-9	2 094	71	267	8.0	9.1	—1.1	0.13
	10-14	1 549	41	231	8.7	6.1	2.6	1.11
	15-19	929	35	115	4.7	4.3	0.4	0.04
	20-29	2 634	108	341	19.1	14.0	5.1	1.86
	30-39	1 900	76	257	12.4	10.3	2.1	0.43
	40-49	1 222	66	172	4.0	9.3	—5.3	3.02
	50-59	724	86	82	19.0	9.7	9.3	8.92
	60 +	333	74	54	15.0	12.0	3.0	0.75
	No data	8	1	7	1.0	0.9	—0.1	0.11
	Total	12 669	744	1 692	117.7	99.9	17.8	16.48 [e]

[a] Persons tested and/or X-rayed in Round I.

[b] All deaths between Rounds I and V.

[c] Samples of 20 villages and of Vayalpad combined after correction for difference in size of samples.

[d] df=8, P=0.40—0.30.

[e] df=9, P=0.10—0.05.

age-groups 15-39 the specific death-rates among females are higher than among males, probably owing to maternity risk. This is in conformity with observations made elsewhere in India.

In order to see whether the Madanapalle rates of deaths from all causes are comparable to rates elsewhere in India, a comparison with death rates in the rural population of Madras State for the year 1950 is given in Table 35. In nearly all age-groups the rates are remarkably similar. For persons aged 60 the death rate in Madanapalle is a little lower than in Madras State. However, owing to the uncertainties in estimating age, differences in rates based upon age-groups can easily arise. The difference in annual death rates among children under one year is much more important.

Table 34

ANNUAL RATES OF DEATHS FROM ALL CAUSES ACCORDING TO SEX AND AGE

Sex	Age-groups	Total sample population 1950 [a]	Deaths				
			Among examined [b]	Among non-examined [c]		Total [d]	Annual deaths per 1000
				(a)	(b)		
Males	0-4	357	21.7	35	2.8	59.5	35.4
	5-9	335	10.3	1	—	11.3	7.2
	10-14	320	4.1	3	0.7	7.8	5.2
	15-19	162	3.2	2	—	5.2	6.8
	20-29	379	6.2	3	0.7	9.9	5.5
	30-39	332	6.0	3	—	9.0	5.8
	40-49	254	12.4	5	0.7	18.1	15.1
	50-59	189	16.1	1	1.4	18.5	20.8
	60 +	167	24.2	17	6.9	48.1	61.1
	No data	38	—	—	—	—	—
	Total	2533	104.2	70	13.2	187.4	15.7
Females	0-4	340	24.2	39	5.5	68.7	42.9
	5-9	312	9.1	2	0.7	11.8	8.0
	10-14	285	6.1	—	—	6.1	4.6
	15-19	165	4.3	2	—	6.3	8.1
	20-29	436	14.0	2	0.7	16.7	8.1
	30-39	306	10.3	1	—	11.3	7.8
	40-49	214	9.3	1	—	10.3	10.2
	50-59	137	9.7	5	—	14.7	22.8
	60 +	117	12.0	14	3.4	29.4	53.4
	No data	27	0.9	—	0.7	1.6	—
	Total	2339	99.9	66	11.0	176.9	16.1

[a] Twenty villages + Vayalpad after adjusting for difference in size of samples.

[b] Deaths observed among total population of persons X-rayed and/or tested after adjustment for size of sample population (cf. Table 23, column 6).

[c] Deaths observed among persons not X-rayed or tested in samples of (a) 20 villages, and (b) Vayalpad (adjusted for difference in size of sample).

[d] During an average observation period of 4.71 years.

Infant mortality

There is a marked difference between the Madanapalle and Madras infant death rates. Deaths among infants under one year of age in the Madanapalle population are not stated, because it was almost impossible for us to ascertain whether a child was under or just over one year when it died. Furthermore, there was an under-enumeration of infants and small children by the field staff. Children born and dying between two censuses were of no interest as subjects for X-ray.

Applying the Madras rates for the age-group under five years to the Madanapalle material, it is estimated that instead of the 59.5 observed deaths among males in the age-group 0-4 years (see Table 34) we should have found 106.4 deaths, and among

TABLE 35
COMPARISON OF RATES OF DEATHS FROM ALL CAUSES (ANNUAL DEATHS PER 1000) IN MADRAS STATE (RURAL)* AND AT MADANAPALLE

Age-groups	Males		Females	
	Madras	Madanapalle	Madras	Madanapalle
0-1	155.4	35.4	134.5	42.9
1-4	33.7		33.5	
5-9	7.6	7.2	7.6	8.0
10-14	5.4	5.2	5.8	4.6
15-19	8.8	6.8	9.7	8.1
20-29	6.3	5.5	7.7	8.1
30-39	8.5	5.8	9.3	7.8
40-49	12.9	15.1	11.5	10.2
50-59	17.6	20.8	15.3	22.8
60+	72.7	61.1	72.2	53.4
All ages	18.9	15.7	18.4	16.1

* Adapted from the *Census of India, 1951*, Vol. I, Part IIA and Vol. III (Madras and Coorg), Part I

females under five years 95.1 deaths instead of the observed 68.7. From this it follows that the annual crude death rate for males should be 19.6 per 1000 instead of 15.7, and for females 18.5 instead of 16.1. With these corrections the Madanapalle annual crude rates of deaths from all causes seem very reasonable.

TUBERCULOSIS MORTALITY

Introduction

Very little is known about the tuberculosis death rates in India. There is no compulsory notification, and official medical statistics give no data. The difficulty is of course scarcity of reliable information.

In Saidapet, a suburb of Madras, Benjamin and associates (1939) encountered 15 deaths from tuberculosis during a six-month survey of 6500 persons—a mortality of 462 per 100 000. In Madanapalle Town Frimodt-Møller (1949) estimated the mortality to be 253 per 100 000.

The present investigation might be expected to provide a good opportunity of collecting data on tuberculosis deaths. However, this has not been an easy task. Some of the difficulties encountered in estimating rates of deaths from all causes also apply to estimating deaths from tuberculosis. However, with regard to tuberculosis deaths we are better placed, as a high proportion of patients in the study population suffering from advanced disease would be specially known to us.

Mortality according to initial X-ray diagnosis (fatality rate)

In order to ascertain the likelihood of a death having been caused by tuberculosis, the prognostic value of the classification of lesions seen on X-ray requires study. All cases with X-ray abnormalities found during Round I (1950-51) have been analysed with respect to risk of death.

The risk of death varies according to type of classification (Table 36). For cases in category A1 the annual death rate between Round I and Round II was 579 per 1000; for cases in A2, 270, and in A3, 105. Among clinically inactive or insignificant cases—categories B and C— death rates of 31 and 22 per 1000, respectively, were found. This does not differ much from the crude death rate for all causes. It is clear that the risk for cases classified under A1, A2 and A3 is different from that for cases in categories B and C.

Follow-up of cases beyond Round II shows that the death rate for cases in categories A2 and A3 decreased between Rounds II and III and increased between Rounds III and IV (Table 36), whereas the annual rate for inactive or insignificant cases increased steadily all the time up to Round IV. This rising mortality suggests that some of the small lesions found in Round I later developed into active lesions which, in some cases, ended fatally.

Case survival rates

On the basis of Table 36 survival rates have been worked out (Table 37 and Fig. 23) which show a striking difference in prognosis among the different categories of cases. It is obvious that category A1 represents very advanced cases, since only 25% were alive after 1¼ years; of A2 cases barely 50%, and of A3 cases 70%, survived 3½ years. Very little difference was found between B and C, the survival rates being practically the same as those seen in non-tuberculous persons.

It would seem from this analysis that, when judging the cause of death, it would be justified to regard fatal cases whose last X-ray photo showed disease classified as A1 or A2 as having died from tuberculosis. The chance of fatal cases classified as

TABLE 36

DEATH RATES AMONG CASES DETECTED BY MASS MINIATURE X-RAY EXAMINATION DURING ROUND I

Group [a]	Observation period [b]	No. Present	No. who left area	No. not traceable	No. at risk	No. Died	Died %	Annual deaths per 1000
A1	I - II	19	0	0	14	10	71.4	579.2
	II - III	9	0	0	9	0	0	—
	III - IV	9	0	0	8 1/2	1	11.8	164.1
A2	I - II	18	0	1	15	5	33.3	270.2
	II - III	12	0	0	11	2	18.2	115.4
	III - IV	10	0	1	9	1	11.1	155.0
A3	I - II	42	0	2	38 1/2	5	13.0	105.3
	II - III	35	3	0	32	3	9.4	59.6
	III - IV	29	2	0	26 1/2	3	11.3	157.9
B	I - II	218	10	4	207	8	3.9	31.3
	II - III	196	9	5	183 1/2	11	6.0	37.9
	III - IV	171	2	6	164	6	3.7	51.0
C	I - II	204	10	17	188	5	2.7	21.6
	II - III	173	7	5	163	8	4.9	31.2
	III - IV	153	5	8	144	5	3.5	48.4

[a] For X-ray categories, see footnote [a] to Table 22.

[b] Average length of observation periods:
Rounds I - II : 14 months and 23 days Rounds II III: - 18 months and 28 days Rounds III - IV: 8 months and 18 days.

A3 having died from tuberculosis is considerably less than for cases classified as A1 or A2 but greater than for cases classified as B or C. To regard all fatal cases under A3 as having died from tuberculosis might lead to an inflation of the death rates. This problem will be discussed below.

Definition of tuberculosis deaths

In assessing the total tuberculosis mortality, the fatal cases have been analysed on the basis of their last available X-ray photo. The great difficulty in making a reliable estimate of the tuberculosis death rate lies in the fact that most cases died in their

TABLE 37

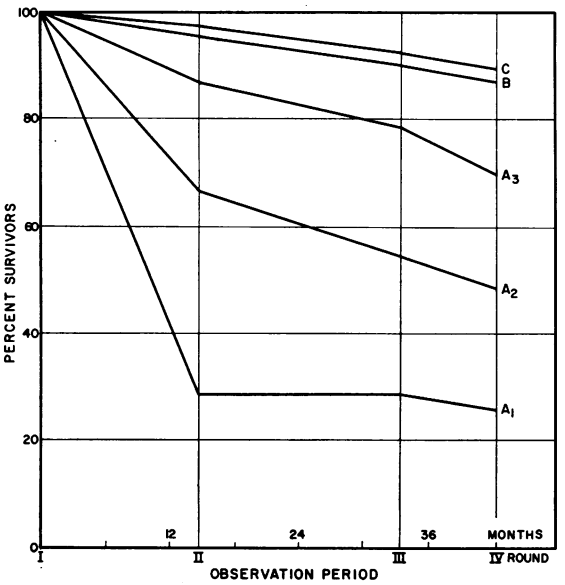
SURVIVAL RATES AS A PERCENTAGE OF CASES DETECTED AT FIRST MASS MINIATURE X-RAY SURVEY 1950-51

X-ray categories [a]	Number of cases detected at Round I	% Survivors			
		Round I	Round II	Round III	Round IV
A1	19	100	28.6	28.6	25.4
A2	18	100	66.7	54.6	48.5
A3	42	100	87.0	78.8	69.9
B	218	100	96.1	90.3	87.0
C	204	100	97.4	92.6	89.4
All A group	79	100	70.4	63.7	56.5

[a] For X-ray categories, see footnote [a] to Table 22.

FIG. 23

SURVIVAL RATES PERTAINING TO VARIOUS DEGREES OF PULMONARY TUBERCULOSIS



A1, A2 and A3 = active tuberculosis varying from very advanced to mild types.

B = observation cases.

C = inactive, clinically insignificant cases.

homes, nearly always without medical attention, and very often a long time after their last examination at the sanatorium. The cause of death must therefore be based upon as good a guess as possible. In cases with moderate lung lesions it is often difficult to say whether the cases died of their disease or died with their disease but from other causes. In view of the above considerations, it was decided to regard cases presenting final X-ray readings described as A1 or A2 as having died from tuberculosis. As far as deaths of A3 patients are concerned, it is difficult to know whether they should be included in or excluded from deaths caused by tuberculosis. In order to get a little closer to the truth, a distribution of 125 fatal cases encountered between Rounds I and IV has been made according to sex, age and X-ray category and is given in Table 38. There is a tendency for the more advanced cases (A1 and A2) to occur in the young or middle-aged people and the less active or clinically insignificant cases (B and C) to occur among the old people. Old people form a fairly high proportion of the deaths under A3—almost as many as under B and C, particularly among the males—which points to the cause of death being to a large extent the same as that of B and C. In the following analysis death rates have been worked out on the as umption that all the patients classified under A1 or A2 died from tuberculosis; with respect to

TABLE 38

DISTRIBUTION OF 125 CASES WHO DIED BETWEEN ROUNDS I AND IV, ACCORDING TO SEX, AGE AND LATEST AVAILABLE X-RAY FINDINGS *

Age	Males					Females				
	A1	A2	A3	B	C	A1	A2	A3	B	C
0-	—	—	—	—	—	—	—	—	—	—
10-	1	1	—	—	—	1	1	—	—	1
20-	4	1	1	1	—	5	—	—	—	3
30-	3	—	—	3	1	4	1	1	—	—
40-	4	2	1	7	4	1	—	2	1	1
50-	4	1	2	3	4	1	1	2	4	2
60+	2	4	4	19	7	—	—	1	6	1
Unknown	—	—	—	—	—	—	1	—	—	—
Total	18	9	8	33	16	12	4	6	11	8

* For X-ray categories, see footnote *a* to Table 22.

deaths among cases classified under A3, final decision has been deferred till after the presentation of mortality rates based upon exclusion as well as inclusion of these cases.

Procedure of analysis

The difficulties arising from the incomplete coverage by the mass miniature X-ray survey of the population at the various rounds, discussed earlier in connexion with the estimate of the prevalence and incidence of tuberculous cases, have also complicated the calculation of tuberculosis mortality. In order to illustrate the difficulties and the methods adopted in overcoming them, the deaths between Rounds I and II may be taken as an example. There were 22 deaths, 18 among cases detected by mass miniature X-ray in Round I and 4 among cases who had come to the sanatorium because of symptoms before the X-ray unit visited the villages. The four " spontaneous " cases have been regarded as drawn from the total population and their mortality has been worked out in relation to the total population. The mortality relating to the 18 cases detected in the X-rayed group has been calculated on the basis of the total number X-rayed. The two rates have then been added. The same result would be obtained by adding a proportion of the number of " spontaneous " cases corresponding to the percentage of people X-rayed in the respective sex and age-groups to the number detected by the mass miniature X-ray and then calculating the mortality with the total number X-rayed as a basis. Which method of computation to use is a matter of convenience.

The results of computation according to the first method are given in Table 39, dealing with cases

TABLE 39

ESTIMATE OF THE MORTALITY BETWEEN ROUNDS I AND II, ACCORDING TO DEATHS OF PATIENTS SUFFERING FROM PULMONARY TUBERCULOSIS *

Sex	Age-groups	Total population (Round I)	Persons not X-rayed		Persons X-rayed			Total deaths [a] per 10 000	Annual deaths per 10 000
			Deaths		Number X-rayed	Deaths			
			No.	per 10 000		No.	per 10 000		
Males	0-	5 517	—	—	2 009	—	—	—	—
	10-	4 051	—	—	2 859	—	—	—	—
	20-	2 861	1	3.50	1 956	2	10.22	13.72	11.12
	30-	2 692	—	—	1 683	1	5.94	5.94	4.82
	40-	1 884	—	—	1 227	2	16.30	16.30	13.22
	50-	1 433	1	6.98	938	1	10.66	17.64	14.30
	60+	1 160	1	8.62	628	4	63.70	73.32	58.64
	Unknown	142	—	—	13	—	—	—	—
	All ages	19 740	3	1.52	11 313	10	8.84	10.36	8.40
Females	0-	5 064	—	—	1 862	—	—	—	—
	10-	3 243	—	—	2 081	1	4.80	4.80	3.91
	20-	3 368	—	—	2 165	2	9.24	9.24	7.49
	30-	2 257	1	4.43	1 620	2	12.35	16.78	13.60
	40-	1 521	—	—	1 077	—	—	—	—
	50-	1 200	—	—	597	3	50.25	50.25	40.72
	60+	723	—	—	273	—	—	—	—
	Unknown	32	—	—	5	—	—	—	—
	All ages	17 408	1	0.57	9 680	8	8.27	9.01	7.30

* The last available X-ray picture indicating lesions in categories A1, A2 and A3.

[a] During an average observation period of 14 months and 23 days.

TABLE 40

DEATHS OF TUBERCULOUS PATIENTS RELATED TO THE THREE INTERVALS BETWEEN ROUNDS I AND IV, AND THE ANNUAL MORTALITY ACCORDING TO SEX AND AGE

Sex	Age-groups	Person - years [a]				Deaths [b]									Total deaths	
						Observations in categories A1-A2				Rate per 10 000 per year	Observations in Category A3				Observations A1 + A2 + A3	Rate per 10 000 per year
		P_1	P_2	P_3	Total	P_1	P_2	P_3	Sub-total		P_1	P_2	P_3	Sub-total		
Males	0-	2 478	3 265	1 509	7 252	—	—	—	—	—	—	—	—	—	—	—
	10-	3 526	3 386	1 395	8 307	—	0.54	—	0.54	0.65	—	—	—	—	0.54	0.65
	20-	2 412	2 170	870	5 452	2.68	0.99	0.22	3.89	7.13	—	—	—	—	3.89	7.13
	30-	2 076	1 750	718	4 544	1.00	1.00	0.38	2.38	5.24	—	—	—	—	2.38	5.24
	40-	1 513	1 348	528	3 389	1.00	1.82	0.53	3.35	9.88	1.00	—	—	1.00	4.35	12.84
	50-	1 157	991	403	2 551	1.65	2.32	—	3.97	15.57	—	—	0.82	0.82	4.79	18.79
	60-	774	699	246	1 719	2.54	1.45	0.44	4.43	25.76	2.00	1.45	—	3.45	7.88	45.83
	Unknown	16	5	6	27	—	—	—	—	—	—	—	—	—	—	—
	All ages	13 952	13 614	5 675	33 241	8.87	8.12	1.57	18.56	5.76	3.00	1.45	0.82	5.27	24.09	7.25
Females	0-	2 296	2 898	1 416	6 610	—	—	—	—	—	—	—	—	—	—	—
	10-	2 566	2 479	1 050	6 095	1.00	—	0.54	1.54	2.53	—	—	—	—	1.54	2.53
	20-	2 670	2 352	976	5 998	2.00	1.08	—	3.08	5.14	—	—	—	—	3.08	5.14
	30-	1 998	1 836	717	4 551	2.72	2.00	—	4.72	10.37	—	—	0.43	0.43	5.15	11.31
	40-	1 328	1 101	451	2 880	—	0.36	—	0.36	1.25	—	1.00	—	1.00	1.36	4.72
	50-	737	707	281	1 725	2.00	—	—	2.00	11.59	1.00	—	0.38	1.38	3.38	19.60
	60-	337	348	142	827	—	—	—	—	—	—	—	0.23	0.23	0.23	2.78
	Unknown	6	3	4	13	—	—	0.16	0.16	—	—	—	—	—	0.16	—
	All ages	11 938	11 724	5 037	28 699	7.72	3.44	0.70	11.86	4.13	1.00	1.00	1.04	3.04	14.90	5.19

[a] P_1, P_2 and P_3 indicate round intervals I-II, II-III, and III-IV respectively.

[b] A1 = Far advanced; A2 = Advanced; A3 = Moderately or slightly advanced cases.

found in Round I who died before Round II. Patients with X-ray readings corresponding to categories A1, A2 and A3 according to their last X-ray films have here been regarded as dying from tuberculosis, although some might not have died *from* the disease but only *with* the disease. The death rates among persons who were not X-rayed have been worked out with the total population as base, and those of the X-rayed persons with the number of people X-rayed as base. The sum of the death rates gives the total death rate for the observation period (last column but one). As the average observation period between Rounds I and II was 14 months and 23 days, the annual death rate can be calculated (last column of the table).

In Table 40 the other method of calculation has been adopted: deaths among "spontaneous" cases have been allotted to deaths among miniature X-ray cases in fractions corresponding to the attendance rates. This explains the fractions appearing in the table. The annual death rate per 10 000 has been worked out with and without the inclusion of patients classified as A3 on their last X-ray photo. It is mainly males of 60 years and over who are affected; excluding the A3 group their death rate is 26, and including A3 it is 46 per 10 000. It therefore seems most likely that the cause of death among A3 patients is more often due to old age than to tuberculosis and that to include this group would constitute a greater error than to exclude it. Furthermore, it might be that a few of the A2 group patients would also have died of causes other than their tuberculous illness, so this might compensate for a possible loss in tuberculous deaths due to the exclusion of the A3 cases. Consequently, only deaths among patients classified as A1 and A2 according to their last photo have been attributed to tuberculosis.

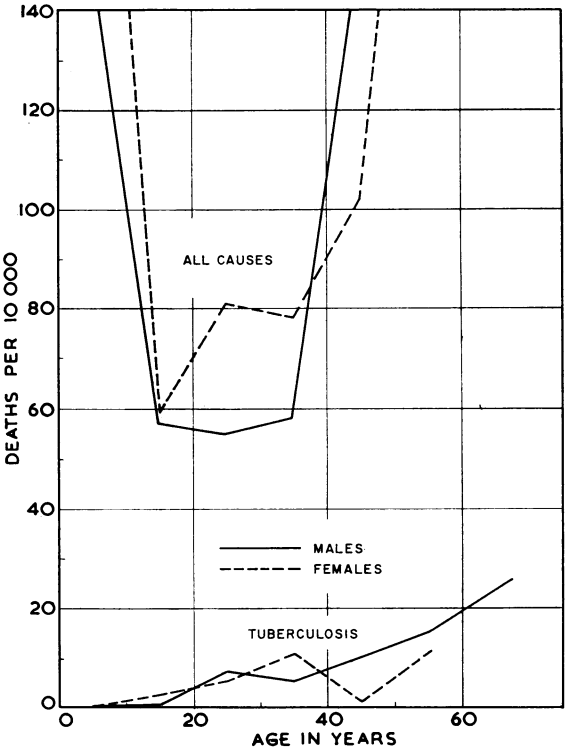
Tuberculosis mortality rates

The death rates among males is higher than among females (Fig. 24, Tables 40 and 41). The mortality rises steadily from the younger age-groups up to the older age-groups without any special peak in the younger years; an exception are females of 30-39 years of age who have a death rate of 10.4, but then the next older age-group shows an unusually low tuberculosis mortality, so the "peak" may be artificial and due to error in the age estimation.

Relating the tuberculosis mortality to deaths from all causes (Table 41), the highest proportions

FIG. 24

MORTALITY CURVES SHOWING AVERAGE ANNUAL RATES OF DEATHS FROM ALL CAUSES AND DEATHS FROM TUBERCULOSIS IN THE MADANAPALLE VILLAGE POPULATION, 1950-54



of deaths caused by tuberculosis are found in males in the age-group 20-29 years and in females in the age-group 30-39 years, but in both instances the proportion is only 13%. In other countries the proportion of tuberculosis deaths to other deaths in the same two age-groups is considerably higher. However, the rate of deaths from all causes at Madanapalle is about twice as high as it is in most countries in the West, so this may account for the relatively lower proportion of tuberculosis deaths.

The tuberculosis mortality found in the villages at Madanapalle for the period after 1950 is much lower than expected, and also lower than the mortality in Madanapalle in 1949. Application of the present estimate to the rest of India is not permissible. The special circumstances pertaining to the Madanapalle study population do not apply to other parts of India. The present death rates are based upon the experience of nearly four years during which a large proportion of all tuberculosis

TABLE 41
TUBERCULOSIS MORTALITY AT MADANAPALLE RELATED TO THE MORTALITY FROM ALL CAUSES

Age-groups	Males			Females		
	Annual death rate per 10 000		% Tuberculosis deaths	Annual death rate per 10 000		% Tuberculosis deaths
	All causes	Tuberculosis		All causes	Tuberculosis	
0-	217	—	—	262	—	—
10-	57	0.6	1.1	59	2.5	4.3
20-	55	7.1	13.0	81	5.1	6.3
30-	58	5.2	9.0	78	10.4	13.3
40-	151	9.9	6.5	102	1.2	1.2
50-	208	15.6	7.5	228	11.6	5.1
60+	611	25.8	4.2	534	—	—
All ages	157	5.8	3.7	161	4.1	2.6

cases in the community had treatment in hospital with modern antibiotics; such conditions do not prevail in other communities in the country. The mortality elsewhere in India is likely to be considerably higher.

Decline in tuberculosis mortality

The tuberculosis mortality in Madanapalle Town in 1949 was 253 per 100 000 (Frimodt-Møller, 1949). It is likely that the mortality in the villages surrounding the town would have been nearly the same before the present control programme was introduced. A mortality of 64 per 100 000 between Rounds I and Round II (Table 42) therefore indicates a very substantial drop as a result of the detection and treatment of most of the advanced cases. The further decline in the rate from 64 through 46 in the second period to 21 per 100 000 in the third period (between Round III and Round IV) must also be regarded as a direct result of keeping advanced cases alive with modern antibiotics; whether a significant lowering of the prevalence of the disease, which could also have contributed to the reduction of the mortality, had taken place during the same period of observation is discussed in the following section.

Summing up, it would appear that the mortality from tuberculosis has been brought down from well over 200 in 1949 to 21 per 100 000 in 1954 as a result of the control programme.

TABLE 42
TUBERCULOSIS MORTALITY AT MADANAPALLE ACCORDING TO INTERVALS BETWEEN ROUNDS

Observation period	Person-years	Deaths from pulmonary tuberculosis	Annual deaths per 100 000
Rounds I-II	25 891	16.59	64.1
Rounds II-III	25 339	11.56	45.7
Rounds III-IV	10 711	2.27	21.2

XVIII. RESULTS OF THE TUBERCULOSIS CONTROL CAMPAIGN

INTRODUCTION

There are various ways of measuring the effect of a tuberculosis control programme on a community. The three most commonly used are: (*a*) to study changes in the rate of tuberculin-sensitive persons; (*b*) to count the existing number of tuberculous patients before and after the control measures have been in operation; and (*c*) to note changes in the tuberculosis mortality. A fourth and more sensitive but also more difficult and slow method is to assess changes in the attack rate.

Applying these methods to the present investigation, which also aimed at the eradication of tuberculosis in the study population, is there any indi-

cation that the control programme based upon case-finding by repeated mass miniature X-ray examinations and isolation and treatment of the detected cases has had any measurable effect ?

The method of studying the rates of tuberculin reactors is not easily applicable because of the high rate of low-grade sensitivity in the present population, and also because a high proportion of the non-reactors have been BCG vaccinated.

In the previous section, on tuberculosis mortality, it was stated that the mortality had been reduced from 200 to 21 per 100 000 during the time of observation. However, this may not mean very much unless the existing number of cases has also been reduced.

The only way in the present circumstances is to study changes in the prevalence. This method, too, is not easy to apply as the counting of existing cases at the fourth and last round is complicated by the low attendance rate at the mass miniature X-ray examination and the creation of a great number of incongruent groups of persons. Also, it is difficult to produce data that are not biased for one reason or another and are comparable with those obtained during Round I. Nevertheless, an attempt has been made to analyse the Round IV results as if the population had been a fresh, not previously investigated, community.

MATERIAL

The population at the time of Round IV is estimated to be 38 575 (see Table 20, page 108); excluding children under five years, there were 32 847 eligible for X-ray. Of these 11 229, or 34.2%, were photographed; 9300 were repeat X-rays, 1929 initial X-rays. Of the 21 618 eligible for but not undergoing X-ray examination in Round IV, about 16 000 had already been X-rayed in the previous rounds. Any information available regarding their lung condition has been ignored in calculating the prevalence rates, the only exception being that persons who were in-patients in the isolation hospital at Madanapalle or in the Sanatorium and therefore could not be X-rayed when the mass miniature X-ray unit visited their villages have also been counted.

Of the 11 229, 115 whose age was not recorded have been excluded; the remainder have been distributed according to age and sex, and the cases with lung pathology detected by miniature X-ray, as well as cases in hospital or " spontaneous " cases, are enumerated in Table 43.

TABLE 43
PREVALENCE OF TUBERCULOUS CASES* AT ROUND IV

Age	Total	Number of " spontaneous " cases			Number X-rayed [a]	Number of cases			Prevalence rates per 1000		
		A	B	C		A	B	C	A	B	C
				Males							
0-9	5 594	—	2	—	1 104	—	4	3	—	4.0	2.7
10-19	4 479	—	2	—	2 005	—	9	2	—	5.0	1.0
20-29	2 928	1	—	1	1 011	4	9	10	4.3	8.9	10.2
30-49	4 407	5	5	—	1 554	9	26	31	6.9	17.9	20.0
50+	2 378	3	2	1	591	14	27	24	25.0	46.5	41.1
All ages	19 785	9	11	2	6 265	27	75	70	4.8	12.5	11.3
				Females							
0-9	4 897	—	1	—	926	—	—	2	—	0.2	2.2
10-19	4 308	1	1	—	1 356	—	2	3	0.2	1.7	2.2
20-29	3 660	1	1	—	1 015	—	4	8	0.3	4.2	7.9
30-49	4 051	2	2	1	1 182	4	15	17	3.9	13.2	14.6
50+	1 780	—	—	—	370	2	12	7	5.4	32.4	18.9
All ages	18 696	4	5	1	4 849	6	33	37	1.4	7.0	7.7

* For X-ray categories, see footnote [a] to Table 22.

[a] 115 persons whose age was not recorded are excluded.

RESULTS

The prevalence rates have been worked out as described earlier: "spontaneous" cases were considered as being drawn from the total population and those detected by mass miniature X-ray as being from the population thus X-rayed (Table 43).

The prevalence rates obtained in Round IV may now be compared with the rates obtained in Round I. For the sake of convenience the two sets of rates are shown in Table 44, and plotted together in Fig. 25.

It will be seen that there is no striking difference between the two sets of curves, yet they are not quite alike. The main differences between Round IV and Round I are, considering first the active or probably active cases in category A: in males a lower rate up to the age of 49, then a marked increase in old men above 50 years; in females, a marked decrease below 30, a moderate decrease between 30-49, and a marked decrease after the age of 50. Taking category B cases, there is a marked increase among young males below 20 years, then a moderate but probably insignificant increase in ages above

TABLE 44

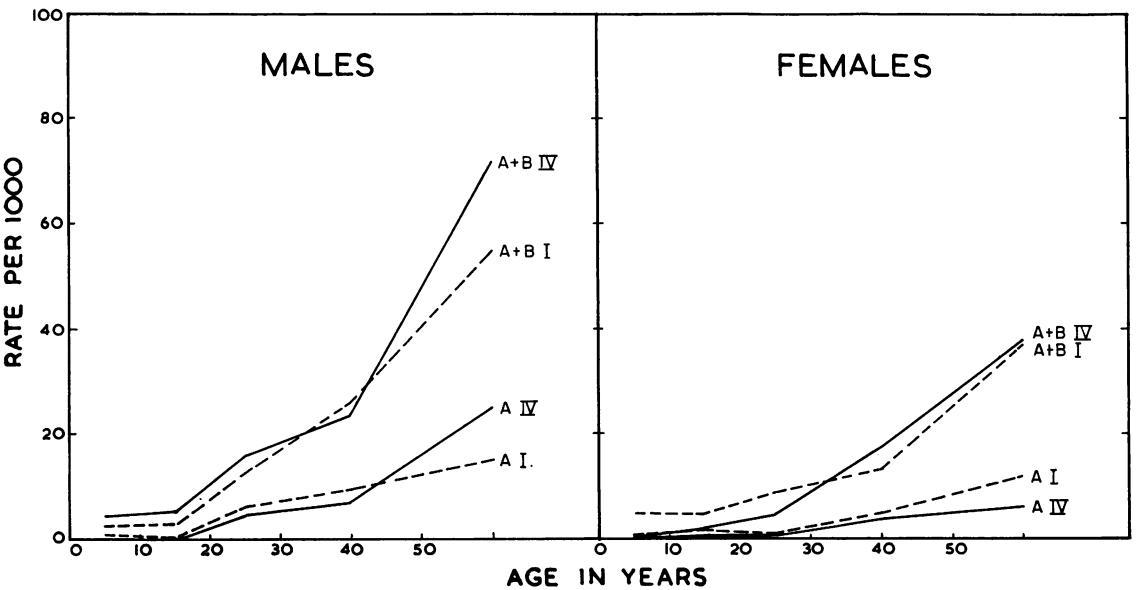
COMPARISON OF PREVALENCE RATES PER 1000 IN STUDY POPULATION AT MADANAPALLE IN 1950-51 (ROUND I) AND 1954-55 (ROUND IV)

Sex	Age	Category A [a]		Category B [a]		Category C [a]	
		I	IV	I	IV	I	IV
Males	0- 9	0.5	—	1.5	4.0	2.0	2.7
	10-19	0.2	—	2.1	5.0	3.2	1.0
	20-29	5.6	4.3	7.0	8.9	5.6	10.2
	30-49	9.0	6.9	19.9	17.9	18.2	20.0
	50+	14.4	25.0	40.2	46.5	31.1	41.1
Females	0- 9	0.5	—	3.8	0.2	2.2	2.2
	10-19	1.4	0.2	2.9	1.7	3.4	2.2
	20-29	0.9	0.3	7.7	4.2	4.2	7.9
	30-49	4.2	3.9	8.9	13.2	11.1	14.6
	50+	11.5	5.4	25.3	32.4	32.2	18.9

[a] For X-ray categories, see footnote [a] to Table 22.

FIG. 25

PREVALENCE RATES PER 1000 AT ROUND I AND ROUND IV RESPECTIVELY IN THE MADANAPALLE VILLAGE POPULATION, INDICATING THE RESULT OF A TUBERCULOSIS CONTROL PROGRAMME OVER AN AVERAGE PERIOD OF 3.6 YEARS



A = active or probably active pulmonary tuberculosis.
B = observation cases.

20 years; in females there is a marked decrease below 30, but conversely a marked increase above 30 years.

In order to compare the total effect, the prevalence rates for both rounds have been applied to the Round IV population (first column of Table 43), and then the total prevalence rates for all males and all females have been calculated. The results are as follows:

	Prevalence rates per 1000			
	Category A		*Category B*	
	I	*IV*	*I*	*IV*
Males . .	4.8	5.2	11.2	13.2
Females . .	2.6	1.5	7.5	7.2
All	3.7	3.4	9.4	10.3

The net result is therefore that any reduction obtained in the prevalence rates in the younger age-groups, males as well as females, is compensated for by an increase in the older age-groups. What has happened is probably that the elderly patients have been kept alive by the drug therapy, and that active forms of the disease have become rarer among the young.

DISCUSSION

Whether the differences just described should be taken as an expression of genuine changes in the prevalence of the disease or whether they could have arisen because of various factors introducing bias is difficult to determine. Two possible sources of bias have been analysed. One could be that former patients have been X-rayed more often or more seldom than the rest of the population. There were 298 male and 148 female patients or persons already diagnosed as having X-ray lung lesions known to be alive and residing in their villages at the time of the fourth X-ray survey. Table 45 shows how many in each category attended and the expected number calculated according to an over-all attendance rate of 34.2%. The male attendance was a little better than expected, the female a little worse, but the differences are not significant; thus it seems unlikely that this factor could have affected the prevalence rates materially.

Another source of bias might be the effect of the intensive work in the village population—entailing numerous visits of the field staff to the homes and numerous opportunities of increased contact between the Sanatorium and the people, resulting in a greater response or better understanding among the population so that more cases would be discovered at Round IV than Round I; or, conversely, that people could have developed a certain apathy towards the work, which resulted in poorer attendance. A coverage by the mass miniature X-ray at Round IV as low as 34% would in itself suggest increased negative response on the part of the population.

In order to obtain a measure of the co-operation enlisted in the population from round to round, the percentages of patients detected by mass miniature X-ray responding favourably to advice given them

TABLE 45

ATTENDANCE OF PREVIOUSLY DIAGNOSED CASES AT THE MASS MINIATURE X-RAY SURVEY, ROUND IV

X-ray category [a]	Males			Females		
	Present	X-rayed		Present	X-rayed	
		Observed	Expected [b]		Observed	Expected [b]
A1	12	2	4.1	0	0	0
A2	8	7	2.7	1	1	0.3
A3	32	10	10.9	14	3	4.8
B	126	46	43.1	52	15	17.8
C	120	52	41.0	81	24	27.7
Total	298	117	101.8	148	43	50.6

[a] For X-ray categories, see footnote [a] to Table 22.

[b] According to an over-all attendance rate of 34.2%, persons at Round IV eligible for X-ray being 32 847 and persons X-rayed 11 299.

with regard to hospital treatment or to further investigations by large X-ray photo and bacteriology are shown for each round in Table 46. The findings suggest no change in the attitude of the people, the percentages being nearly the same throughout the period. This observation is in keeping with our general impression, gained by moving among the population, that the reasons why people do not avail themselves of the opportunities offered them for treatment and diagnosis are deep and not easy to uproot. Fundamentally it is an economic question, as the great majority of the patients come from the poorer strata of the community, and each adult person occupies a place in the family where he or she is indispensable. Besides, there is widespread lack of understanding of the need for treatment, particularly in asymptomatic cases with lesions detected merely by mass miniature X-ray. In conclusion it seems likely that the difference in prevalence rates between Rounds I and IV has not been influenced by selection.

TABLE 46
RESPONSE OF PATIENTS DETECTED BY MASS MINIATURE X-RAY TO ADVICE GIVEN

Round	Patients advised hospital treatment	Advice accepted		Patients advised further examination	Advice accepted	
		No.	%		No.	%
I	102	79	77.5	232	149	64.2
II	42	31	83.8	112	73	65.2
III	15	14	93.3	56	33	58.9
IV	9	6	66.7	43	27	62.8

CONCLUSION

The present data point to what small likelihood there is of obtaining quick results in controlling or eradicating tuberculosis in a community like the one described by active and planned efforts. Although the present control methods may not have been applied as thoroughly and systematically as could be wished and was originally visualized, they represent an effort which it may not be possible to emulate in an ordinary service programme.

XIX. EFFECT OF A TUBERCULOSIS CONTROL PROGRAMME ON THE TOTAL TUBERCULOSIS POPULATION

An attempt has been made to construct data based upon the various rates pertaining to prevalence, incidence, births, deaths, and population movements, given in the preceding sections, and apply them to a hypothetical population of 50 000 people. It is assumed that these people live and behave exactly like those observed in the present investigation. By calculating the number of cases of tuberculosis existing at the beginning of the control programme and the fate of these cases during the following 12 months, and by calculating the number of fresh cases that can be expected to arise either from those with suspect X-ray shadows or from the much larger population with normal chest X-rays, it is possible to form an idea of the success of such a control programme.

In this hypothetical population of 50 000 there may be 200 active cases (Table 47), 500 observation cases that do not appear active, and 468 clinically insignificant cases which most probably are inactive.

Reading Table 47 from left to right the fate of the X-ray abnormal cases during the next 12 months can be seen: of the 200 active or probably active cases, 35 are likely to die, 24 to become inactive or probably inactive, and 137 may still be active or probably active. Altogether, the group of active cases would be reduced from 200 to 137, giving a decrease of about 32%. It is rather sobering to note that the major part of this reduction is due to half of the most advanced cases being removed by death. The gain from a public health point of view of this reduction is offset by the simultaneous development of 64 fresh active or probably active cases from various sources, as discussed later, leading to a slightly higher number of active cases at the end of the year—namely, 203 instead of the original 200. There has been a moderate shift in the type of active cases caused by a slight decrease in the number of more active cases and a small increase in the less active cases, but the change is small and would not materially affect the prevalence of infective cases.

Considering group B, with 500 observation cases, it may be expected that 33 will develop lesions;

TABLE 47

CHANGES IN THE TUBERCULOUS POPULATION IN A HYPOTHETICAL RURAL COMMUNITY OF 50 000 DURING ONE YEAR

Position at beginning of year		Position at end of year								
Category	Number of cases	Died	Left area or fate unknown	A1	A2	A3	A sub-total	B	C	Normal
A. Active:										
A1	60	19	—	30	1	3	34	6	—	1
A2	43	8	2	3	19	5	27	4	1	1
A3	97	8	2	2	2	72	76	6	2	3
Sub-total	200	35	4	35	22	80	137	16	3	5
B. Observation cases	500	15	15	7	12	14	33	370	25	42
C. Inactive	465	10	37	1	1	3	5	24	345	44
Normal	48 835	742	1 925	9	9	2	20	96	87	49 165
Born	1 295			—	—	—	—	—	—	
New arrivals	1 950			2	2	4	8	19	18	
Total		802	1 981	54	46	103	203	525	478	49 256

15 are likely to die, and as this number is higher than would be expected from the crude death rate in the population, some of these deaths may be caused by active tuberculosis also. So the number of active cases arising from this group might be a little higher than 6% or 7%, possibly about 8%. Also from group C, representing probably inactive or clinically insignificant cases, 5 cases, or 1%, with active tuberculosis may be expected to arise. These fresh active cases have therefore come from individuals already known to have had some lesions in their lungs at the beginning of the year. In all, about 38 cases may be expected to develop from already existing lesions which at the time of detection were not sufficiently advanced to be considered active.

To this should be added active cases arising among persons who were found to have normal X-ray films. These have been estimated to be 20, corresponding to an annual incidence of 0.43 per 1000. Add to these another 8, which might have come through the arrival of new people whom it is assumed have the same prevalence as the original population. Altogether, 28, or 42%, of the 66 fresh active cases expected to develop during the year come from the general population and are quite unpredictable, except that the majority may develop among adults with Mantoux 5 TU reactions of 10 mm or more.

The total rate of fresh active cases per year is therefore estimated to be about 12-13 per 10 000. Half, or a little more than half, of these would be known at the beginning of the year since they would arise among persons with X-ray abnormalities, the majority coming from the 522 in category B. Of these 1:15 would develop active disease during the following 12 months. As for the other group of " inactive " cases, 1:103 may be expected to develop active tuberculosis.

The implications of these observations with respect to the possibility of chemoprophylaxis are self-evident. If it were possible to persuade the observation cases to take drugs prophylactically, and if it is assumed that drugs could prevent active tuberculosis from developing in all the cases, the incidence of fresh tuberculosis could be reduced by 50% or so. This would mean that for each case prevented another 14 would have to be treated. However, if the people did not adhere faithfully to the prophylactic regimen, such a result could not be expected, however potent the drug.

The fact that isolation and treatment of active cases in hospital have not yielded quick and specta-

cular results within the observation period, according to our experience, does not necessarily imply that domiciliary drug therapy and chemoprophylaxis would not be more successful. One of the major drawbacks in treating patients in a hospital, even if it is a local one, centrally placed and within easy reach of the relatives of the patients, is the fact of removal of the patients from their homes. It is possible that when patients are not required to move away from their homes their co-operation may be better. On the other hand, since the drugs have to be self-administered instead of being given under hospital routine, there may be so many interruptions or failures in taking them that the general results from a community point of view may be poorer than under the present system of treatment in a hospital.

The findings suggest that (*a*) one-third of existing active cases have occurred during the previous year, or, with the present situation, the tuberculous population renews itself every third year; (*b*) if drug administration prevents deaths from active tuberculosis but cannot gain complete control of the disease, the result may be an increase in the number of patients from year to year; and (*c*) since the majority of fresh cases arise in adults—particularly among elderly males—it may be considered appropriate to submit only the adult population to X-ray examination.

XX. GENERAL DISCUSSION

THEORETICAL CONSIDERATIONS

The really critical question arising from the present investigation is how to explain the highly prevalent low-degree sensitivity to tuberculin. This problem dominates all the other problems; it affects the use of the tuberculin test as a diagnostic tool and as a guide in screening persons for eligibility for BCG vaccination; it confounds all estimates concerning prevalence and incidence of tuberculosis based upon tuberculin tests. The magnitude of the problem is borne out by the fact that 95% of the whole Madanapalle study population react to a dose of 100 TU tuberculin (with reactions of 5 mm and more), and that young children also appear heavily infected: at the age of 10 years 80% and even at the age of five years as much as 60%, react to 100 TU. How is this very high rate of tuberculin sensitivity compatible with a low prevalence of bacillary tuberculosis?

The hypothesis that much of this allergy, particularly that which is reflected in small reactions to a low dose of tuberculin, is the result of infection with a non-pathogenic, ubiquitous, still unknown organism, related to *Mycobacterium*, which may exist normally in soil, water or on plants and which easily invades the human organism, is very attractive. It offers a logical explanation of many of the problems posed in the course of the present investigation. According to this hypothesis most of the low-degree allergy is caused by the unknown organism and most of the high-degree allergy by the tubercle bacillus. Using the skin sensitivity found in patients with proved pulmonary tuberculosis as an indication of the type of reaction associated with the high-degree allergy set up by the tubercle bacillus (see Fig. 15, page 90) it can be estimated from the distributions of reactors in the general population that about one-quarter (24%) have specific allergy and two-thirds (about 70%) have " non-specific " allergy only. In view of the evidence accumulating from research in tropical and subtropical countries that " non-specific " allergy is common, it seems reasonable to accept the theory that much of the tuberculin sensitivity encountered at Madanapalle is also due to causes other than the classic tubercle bacillus.

The strongest argument in favour of this theory is that it can explain the extraordinarily high rate of reactors among small children. It is also in children—but only in children—that the frequency distributions of reactors to tuberculin at Madanapalle appear to have a bimodal character (see Fig. 13 and 14, page 88), suggesting that less than 10% of the reactions are specific. In adults it is very difficult to discern any bimodal distribution, so it must be assumed that there is great overlapping between the two types of distribution or that most persons are infected with both types of organism; it seems that with advancing age the " non-specific " reactions have a tendency to shift to the right on the scale of indurations and the " specific " to the left until they coalesce into one distribution with a mode as low as 7-9 mm (see Fig. 13,

age-groups 30-49, page 88). Judging from the distributions in adults only it would be difficult to suspect that we may be dealing with composite distributions and not merely with one distribution of reactions representing one type of sensitivity or an admixture of several types of sensitivity.

The significance of the " non-specific " allergy can be understood best by considering the sensitivity in children. Of children in the age-group below 5 years 20% reacted to 5 TU and another 40% to 100 TU (see Fig. 10, page 85). Presuming for the sake of argument that reactions produced by 100 TU among children not reacting to 5 TU are exclusively due to " non-specific " allergy it means that nearly half the children at the early age of about 2-3 years have been infected with the unknown organism. This would indicate an annual infection rate of not less than 20%; as some of the 5 TU reactions of 5 mm and more would also be caused by this organism, the infection rate must be considerably higher. In any case, it seems certain that practically everybody must have been exposed to infection with the unknown organism before the age of 10-15 years and that the majority have acquired the low-grade " non-specific " allergy by that age.

Turning to the infection with tubercle bacilli and assuming, again for the sake of argument, that persons reacting with 10 mm and more to 5 TU represent persons possessing " specific " allergy, the prevalence rate of infections with tubercle bacilli is as follows: 10% at the age of 10 years, 21% at 20, 31% at 30, and 34% at 40 years; graphically they would be represented by a curve a little lower than the 1 TU curve shown in Fig. 9 (page 84). This estimate does not take into account " specific " sensitivity giving reactions less than 10 mm nor that some of the reactions of 10 mm and above could also be due to the " non-specific " sensitivity; the prevalence rates can therefore be only rough approximations. However, using these as a basis the average annual infection rate with tubercle bacilli works out to about 1:100, or 1%. The increase in prevalence rate from year to year according to age is greatest between 10 and 20 years, corresponding to a maximal annual infection rate of about 1.5% at the age of 15 years.

The annual infection rate here estimated as 1% is considerably lower than the rate of 4% found by direct observation among unvaccinated controls in the BCG control trial described in section X. Since the criterion for " specific " reactions—viz. 10 mm to 5 TU—is the same for both estimates, the rates should have been the same. It is possible that the rate of 4% represents an over-estimate, a fairly high proportion of large reactions being due to chance distribution within the limits of the experimental error. Perhaps some of the " specific " allergy induced by fresh primary infections might tend to wane in the course of time; this is also suggested by the observation that many persons with large reactions at the initial test show smaller reactions at repeat tests (see Fig. 16, page 96). It seems, therefore, that 4% may be an over-estimate and 1% possibly an under-estimate, so perhaps the annual infection rate is nearer 2%. In any case, these considerations suggest that (*a*) the infection rate with tubercle bacilli is not nearly as high as that relating to the unknown agent responsible for the " non-specific " sensitivity, and (*b*) when infection with tubercle bacilli takes places most people already possess a low-degree allergy.

The incidence of fresh lesions is low, particularly in children and young persons. The reason is undoubtedly the low infection rate and the low prevalence of bacillary tuberculosis. But the presence of a low-degree tuberculin sensitivity may also be a contributory factor. It seems reasonable to assume that this low-degree allergy may be associated with a certain degree of protection against superinfection with virulent tubercle bacilli, in the same manner as BCG allergy is associated with a certain immunity induced by the BCG. It is also possible that the " non-specific " allergy may retard the development of demonstrable lesions due to virulent bacilli, if it does not prevent it altogether. This may be one reason why tuberculosis occurs rather late in life, another being the possibility that many are infected only late in life.

In the British BCG trial and in the United States Public Health Service nurses study (Palmer, 1957) a close association is found between the incidence of tuberculosis and the degree of tuberculin sensitivity. As in the present study (see Fig. 22, page 124) there is a positive correlation between the size of reactions to small doses of tuberculin (3 or 5 TU) and the incidence of fresh cases: the smaller the reactions the lower is the incidence, the larger the reactions the higher is the incidence. The present material, however, differs from the other two groups studied by the absence of a high incidence of fresh lesions among persons with very small or no reactions. In the British and American studies the incidence is higher among persons with small or no reactions

(0-4 mm) to 100 TU and 250 TU than among persons with slightly larger reactions. This is not found at Madanapalle. Perhaps this absence of a high incidence among non-reactors (0-4 mm reactions to 5 TU) is due mainly to the low infection rate and the limited period of observation; perhaps it is due also to a protective effect of the low-degree allergy present among such persons as revealed by a second test with 100 TU (see Fig. 13 and 14, page 88).

Besides a low infection rate with tubercle bacilli and a high prevalence of " non-specific " allergy, another factor may contribute to the low incidence of tuberculosis at Madanapalle—namely, a low virulence of the tubercle bacilli. Strains of tubercle bacilli isolated from patients admitted to the UMT Sanatorium without any prior treatment have often shown a much lower virulence than is normally found in strains isolated from European patients (Frimodt-Møller, Mathew & Barton, 1956). Of 60 strains isolated from untreated patients (of which a high proportion belong to the present study population) and tested for virulence in guinea-pigs, the provisional results are: 13 showed high virulence, 20 moderate and 27 a low virulence; of 22 strains recently isolated from untreated patients in the United Kingdom and West Germany and tested for virulence at our laboratory, 20 had high, two moderate and nil a low virulence. Although it is not certain that the virulence for guinea-pigs necessarily reflects the level of virulence for man, there is usually a fairly close association between the two. It appears, therefore, that a high proportion of bacilli infecting Indian patients and capable of setting up progressive lesions are attenuated in comparison with bacilli recovered from European patients. It is too early to speculate about the implications of this observation but it is another pointer to the unusual features characterizing the tuberculosis epidemiology pertaining to the Madanapalle population. Whether there is any connexion between these abnormal strains and the unknown organism or organisms causing the abnormal tuberculin sensitivity that affects a large proportion of the population is not known. It is obvious that much work has to be done before the complicated pattern of the tuberculosis epidemiology emerging from the present investigation can be fully understood and explained. Specially needed are the isolation and identification of the unknown agent responsible for the " non-specific " allergy and the preparation of special antigens from the same, as well as an improved tuberculin better suited to identify the specific allergy produced by the tubercle bacillus than the present standard tuberculin.

In conclusion the findings may be summarized as follows:

1. Most of the tuberculin sensitivity revealed by small reactions to a small dose of tuberculin is probably caused by infections with a non-pathogenic organism related to the mycobacteria but different from the classic tubercle bacillus. The unknown agent is so common that practically all children, by the time they reach school age, have acquired the " non-specific " allergy.

2. The prevalence of persons infected with the classical tubercle bacillus is low; the annual infection rate may be about 1%-2%.

3. The attack rate of tuberculosis is low; most cases arise in adults, the number increasing with the age of the persons.

4. It is possible that the low-degree " non-specific " allergy may act as a kind of natural vaccination which prevents or retards the development of progressive lesions after infection with the classic tubercle bacillus.

5. The poor response to BCG vaccination observed at Madanapalle and indicated by a low post-vaccination allergy and the inability to reduce significantly the incidence of fresh tuberculous lesions demonstrable by mass miniature X-ray may be due to (*a*) the ineffectiveness of Mantoux tests with standard tuberculin to identify persons eligible for BCG vaccination in the face of a high prevalence of " non-specific " allergy; (*b*) a possible protective effect associated with the " non-specific " allergy which competes with the effect of the BCG vaccination; and (*c*) possible damage to the vaccine itself by local conditions such as exposure to heat during transit and to indirect sunshine at the time of vaccination.

PRACTICAL CONSIDERATIONS

The value of the present investigation is to be found not only in the light it has shed on various aspects of tuberculosis epidemiology but also in the fact that it has served as an exercise in the practical conduct of a tuberculosis control programme. At the time the investigation was planned modern drugs against tuberculosis were not known. Considering isolation of all bacillary cases to be the most effective means of prevention it was decided to make an all-out attack on the tuberculosis

problem by intensive case-finding by means of mass miniature X-ray examination of the whole study population and hospitalization of all bacillary cases detected. As streptomycin and PAS had already become available before the first village survey began, and isoniazid in 1952, all the patients treated in hospital have also had the benefit of modern drugs. Domiciliary treatment with drugs did not form any part of the control programme.

As already outlined in the preceding two sections the results with regard to a reduction of the prevalence of tuberculosis over four years are not very striking. In the first place, the observation period has been too short. Many of the fresh cases have arisen in persons already infected before the present investigation began. The effect on the reduction of incidence of fresh lesions developing in persons infected after the beginning of the investigation has not had time to be felt. Further, any reduction which has actually taken place has been counterbalanced by the keeping alive of a number of advanced cases which would have died if they had not been given drug therapy. As several of these failed to obtain sputum conversion and others relapsed after returning home from an apparently successful hospital treatment, the reduction in the community load of infection may not have been altered very much.

Even in other respects the present system of tuberculosis control has not been as effective as had been expected. The main reasons are, first, the insufficient coverage of the population by X-ray examination; secondly, the refusal of many patients with manifest disease to enter hospital, and, thirdly, the difficulty in keeping many of the patients long enough in hospital for the treatment with drugs to produce a lasting effect. It is estimated that altogether about 50% of the existing bacillary cases could not be brought into hospital and could therefore not be isolated.

Some of the defects mentioned might have been averted or reduced had it been possible to offer some financial help to families where the breadwinner had been stricken down with disease for a long period—but no such funds were available. Further, it would also have been a help if some kind of legislation had been introduced permitting a gentle pressure to be applied in specially obstinate cases, where individuals refused to be either X-rayed or admitted to hospital. All influence had to be exerted through mere moral persuasion. Such legislation should of course apply only to situations where facilities exist for dealing adequately with tuberculous patients detected by the mass miniature X-ray examination.

With the advent of potent antituberculosis drugs which can be given by mouth and which are not too expensive, it is clear that domiciliary drug treatment must occupy a very important place in any comprehensive scheme of tuberculosis control. It is also clear that the system which has been tried out at Madanapalle is not satisfactory and should not be emulated without considerable change in the organization. In view of the costliness of a system where hospital treatment forms a major part, and of the defects here encountered, there can be no doubt that the emphasis must be placed on domiciliary treatment with drugs. Whether institutional treatment can be left out altogether or should form part of the system is a matter for further research. However, in view of the fact that many patients are far advanced when detected and are often very poor, it seems unlikely that some provision for institutional treatment can be avoided.

Even though the present investigation has not made use of domiciliary treatment it can be said, as a general observation, that no scheme based upon domiciliary treatment is likely to make a significant impact upon the tuberculosis problem unless it can be applied to a very high percentage of all existing cases of bacillary tuberculosis and in a manner that ensures that a high percentage become permanently sputum-negative.

To summarize some of the conclusions:

1. In a rural population of low density one mobile X-ray unit can normally photograph 18 000-20 000 persons in a year.

2. The time taken to cover a population by mass miniature X-ray examinations depends upon the response of the people and the attendance rate desired; the higher the attendance rate the longer is the time taken. To round up the chronic absentees takes a disproportionately long time.

3. The main reason for refusing to be X-rayed or to accept hospital treatment is unwillingness on the part of the people to interrupt their gainful occupation. In a community where the average income is low and barely above subsistence level the loss of income even for short periods may be serious.

4. The small change in the prevalence of tuberculosis noticed over an observation period of four years may be attributed to (*a*) too many bacillary

cases remaining at large; (*b*) increase of the tuberculous population by the keeping alive of many advanced cases by drug therapy who would otherwise have died and who did not obtain sputum conversion; (*c*) relapses in patients returning home after apparently adequate hospital treatment with drugs; (*d*) failure of the control programme to prevent fresh cases arising in persons already infected before the investigation began; and (*e*) the observation period being too short to record the effect of a possible reduction in the prevalence of bacillary cases on the incidence of fresh lesions in persons infected after the investigation had started.

5. It is possible markedly to reduce the tuberculosis mortality within a short period if the majority of advanced cases can be brought under a modern drug therapy. In the present investigation the tuberculosis mortality rate fell from over 200 to 21 per 100 000 in four years.

6. The present control programme based upon intensive case-finding and hospitalization of all bacillary cases was planned before the modern drugs were known. With the advent of potent drugs which can be given by mouth the emphasis in any future control programme should be laid on domiciliary treatment. It will permit the patients to continue their work and to earn unless they are too sick to begin with. Whether such patients would be able to continue to take drugs at home over a sufficiently long period to ensure a lasting effect is not known.

7. In a case-finding programme by means of mass miniature X-ray it may be profitable, when funds are limited, to concentrate on the population groups having the highest prevalence of bacillary tuberculosis. In the present study 90% of all clinically active cases were found among the adults of 20 years of age and above—i.e., in 50% of the total population. Men were affected more often than women, elderly persons more often than young.

8. As more than 50% of all fresh active lesions appeared among persons already showing some X-ray pathology, such persons may be especially suitable for chemoprophylaxis.

9. Practically all cases with fresh disease observed within the first year after a survey occur among persons having a high tuberculin sensitivity. Tuberculin tests may therefore be helpful in indicating those persons who are most likely to fall ill.

10. For BCG vaccination to be effective it is necessary to ensure a high potency of the vaccine at the time of vaccination by preventing damage in transit from exposure to heat, sunshine and other adverse factors. It would be of great value if new antigens could be developed which could distinguish the sensitivity caused by the tubercle bacillus from that caused by non-pathogenic organisms different from the tubercle bacillus. It would be desirable to carry out a BCG control trial in an area with a high prevalence of low-grade allergy, where the rate of infection with tubercle bacilli is higher than that found in the Madanapalle area.

11. It has been shown that the factors influencing tuberculosis epidemiology are numerous, and some were unknown hitherto. It has also been shown that the forces determining the incidence of tuberculosis are delicately balanced, so that it is difficult to predict the outcome of a tuberculosis control programme. It is therefore essential that carefully conducted research should always accompany any new programme aimed at controlling or eradicating tuberculosis in a community, and that the effect of the programme, in all its aspects, should be analysed and assessed.

XXI. SUMMARY

INTRODUCTION

In 1948-49 a tuberculosis survey by mass miniature X-ray examination and tuberculin testing was carried out in Madanapalle, a small town in Andhra Pradesh, South India. In 1950 about 200 villages were included in the study making a total population of about 60 000. The investigation was sponsored by the Government of India and the WHO Tuberculosis Research Office and conducted by the Union Mission Tuberculosis Sanatorium, Arogyavaram. Cases detected with infectious forms of tuberculosis were admitted and treated in a special isolation hospital at Madanapalle. The present report deals with the findings in the villages during four consecutive rounds of examinations by X-ray and tuberculin testing between May 1950 and February 1955. The observation period was on an average 3½ years.

THE STUDY POPULATION

A census was taken at each round of investigation. Two card indexes were set up, one containing individual cards for each person tested and/or X-rayed, and one listing the members of each household. This household roster was brought up to date at each census. A special study was made of the movements in the population between 1950 and 1955 based upon the census records in a 10% sample of the villages and a 20% sample of the households in Vayalpad, the second largest town in the study area. Whereas the study population (excluding Madanapalle town) was about 37 000 in 1950, the number of persons living in the area at one time or another increased by 30% to 47 815, owing to 4470 births (12%) and 6662 fresh settlers in the area (18%). At the same time 2782 were lost by death and 6711 by departures from the area, leaving in 1955 a population of 39 000. Further, about 10 000 changed address within the study area; only 23 800, or 64%, occupied the same house during the whole period of investigation. All these changes, besides a high degree of illiteracy and relatively primitive living conditions, made the task of identification of individuals and keeping order in the records rather laborious.

COVERAGE

During the observation period 39 496 persons were tested with tuberculin; 25 092 were retested at least once. The total number of tests given was 84 137. During the same period 31 889 persons were X-rayed and 18 711 had additional X-rays, the total number of X-ray photographs amounting to 63 261. The attendance rate at Round I was 72.6% tested and/or X-rayed; 62.3% were tested and 56.5% X-rayed. At the end of Round IV, 85% of all present at one time or another had received at least one tuberculin test and/or X-ray examination. Of the persons who had not moved 93% had been examined at least once.

TUBERCULIN TESTING

At Round I, 9349 persons were tested with 1, 10 and 100 TU (Danish PPD, batch RT 19-20-21), the criterion for giving the next higher dose being indurations of 5 mm or less in diameter. Another 13 656 were tested with 5 TU followed by 100 TU if their reactions were 4 mm or less in size. Tests were read at 2, 3 or 4 days in 71%, and at 5 days or after in 18%; in 11% readings were unobtainable.

TUBERCULIN SENSITIVITY

The majority of the reactions to 1 and 5 TU, especially in children, showed small indurations about 4-10 mm in diameter and few only showed strong reactions of 10-30 mm. Tests with 10 and 100 TU in persons with very small or no reactions after the first test produced quite strong reactions. The percentage of reactors (as defined above) at the ages of 5, 10 and 20 years respectively were as follows: reactions to 1 TU: 9%, 12%, 28%; to 10 TU: 27%, 35%, 72%, and to 100 TU: 58%, 80% and 98%; to 5 TU: 22%, 28% and 54%. In children the number of reactors to small doses of tuberculin is low, while the number of reactors to the large doses is remarkably high. From the sensitivity observed in patients with proved tuberculosis at Madanapalle, and from observations elsewhere in tropical and subtropical countries, it is suggested that most of the low-grade sensitivity is due to infection with unknown acid-fast organisms producing a "non-specific" allergy, while true "specific" allergy is found only in a relatively small proportion (perhaps in not more than 25%). The two types of sensitivity are difficult to distinguish by means of Mantoux tests with standard PPD, the distributions according to size of indurations apparently overlapping greatly. Under such conditions the tuberculin test is therefore not of much practical value as a diagnostic tool or as a screen for selecting persons for BCG vaccination.

FLUCTUATIONS IN TUBERCULIN SENSITIVITY

Retests carried out at Rounds II, III and IV showed distinct positive correlations as compared with the initial test. However, the degree of variation observed was quite remarkable; how much of this is due to genuine fluctuations in the allergy and how much to unavoidable and uncontrollable variations in the testing technique is difficult to assess. However, it appears that the experimental error attached to tuberculin testing is much higher than ordinarily realized, so much so that it is considered very difficult to draw any valid conclusions about the development of allergy in individual cases unless the differences observed are quite considerable.

INFECTION RATE

Owing to the high prevalence of low-grade allergy and the inaccuracy of the tuberculin test it is difficult to estimate the infection rate on the basis of repeat

tuberculin tests. However, the rate of persons with initial reactions of 4 mm and less to 5 TU who showed 10 mm or more at later retests was 4% per year. As this change may be due mostly to infection with tubercle bacilli, it is suggested that the infection rate may be 2%-4% per year.

PREVALENCE OF TUBERCULOSIS

Grouping cases with X-ray pathology suggestive of tuberculosis into three categories—A: active or probably active pulmonary tuberculosis; B: observation cases; and C: clinically insignificant lesions—the prevalence in 1950-51 was as follows:

		Males	*Females*
Category	A	5.4 per 1000	2.8 per 1000
,,	B	12.7 ,, ,,	7.8 ,, ,,
,,	C	11.2 ,, ,,	8.1 ,, ,,

The prevalence in children was very low: 0.5 A cases per 1000 in boys and girls below 10 years. The rate increased with age, the highest rate being found in the age-group 50+: men 14.4 and women 11.5 A cases per 1000. Of all A cases observed 93% were found in adults 20 years of age or older. The proportion of males to females in category A was 2.2 : 1.

The prevalence of bacillary tuberculosis was between 2.3 and 4.1 per 1000.

Compared with findings in later surveys in the neighbouring districts the prevalence of tuberculosis in the Madanapalle villages is definitely low.

FOLLOW-UP RESULTS IN X-RAY ABNORMAL CASES

Dividing the cases in category A into three subgroups according to severity, the average annual fatality rate was: A1 (very extensive) 31%, A2 (moderately extensive) 19% and A3 (mild cases) 8%. In category B (observation cases) 3% died and 6.5% developed A-type lesions in a year. In category C, 1.1% per year developed A-type lesions.

ANNUAL ATTACK RATE

The annual incidence of fresh category A cases following a normal chest X-ray was 0.46 and 0.41 per 1000, and of category B cases 2.31 and 1.97 per 1000 for males and females respectively.

It is noteworthy that the attack rate was low in young people, the incidence of A cases in the age-group 20-29 years being 0.54 and 0.59 per 1000 only for males and females respectively. The rate increased gradually with age, elderly people of 50 years or more showing an incidence of 0.89 and 0.67 A cases per 1000 in men and women respectively.

THE ATTACK RATE AND INITIAL LEVEL OF TUBERCULIN SENSITIVITY

Fresh cases in category A following a normal chest X-ray were observed only in persons showing initial reactions of 10 mm or more to 5 TU, whereas B-type cases developed at all levels of allergy. The incidence in both categories was directly proportionate to the size of the reactions.

EFFECT OF BCG VACCINATION

Postvaccination allergy

A BCG control trial was set up in November 1950. Non-reactors (persons with indurations of 4 mm or less to 5 TU) were divided at random into two groups, one which was vaccinated and one which was left unvaccinated. During Round I, 4768 persons were found eligible for admission to the trial, 195 refused vaccination and are excluded, 2082 were vaccinated and 2491 were not vaccinated. At later rounds retests were done in 1555 vaccinated and 1817 unvaccinated. The mean sizes of reactions obtained at Rounds II, III and IV were as follows: in the vaccinated 5.53, 6.15 and 6.46 mm, and in the unvaccinated 4.37, 4.34 and 4.80 mm respectively. Retests of persons admitted to the trial during Rounds II and III showed practically the same results—namely, small reactions indicating a very low level of postvaccination allergy. As the unvaccinated also developed a certain degree of tuberculin sensitivity, though not quite so much as the vaccinated, it is evident that exposure to infection with the microbes responsible for producing "non-specific" allergy is very high. How this "non-specific" allergy may affect the development of BCG allergy is not known. Although special precautions were taken to avoid damage to the BCG vaccine the possibility cannot be entirely excluded that the vaccine was exposed to excessive heat in transit from Madras or to indirect sunlight at the time of vaccination. This may partly account for the inability of the vaccine to set up a strong allergy.

Incidence in the BCG control trial

Of the 4573 persons admitted to the trial in Round I, 48 (24 in each group) showed abnormal X-ray findings; 9 cases (4 among the vaccinated and 5 among the unvaccinated) were classified as non-

tuberculous. Of the 39 considered to be of tuberculous origin (20 among the vaccinated and 19 among the unvaccinated) 23 were seen on the first X-ray taken during Round I itself (11 among the vaccinated and 12 among the unvaccinated). Of the 16 cases detected during Rounds II, III or IV on X-ray examination, 9 were among the vaccinated and 7 among the unvaccinated. This gives an annual incidence of 1.9 per 1000 in the vaccinated and 1.4 per 1000 in the unvaccinated. Excluding cases in category C (clinically insignificant)—3 among the vaccinated and 4 among the unvaccinated—the incidence of A- and B-type cases was 1.2 per 1000 among the vaccinated and 0.6 per 1000 among the unvaccinated. Thus it has not been possible to demonstrate any reduction of the incidence among the vaccinated as compared with the unvaccinated. This result is in keeping with the very low degree of tuberculin sensitivity attributable to the BCG vaccination.

It is suggested that several factors may have interfered with the effect of the vaccine: (*a*) possible loss of potency owing to damage by heat or indirect sunlight; (*b*) possible failure of the tuberculin test to separate persons infected with tubercle bacilli from persons not so infected; (*c*) low-grade "non-specific" allergy possibly existing already at the time of vaccination or acquired shortly afterwards; (*d*) low prevalence of infectious bacillary tuberculosis, and, concomitantly, a very low infection rate with tubercle bacilli; and finally (*e*) the shortness of the observation period.

TUBERCULOSIS MORTALITY

The rate of deaths from all causes was 15.7 for males and 16.1 for females per 1000 per year (infant mortality not recorded). The average annual death rate for tuberculosis was 49 per 100 000. This figure, it should be recalled, applies to a population in which tuberculous patients had full access to hospital and modern drug treatment. The tuberculosis mortality before the investigation began was probably 200 or more per 100 000. During the three intervals between the four rounds the rate was 64, 46 and 21 respectively. This dramatic fall in less than four years must be ascribed to the detection of the cases in earlier stages of the disease and the wide use of antibiotics. The ratio of deaths from tuberculosis to deaths from all causes was highest in males in the age-group 20-29 years and in females in the age-group 30-39 years, it being 13% in both groups.

EFFECT OF THE CONTROL PROGRAMME

Despite the great fall in mortality no significant change in the prevalence of tuberculosis between Rounds I and IV could be found. While the prevalence of A-type cases at Round I was 3.7 per 1000, at Round IV it was 3.4 per 1000. However, there were fewer A cases among young people and more among old people at Round IV than at Round I. The keeping alive of a number of advanced cases by drug therapy may have compensated for a fall in the incidence of the disease.

The control programme based upon case-finding and hospitalization of all bacillary cases was greatly handicapped by the unwillingness of patients to be prevented from working and earning, and to be separated from their families for long periods. In this respect domiciliary treatment with drugs may prove a definite advantage.

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RÉSUMÉ

Introduction

En 1948-1949, une enquête systématique sur la tuberculose par micro-radiophotographies et épreuves tuberculiniques a été exécutée à Madanapalle, localité de l'Andhra Pradesh (Inde méridionale). En 1950, environ 200 villages furent englobés dans l'enquête, ce qui porta à 60 000 le chiffre de la population étudiée. Cette enquête était patronnée par le Gouvernement de l'Inde et par le Bureau de Recherches sur la Tuberculose de l'OMS; elle a été effectuée par le « Union Mission Tuberculosis Sanatorium » d'Arogyavaram. Les cas contagieux ont été traités à Madanapalle dans un hôpital spécial où ils étaient isolés. Le présent rapport expose les observations faites dans les villages étudiés pendant quatre cycles consécutifs d'examens radiographiques et tuberculiniques entre mai 1950 et février 1955. La période d'observation a été, en moyenne, de trois ans et demi.

Population étudiée

Un recensement a été effectué à chaque cycle d'enquête. Deux fichiers ont été établis: l'un contenait la carte individuelle de chaque sujet examiné, l'autre la liste des membres de chaque ménage. Ce fichier des ménages a été mis à jour à chaque recensement. Les mouvements de la population entre 1950 et 1955 ont fait l'objet d'une étude spéciale, pour laquelle on a utilisé les résultats des recensements successifs dans deux échantillons: l'un comprenant 10% des villages, l'autre 20% des ménages de Vayalpad, seconde localité de la circonscription par ordre d'importance. La population étudiée (à l'exclusion de la ville de Madanapalle) se composait d'environ 37 000 personnes en 1950. Ce nombre a augmenté par moments, allant jusqu'à 47 815 habitants (+ 30%); cet accroissement était dû à 4470 naissances (12%) et à l'arrivée de 6662 immigrants venus se fixer dans la circonscription (18%). D'autre part, il y a eu 2782 décès et 6711 départs, ce qui a laissé, en 1955, une population de 39 000 habitants. En outre, quelque 10 000 personnes ont changé de domicile à l'intérieur de la circonscription; 23 800 seulement — soit 64% — ont résidé au même lieu, pendant toute la durée de l'enquête. Tous ces mouvements, joints à l'analphabétisme et aux conditions d'existence relativement primitives, ont compliqué l'identification des individus et la tenue à jour des fichiers.

Etendue de l'enquête

Au cours de la période d'observation, des épreuves tuberculiniques ont été exécutées sur 39 496 personnes dont 25 092 ont été soumises au moins à une deuxième épreuve; le nombre total des tuberculino-réactions pratiquées a été de 84 137. Durant la même période, 31 889 personnes ont été radiographiées, dont 18 711 au moins deux fois; le nombre total des radiographies a été de 63 261. Lors du premier cycle d'enquête, la proportion de la population examinée a été de 72,6%; sur ce nombre 62,3% ont fait l'objet d'un examen tuberculinique et 56,5% d'un examen radiographique. A la fin du quatrième cycle d'enquête, 85% de toutes les personnes présentes à un moment quelconque avaient été examinées une fois au moins par tuberculino-réaction ou par radiographie. Des personnes qui n'avaient pas changé de domicile, 93% ont été examinées une fois au moins.

Epreuves à la tuberculine

Lors du premier cycle, des épreuves à la tuberculine ont été exécutées sur 9349 personnes, qui ont reçu 1, 10 ou 100 UT (PPD d'origine danoise, lot RT 19-20-21). Le critère adopté pour le passage à la dose immédiatement supérieure était la présence d'une induration de 5 mm de diamètre au moins. Un autre groupe de 13 656 personnes a reçu 5 UT, puis 100 UT quand les premières réactions avaient un diamètre de 4 mm ou moins. La lecture se faisait après 2, 3 ou 4 jours dans 71% des cas, après 5 jours ou plus dans 18% des cas; la lecture n'a pas été possible dans 11% des cas.

Sensibilité tuberculinique

Les réactions à 1 UT et 5 UT, notamment chez les enfants, ont été en majorité de petites indurations de 4 à 10 mm de diamètre; les fortes réactions de 10 à 20 mm

ont été rares. Les épreuves exécutées avec 10 et 100 UT ont provoqué des réactions très fortes chez les personnes qui n'avaient donné que des réactions faibles ou nulles la première fois. Les pourcentages de réactions positives (définies par les dimensions indiquées plus haut) chez les individus âgés de 5, 10 et 20 ans ont été les suivants: réactions à 1 UT: 9%, 12%, 28%; à 10 UT: 27%, 35%, 72%; à 100 UT: 58%, 80%, 98%, à 5 UT: 22%, 28%, 54%. Chez les enfants, il n'y a eu qu'un petit nombre de réactions positives aux faibles doses de tuberculine; en revanche, le nombre de réactions positives aux doses fortes a été remarquablement élevé. De la sensibilité observée à Madanapalle parmi les cas avérés de tuberculose, et des constatations faites ailleurs en milieu tropical et subtropical, il apparaît que, le plus souvent, la faible sensibilité est due à une infection par des organismes acido-résistants inconnus qui provoquent une allergie non spécifique, alors que l'allergie véritablement spécifique se rencontre chez un nombre relativement faible d'individus (peut-être pas plus de 25%). Le test de Mantoux exécuté avec le PPD standard permet difficilement de distinguer entre les deux types de sensibilité, le classement d'après le diamètre de l'induration aboutissant apparemment à un large chevauchement. Dans ces conditions, la tuberculino-réaction est de peu d'utilité pratique soit pour le diagnostic, soit pour sélectionner les sujets à vacciner par le BCG.

Variations dans la sensibilité tuberculinique

On a constaté une nette corrélation entre les résultats de l'examen initial et ceux des épreuves de contrôle exécutées lors des II^{me}, III^{me} et IV^{me} cycles d'enquête. Cependant, on a enregistré des variations remarquables. Il est difficile de savoir dans quelle mesure elles étaient dues à de véritables fluctuations de l'allergie ou à des différences inévitables et incontrôlables dans la technique d'épreuve. Il semble cependant que la tuberculino-réaction comporte une marge d'erreur expérimentale beaucoup plus grande qu'on ne le croit d'ordinaire; il y a même lieu de penser qu'il est très difficile de tirer des conclusions valables quant au développement de l'allergie dans des cas individuels, à moins que les différences enregistrées ne soient très considérables.

Taux d'infection

L'allergie de faible degré étant très fréquente et les résultats fournis par la tuberculino-réaction étant incertains, il est malaisé d'estimer le taux d'infection sur la base d'épreuves tuberculiniques répétées. Cependant, la proportion d'individus ayant présenté des réactions initiales de 4 mm et moins avec 5 UT et des indurations de 10 mm et plus lors de la répétition de l'épreuve était de 4% par an. Comme ce changement peut être principalement dû à l'infection par le bacille de la tuberculose, on peut penser que le taux d'infection est de 2% à 4% par an.

Fréquence globale de la tuberculose

On peut répartir en trois catégories les cas pour lesquels la radiographie donne une présomption de tuberculose, à savoir: A) tuberculose pulmonaire certainement ou probablement active; B) cas à surveiller; C) lésions cliniquement non significatives. D'après ce classement, la fréquence des cas était, en 1950-1951, la suivante:

	Hommes	*Femmes*
Catégorie A	5,4 pour 1000	2,8 pour 1000
Catégorie B	12,7 pour 1000	7,8 pour 1000
Catégorie C	11,2 pour 1000	8,1 pour 1000

Chez les enfants, la fréquence globale était très faible: 0,5 cas A pour 1000 garçons et filles de moins de 10 ans. La proportion augmentait avec l'âge, la plus forte se rencontrant au-dessus de 50 ans: 14,4 cas A pour 1000 hommes et 11,5 pour 1000 femmes. De tous les cas A observés, 93% étaient des adultes ayant atteint ou dépassé 20 ans. Le rapport numérique entre hommes et femmes était de 2,2 à 1.

La fréquence de la tuberculose bacillaire était comprise entre 2,3 et 4,1 pour 1000.

Comparée avec les renseignements fournis par des enquêtes ultérieures faites dans les districts voisins, la fréquence globale de la tuberculose à Madanapalle paraît donc nettement faible.

Evolution des cas à radiologie positive

Si l'on répartit les cas de catégorie A en trois sous-groupes d'après leur gravité, on obtient les taux moyens annuels suivants de mortalité: A1 (tuberculose très étendue) 31%; A2 (modérément étendue) 19%; A3 (cas bénins) 8%. Dans la catégorie B (cas à surveiller), il y a eu 3% de décès et 6,5% des cas ont donné des lésions du type A dans l'année. Dans la catégorie C, 1,1% des cas ont donné des lésions du type A dans l'année.

Fréquence annuelle des cas nouveaux

La fréquence annuelle des cas nouveaux de catégorie A, apparus alors que la première radiographie avait donné une image normale des poumons, a été de 0,46 pour 1000 hommes, de 0,41 pour 1000 femmes; celle des cas de catégorie B a été de 2,31 pour 1000 hommes et de 1,97 pour 1000 femmes.

Le taux est remarquablement faible chez les jeunes, la fréquence des cas A nouveaux dans la classe d'âge de 20 à 29 ans étant seulement de 0,54 pour 1000 hommes et de 0,59 pour 1000 femmes. Le taux augmente progressivement avec l'âge, la fréquence des cas A atteignant, à partir de l'âge de 50 ans, 0,89 pour 1000 hommes et 0,67 pour 1000 femmes.

Fréquence des cas nouveaux et sensibilité tuberculinique initiale

L'apparition d'un cas de catégorie A après une radiographie pulmonaire initialement normale, n'a été observée que chez les sujets ayant donné des réactions initiales de 10 mm ou plus avec 5 UT; des cas de catégorie B

sont apparus chez des sujets de tous degrés d'allergie. La fréquence des cas nouveaux de l'une et de l'autre catégorie a été en proportion directe de la dimension des réactions.

Effets de la vaccination BCG

Allergie postvaccinale. Un essai de prophylaxie antituberculeuse par la BCG a été entrepris en novembre 1950. Un certain nombre de sujets tuberculino-négatifs (induration de 4 mm ou moins avec 5 UT) ont été répartis au hasard en deux groupes, dont l'un a été vacciné et l'autre a servi de témoin. Au cours du premier cycle d'enquête, 4768 personnes se sont trouvées remplir les conditions fixées; 195 refusèrent de se laisser vacciner et furent exclues de l'expérience, 2082 furent vaccinées et 2491 ne le furent pas. Lors des cycles ultérieurs, des épreuves de contrôle furent exécutées sur 1555 personnes vaccinées et 1817 non vaccinées. Les diamètres moyens des réactions notées lors des cycles II, III et IV ont été respectivement les suivants: chez les vaccinés 5,53, 6,15 et 6,46 mm; chez les non-vaccinés 4,37, 4,34 et 4,80 mm. Les épreuves de contrôle faites sur les sujets admis à participer à l'essai lors des cycles II et III ont donné pratiquement les mêmes résultats, à savoir: réactions de petit diamètre indiquant un très faible degré d'allergie postvaccinale. Comme une certaine sensibilité tuberculinique s'est également manifestée chez des sujets non vaccinés — bien qu'un peu moindre que chez les vaccinés — il semble évident que l'exposition aux micro-organismes responsables de l'allergie « non spécifique » est très forte. On ignore comment cette allergie « non spécifique » peut retentir sur le développement de l'allergie due au BCG. Bien que des précautions spéciales aient été prises pour éviter toute altération du vaccin, on ne peut entièrement exclure la possibilité d'une exposition excessive à la chaleur lors du transport à partir de Madras ou encore une exposition indirecte à la lumière du soleil au moment de la vaccination, ce qui pourrait expliquer en partie l'inaptitude du vaccin à produire une forte allergie.

Fréquence des cas nouveaux de tuberculose lors de l'essai de prophylaxie par le BCG. Sur les 4573 personnes admises à participer à l'essai lors du cycle I, 48 (24 de chaque groupe) présentaient des images radiographiques anormales, 9 cas (4 parmis les vaccinés, 5 parmi les non-vaccinés) étant classés comme non tuberculeux. Sur les 39 cas considérés comme d'origine tuberculeuse (20 parmi les vaccinés, 19 parmi les non-vaccinés), 23 furent décelés par la radiophotographie initiale prise lors du premier cycle d'enquête (11 cas parmi les vaccinés, 12 parmi les non-vaccinés). Des 16 cas dépistés lors des examens radiographiques des cycles II, III et IV, 9 étaient des vaccinés et 7 des non-vaccinés. Il s'ensuit que la fréquence annuelle des cas nouveaux a été de 1,9 pour 1000 chez les vaccinés et de 1,4 pour 1000 chez les non-vaccinés. Si l'on exclut les cas de catégorie C (cliniquement insignifiants) — dont 3 chez les vaccinés et 4 chez les non-vaccinés —, la fréquence des cas nouveaux de catégorie A et B a été de 1,2 pour 1000 chez les vaccinés et de 0,6 pour 1000 chez les non-vaccinés. Il n'a donc pas été possible de mettre en évidence une diminution de la fréquence des cas nouveaux chez les vaccinés. Ce résultat concorde avec le très faible degré de sensibilité tuberculinique attribuable au BCG.

Il y a lieu de penser que plusieurs facteurs peuvent avoir contrecarré l'effet du vaccin: a) perte d'activité due à l'action de la chaleur ou d'un éclairage indirect; b) inaptitude de la tuberculino-réaction à faire le départ entre les sujets infectés par des bacilles tuberculeux et les autres; c) préexistence d'une allergie « non spécifique » de faible degré au moment de la vaccination ou acquisition d'une telle allergie peu après la vaccination; d) faible fréquence globale de la tuberculose bacillaire infectieuse et, simultanément, très faible taux d'infection par des bacilles de la tuberculose; e) brièveté de la période d'observation.

Mortalité par tuberculose

La mortalité (toutes causes) a été de 15,7 pour 1000 chez les hommes et de 16,1 chez les femmes (mortalité infantile non enregistrée). La mortalité annuelle moyenne par tuberculose a été de 49 pour 100 000 habitants. Ce chiffre, il faut le rappeler, s'applique à une population où les tuberculeux pouvaient recevoir à l'hôpital un traitement médicamenteux moderne. La mortalité par tuberculose avant le début de l'enquête était probablement de 200 ou plus pour 100 000 habitants. Au cours des trois intervalles de temps compris entre les quatre cycles d'enquête, les taux ont été respectivement de 64, 46 et 21 pour 100 000. Cette diminution spectaculaire en moins de 4 ans doit être attribuée au dépistage des cas aux stades initiaux de la maladie et à un large recours à l'antibiothérapie. C'est chez les hommes de 20 à 29 ans et chez les femmes de 30 à 39 ans que le rapport entre la mortalité par la tuberculose et la mortalité de toute origine a été le plus élevé, soit 13% dans les deux cas.

Résultats du programme antituberculeux

Malgré la diminution considérable de la mortalité, il n'a été enregistré aucun changement significatif dans la fréquence globale entre le cycle I et le cycle IV. Alors que la fréquence globale des cas de catégorie A était de 3,7 pour 1000 au cycle I, elle était encore de 3,4 pour 1000 au cycle IV. Cependant, par comparaison avec le cycle I, le nombre des cas enregistré au moment du cycle IV était moindre chez les jeunes et plus élevés chez les vieillards. La survie d'un certain nombre de cas avancés, grâce au traitement médicamenteux, peut avoir compensé une diminution de la fréquence des cas nouveaux.

Le programme antituberculeux, dont la méthode fondamentale était le dépistage et l'hospitalisation de tous les cas bacillaires, a été sérieusement entravé par l'opposition des malades à cesser de travailler pour gagner leur vie et à être longtemps séparés de leur milieu familial. A cet égard, le traitement médicamenteux à domicile peut présenter un net avantage.

REFERENCES

Aspin, J. (1946) *Tubercle (Lond.)*, **27**, 25

Benjamin, P. V. (1938) *Indian med. Gaz.*, **73**, 540

Benjamin, P. V. (1952) In: Tuberculosis Association of India, *Proceedings of the Ninth Tuberculosis Workers' Conference, held in Lucknow*, New Delhi, p. 43

Benjamin, P. V. (1956) *Bull. int. Un. Tuberc.*, **26**, 563

Benjamin, P. V. (1957) *Tuberculosis in the tropics.* In: Heaf, F. R. G., ed., *Symposium of tuberculosis*, London, Cassell, p. 611

Benjamin, P. V., Jesudian, K. T., Verghese, M. C. & Varkkey, C. E. (1939) *Indian med. Gaz.*, **74**, 516

Cochrane, A. L., Cox, J. G. & Jarman, T. F. (1955) *Brit. med. J.*, **1**, 371

D'Arcy Hart, P., Pollock, T. M. & Sutherland, I. (1957) *Advanc. Tuberc. Res.*, **8**, 171

Edwards, L. B. & Dragsted, I. (1952) *Bull. Wld Hlth Org.*, **5**, 333

Edwards, L. B. & Palmer, C. E. (1953) *Lancet*, **1**, 53

Edwards, L. B., Palmer, C. E. & Magnus, K. (1953) *BCG vaccination*, Geneva (*World Health Organization: Monograph Series*, No. 12)

Edwards, L. B. & Tolderlund, K. (1952) *Bull. Wld Hlth Org.*, **5**, 245

Ferguson, R. G. (1955) *Studies in tuberculosis*, Toronto, University of Toronto Press

Frimodt-Møller, J. (1949) In: Tuberculosis Association of India, *Proceedings of the Seventh Tuberculosis Workers' Conference, held in Bombay*, New Delhi, p. 80

Frimodt-Møller, J. (1953) In: Tuberculosis Association of India, *Proceedings of the Tenth Tuberculosis Workers' Conference, held in Mysore*, New Delhi, p. 40

Frimodt-Møller, J., Mathew, K. T. & Barton, R. M. (1956) In: Tuberculosis Association of India, *Proceedings of the Thirteenth Tuberculosis Workers' Conference, held in Trivandrum*, New Delhi, p. 157

Great Britain, Medical Research Council (1956) *Brit. med. J.*, **1**, 413

Groth-Petersen, E., Knudsen, J. & Wilbek, E. (1957) *Nord. Med.*, **58**, 1361

Guld, J. (1953) *Acta tuberc. scand.*, **28**, 222

Hertzberg, G. (1952) In: Tuberculosis Association of India, *Proceedings of the Ninth Tuberculosis Workers' Conference, held in Lucknow*, New Delhi, p. 101

Lal, R. B., Majumdar, S. M. & Ahmed, J. (1943) *Indian med. Gaz.*, **78**, 477

Nissen Meyer, S., Hougen, A. & Edwards, P. (1951) *Publ. Hlth Rep. (Wash.)*, **66**, 561

Palmer, C. E. (1957) *Bull. int. Un. Tuberc.*, **27**, 106

Palmer, C. E., Shaw, L. W. & Comstock, G. W. (1958) *Amer. Rev. Tuberc.*, **77**, 877

Philip, S. (1952) In: Tuberculosis Association of India, *Proceedings of the Ninth Tuberculosis Workers' Conference, held in Lucknow*, New Delhi, p. 125

Rao, S. & Cochrane, R. G. (1943) *Indian med. Gaz.*, **78**, 191

Sikand, B. K. & Raj Narain (1952) In: Tuberculosis Association of India, *Proceedings of the Ninth Tuberculosis Workers' Conference, held in Lucknow*, New Delhi, p. 106

Tuberculosis Program, Public Health Service, USA (1955) *Bull. Wld Hlth Org.*, **12**, 31

Tuberkulose-Jahrbuch 1954/55, Berlin, 1957, pp. 126-131

Ukil, A. C. (1930) *Indian J. med. Res.*, **17**, 821

WHO Tuberculosis Research Office (1955a) *Bull. Wld Hlth Org.*, **12**, 63

WHO Tuberculosis Research Office (1955b) *Bull. Wld Hlth Org.*, **12**, 101

WHO Tuberculosis Research Office (1957) *Bull. Wld Hlth Org.*, **17**, 203

APPENDIX TABLE 1

TEST OF ADEQUACY OF SAMPLING FOR POPULATION MOVEMENT STUDY: COMPARISON OF SAMPLE POPULATIONS ACCORDING TO SEX AND AGE IN (A) 20 SAMPLE VILLAGES AND (B) 20% OF HOUSES IN VAYALPAD TOWN, WITH EXPECTED VALUES CALCULATED FROM ALL PERSONS TUBERCULIN TESTED AND/OR X-RAYED DURING FIRST FOUR ROUNDS OF INVESTIGATIONS

	Estimated birth year	Base population	Sample population		χ_2		Estimated birth year	Base population	Sample population		χ_2
			Observed	Expected					Observed	Expected	
(A) Villages	1950	1 452	840	851.4	0.153	(B) Vayalpad	1950	225	35	41.1	0.905
	1940-49	5 643					1940-49	919	147	167.9	2.593
	1930-39	3 240+105 [a]	400+8 [a]	401.4	0.109		1930-39	810+10 [c]	139+4 [c]	149.8	0.306
Males	1920-29	3 029	321	363.5	4.972	Males	1920-29	580	108	105.9	0.040
	1910-19	2 252	271	270.2	0.002		1910-19	316	62	57.7	0.317
	1900-09	1 664	196	199.7	0.069		1900-09	279	65	51.0	3.868
	1890-99	1 135	132	136.2	0.130		1890-99	138	26	25.2	0.025
	Before 1890	363	62	43.6	7.765		Before 1890	48	12	8.8	1.190
	Sub-total	18 883	2 230	2 266.0			Sub-total	3 325	598	607.4	
	1950	1 465	772	777.8	0.043		1950	215	40	39.3	0.014
	1940-49	5 017					1940-49	785	144	143.4	0.003
	1930-39	3 375+62 [a]	430+7 [a]	412.4	1.467		1930-39	732+2 [a]	137+4 [a]	134.1	0.358
Females	1920-29	3 417	427	410.0	0.705	Females	1920-29	530	94	96.8	0.082
	1910-19	1 830	227	219.6	0.249		1910-19	292	46	53.3	1.007
	1900-09	1 342	150	161.0	0.752		1900-09	222	42	40.5	0.052
	1890-99	701	81	84.1	0.114		1890-99	82	21	15.0	2.419
	Before 1890	202	32	24.2	2.514		Before 1890	29	9	5.5	2.583
	Sub-total	17 411	2 126	2 089.1			Sub-total	2 889	537	527.7	
Males and Females	Total	36 294	4 356	4 355.1	21.216 [b]	Males and Females	Total	6 214	1 135	1 135.1	15.762 [d]

[a] No age recorded. [b] df.: 13, P = 0.10-0.05 [c] No age recorded. [d] df. : 15, P = 0.40-0.30

APPENDIX TABLE 2a

BCG CONTROL TRIAL
SIZE OF INDURATION AFTER MANTOUX 5 TU REPEATED AT ROUNDS II, III AND IV IN PERSONS TESTED FOR THE FIRST TIME IN ROUND I AND HAVING INDURATION OF 4 mm AND LESS; TESTS READ AT 2, 3 OR 4 DAYS

Induration in mm	Vaccinated			Controls		
	Retested			Retested		
	Round II	Round III	Round IV	Round II	Round III	Round IV
0	41	50	22	94	109	49
1	—	—	—	—	—	—
2	95	79	55	176	170	121
3	81	45	56	84	88	96
4	37	37	46	39	48	78
5	120	48	57	157	58	73
6	131	76	56	120	74	32
7	74	57	44	65	48	42
8	46	32	33	26	23	16
9	14	22	19	13	10	12
10	19	32	18	12	11	10
11	9	11	13	8	5	10
12	18	19	14	9	6	5
13	8	5	9	4	4	3
14	3	5	7	3	1	9
15	10	12	4	4	7	2
16	4	3	7	1	7	1
17	2	7	6	1	—	4
18	1	3	3	—	4	4
19	1	2	2	—	—	2
20	1	6	2	—	5	3
21	—	—	4	—	1	—
22	1	—	1	—	2	—
23	—	1	1	—	1	2
24	—	—	—	—	—	1
25	—	1	—	1	2	1
26	—	—	1	—	—	—
27	—	—	—	—	—	—
28	—	—	—	—	—	1
29	—	—	—	—	—	—
30	—	—	—	—	—	—
Sub-total	716	553	480	817	684	577
Retests read after 5 days or more	214	147	112	290	164	130
Not retested	625	855	963	710	969	1110
Total	1 555	1 555	1 555	1 817	1 817	1 817
Mean	5.53	6.15	6.46	4.37	4.34	4.80
Standard deviation	3.27	4.42	4.41	3.01	4.05	4.16

APPENDIX TABLE 2b

BCG CONTROL TRIAL

SIZE OF INDURATION AFTER MANTOUX 5 TU REPEATED AT ROUNDS III AND IV IN PERSONS TESTED FOR THE FIRST TIME IN ROUND II AND HAVING INDURATION OF 4 MM AND LESS; TESTS READ AT 2, 3 OR 4 DAYS

Induration in mm	Vaccinated		Controls	
	Retested		Retested	
	Round III	Round IV	Round III	Round IV
0	16	7	48	25
1	—	—	—	—
2	30	24	92	63
3	19	16	58	31
4	12	17	19	36
5	26	13	27	27
6	28	27	14	13
7	29	28	8	13
8	20	28	9	6
9	12	5	4	2
10	13	11	2	3
11	7	12	3	3
12	5	6	3	2
13	11	8	1	1
14	4	5	—	2
15	2	—	2	—
16	3	1	1	1
17	3	4	—	2
18	1	2	—	2
19	—	—	—	—
20	—	1	1	—
21	—	—	—	—
22	—	1	—	—
26	—	—	—	1
30 +	—	—	1(32)	—
Sub-total	241	216	293	233
Retests read after 5 or more days	64	42	66	45
Not retested	341	388	427	508
Total	646	646	786	786
Mean	6.42	6.97	3.47	4.18
Standard deviation	3.97	3.66	3.42	3.61

APPENDIX TABLE 2c

BCG CONTROL TRIAL

SIZE OF INDURATION AFTER MANTOUX 5 TU REPEATED AT ROUND IV IN PERSONS TESTED FOR THE FIRST TIME IN ROUND III AND HAVING INDURATION OF 4 mm AND LESS; TESTS READ AT 2, 3 OR 4 DAYS

Induration in mm	Vaccinated	Controls
	Retested	Retested
	Round IV	Round IV
0	36	96
1	—	—
2	47	189
3	55	86
4	50	57
5	49	45
6	56	38
7	44	27
8	51	7
9	12	7
10	21	3
11	11	3
12	14	3
13	7	5
14	4	4
15	5	2
16	3	3
17	1	2
18	2	1
19	1	1
20	—	2
21	—	—
22	1	—
26	1	—
27	—	1
Sub-total	471	582
Retests read after 5 or more days	60	90
Not retested	605	825
Total	1 136	1 497
Mean	5.85	3.54
Standard deviation	3.79	3.40

APPENDIX TABLE 3

RESULTS OF BACTERIOLOGICAL EXAMINATION OF 1322 CASES WITH X-RAY ABNORMALITIES DETECTED DURING A SAMPLE SURVEY IN ANDHRA, MYSORE AND MADRAS STATES BY THE MOBILE X-RAY UNIT OF THE MADANAPALLE FIELD RESEARCH STATION IN 1955-57 (OUTSIDE THE MADANAPALLE STUDY AREA)

Code I	Code II	Code III : Impression regarding etiology																				
		1. Probably non-tuberculous			2. Probably tuberculous but inactive			3. Probably tuberculous, possibly active			4. Probably tuberculous and active			5. Etiology undetermined			Sub-total			Group total		
Type of pathology	Cavity	No.	TB+		No.	TB+		No.	TB+		No.	TB+		No.	TB+		No.	TB+		No.	TB+	
			No.	%		No.	%		No.	%		No.	%		No.	%		No	%		No.	%
2. Minimal	1. Nil	60	1	1.7	97	3	3.1	19	0		1	0		27	2	2.9	204	6	2.9			
parenchymal	2. Doubtful	1	0		..	..		1	1		..	..		..	..		2	1		206	7	3.4
lesion	3. Present	..	..		..	..		..	..		..	..		..	..		..	..				
3. Moderate	1. Nil	141	2	1.4	127	10	7.9	209	21	10.1	42	11	26.2	123	6	4.9	642	50	7.8			
parenchymal	2. Doubtful	7	0		3	0		38	5	13.2	19	5	26.3	9	0		76	10	13.2	753	70	9.3
lesion	3. Present	13	0		..	..		4	1	25.0	15	9	60.0	3	0		35	10	28.6			
4. Extensive	1. Nil	9	1	11.1	5	1	20.0	24	4	16.7	25	14	56.0	11	0		74	20	27.0			
parenchymal	2. Doubtful	2	0		..	..		15	2	13.3	53	31	58.5	2	1		72	34	47.2	218	106	48.6
lesion	3. Present	6	0		..	..		4	1	25.0	59	51	86.4	3	0		72	52	72.2			
5. Lobar pneumonia	—	3	0		..	..		..	..		..	..		2	0		5	0				
6. Atelectasis	—	1	0		2	0		3	0		..	..		5	0		11	0				
7. Fibrotic scar	—	6	0		12	2	16.7	..	..		..	..		2	0		20	2	14.3			
8. Hilar adenitis	—	1	0		9	0		4	0		..	..		7	0		21	0				
9. Pleural scar	—	..	..		16	0		3	0		..	..		0	0		19	0				
10. Pleural effusion (small)	—	..	..		5	0		4	0		..	..		2	0		11	0		145	6	4.1
11. Pleural effusion (moderate or extensive)	—	1	1		1	0		4	0		2	0		1	0		9	1	11.1			
12. Pneumothorax	—	..	..		..	..		..	..		..	..		..	..		..	..				
13. Cardiovascular diseases	—	34	3		..	..		..	..		..	..		4	0		38	3	7.9			
14. Operated	—	..	..		1	0		..	..		..	..		..	..		1	0				
15. Special pathology	—	5	0		..	..		..	..		..	..		5	0		10	0				
Total	—	290	8	2.8	278	16	5.8	332	35	10.5	216	121	56.3	206	9	4.4	1 322	189	14.3	1 322	189	14.3

APPENDIX TABLE 4

TRANSCRIPTION TABLE FOR PUNCH CARDS FROM X-RAY CODES TO A SIMPLIFIED SYSTEM OF X-RAY CLASSIFICATION [a]

I. Type of Pathology	II. Cavity	III. Etiology [b] 1.	2.	3.	4.	5.
2. Minimal parenchymal lesions	Not seen	C	C	B	A3	B
" " "	Doubtful	C	—	B	—	—
" " "	Present	—	—	—	—	—
3. Moderate parenchymal lesions	Not seen	C	B	B	A3	B
" " "	Doubtful	C	B	B	A3	B
" " "	Present	B	—	A3	A2	B
4. Extensive parenchymal lesions	Not seen	B	A3	A3	A2	B
" " "	Doubtful	B	—	A3	A2	B
" " "	Present	A3	—	A2	A1	A3
5. Lobar pneumonia	Not seen	B	—	—	—	B
6. Atelectasis	"	C	C	B	A3	B
7. Fibrotic scar	"	C	C	—	—	B
8. Hilar adenitis	"	C	C	B	A3	B
9. Pleural scar	"	—	C	B	—	—
10. Pleural effusion, small	"	C	C	B	A3	B
11. Pleural effusion, moderate or extensive	"	B	B	B	A3	B
12. Pneumothorax	"	C	C	B	A3	B
13. Cardiovascular disease	"	C	—	—	—	B
14. Operated (thoracoplasty, resection, etc.)	"	C	—	—	—	B
15. Special pathology	"	C	—	—	—	B

[a] A1. Advanced pulmonary tuberculosis with cavity
A2. Moderately advanced, most probably active tuberculosis
A3. Moderately advanced tuberculosis, possibly active
B. Probably tuberculous lesions but inactive
C. Possibly tuberculous lesion but clinically insignificant

[b] 1. Probably non-tuberculous
2. Probably tuberculous but inactive
3. Probably tuberculous, possibly active
4. Probably tuberculous and active
5. Undecided

APPENDIX TABLE 5

CASES FOUND DURING FIRST MASS X-RAY SURVEY 1950-51 ACCORDING TO SEX, AGE, TYPE OF PATHOLOGY AND METHOD OF DETECTION

Age	Base population	"Spontaneous" cases							Number X-rayed	Detected by mass miniature X-ray						
		Pathology [a]								Pathology [a]						
		A1	A2	A3	B	C	D	E		A1	A2	A3	B	C	D	E
Males																
0-4	2 685	—	—	—	—	—	—	—	278	—	—	—	1	—	—	—
5-9	2 832	—	—	—	—	—	—	—	1 731	—	—	1	2	4	2	4
10-14	2 668	1	—	—	—	—	—	—	1 864	—	—	—	3	4	1	3
15-19	1 382	—	—	—	—	—	—	—	995	—	—	—	3	5	2	4
20-29	2 862	1	1	1	1	—	—	—	1 956	2	4	3	13	11	6	3
30-39	2 692	2	—	1	—	—	—	—	1 683	7	1	3	22	27	5	1
40-49	1 884	2	—	—	—	—	—	—	1 227	3	2	7	36	26	3	4
50-59	1 443	3	—	—	—	—	—	—	938	—	4	8	24	25	6	2
60 +	1 160	1	—	—	—	—	—	—	628	—	2	6	39	24	4	5
Not recorded	142	—	—	—	—	—	—	—	13	—	—	—	—	—	—	—
Total	19 740	11	1	2	1	—	—	—	11 313	12	13	28	143	126	29	26
Females																
0-4	2 612	—	—	—	—	—	—	—	220	—	—	—	—	—	1	—
5-9	2 452	—	—	—	—	—	—	—	1 642	—	—	1	7	4	2	2
10-14	1 912	—	—	—	—	—	—	—	1 330	—	—	2	1	3	1	4
15-19	1 331	—	—	—	—	—	—	—	751	1	—	—	5	4	2	3
20-29	3 368	—	—	—	1	—	—	—	2 165	2	—	—	16	9	3	6
30-39	2 257	1	—	—	—	—	—	—	1 620	2	1	1	17	11	2	8
40-49	1 521	1	—	—	—	—	—	—	1 077	1	1	4	7	19	6	3
50-59	1 201	—	—	—	—	—	—	—	597	1	3	5	14	19	3	8
60 +	723	—	—	—	—	—	—	—	273	—	—	1	8	9	4	4
Not recorded	32	—	—	—	—	—	—	—	5	—	—	—	—	—	—	—
Total	17 409	2	—	—	1	—	—	—	9 680	7	5	14	75	78	24	38

[a] For X-ray categories, see footnote [a] to Table 22, page 110.

APPENDIX TABLE 6

FATE OF X-RAY ABNORMALS:* CASES DETECTED DURING ROUNDS I, II AND III BY MASS MINIATURE X-RAY EXAMINATIONS

Category according to first X-ray [a]	Round in which detected	Number cases	Person-observation years	Category [a] on first significant change in condition							
				Died	Left or lost	A1	A2	A3	B	C	Nil
A1	I	19	29.95	11	0	—	1	1	4	0	1
	II	10	16.90	4	0	—	0	1	0	0	0
	III	2	1.43	0	0	—	0	0	1	0	0
	Total	31	48.28	15	0	—	1	2	5	0	1
A2	I	18	33.18	5	1	2	—	3	3	1	0
	II	4	5.08	3	0	1	—	0	0	0	0
	III	6	3.94	0	1	0	—	2	1	0	1
	Total	28	42.20	8	2	3	—	5	4	1	1
A3	I	42	103.89	9	2	1	2	—	5	1	3
	II	12	23.11	1	0	1	0	—	1	1	1
	III	0	..	..	..	..	—	—	..	..	..
	Total	54	127.02	10	2	2	2	—	6	2	4
B	I	218	543.27	12	18	7	11	15	—	19	46
	II	102	185.03	8	2	2	4	6	—	13	11
	III	58	39.78	3	3	1	3	1	—	6	7
	Total	378	768.08	23	23	10	18	22	—	38	64
C	I	204	478.44	8	34	1	1	4	26	—	38
	II	83	149.86	6	9	0	1	0	8	—	22
	III	48	30.81	0	10	0	0	0	0	—	2
	Total	335	659.11	14	53	1	2	4	34	—	62

* Annual incidence per 1000 for each group total is given in Table 26, page 116.

[a] For X-ray categories, see footnote [a] to Table 22, page 110.

APPENDIX TABLE 7

PERSONS WITH NORMAL CHEST X-RAY AT EACH ROUND OF X-RAY EXAMINATION ACCORDING TO SEX AND AGE, AND NUMBER OF CASES DETECTED EITHER ON ACCOUNT OF SYMPTOMS OR BY A SUBSEQUENT MASS MINIATURE X-RAY EXAMINATION

Age	Males									Females								
	Number X-rayed	"Spontaneous" cases				Number X-rayed	Cases detected by X-ray				Number X-rayed	"Spontaneous" cases				Number X-rayed	Cases detected by X-ray			
		A	B	C	D [a]		A	B	C	D [a]		A	B	C	D [a]		A	B	C	D [a]
I. Normal X-ray at Round I, second X-ray at Round II (average observation period: 14.8 months):																				
	Rd. I					*Rd. II*					*Rd. I*					*Rd. II*				
0-	277	—	—	—	—	159	—	—	—	—	219	—	—	—	—	129	—	1	—	—
5-	1722	—	—	—	1	1145	—	1	1	—	1628	—	—	—	—	1084	—	1	—	—
10-	1856	1	—	—	1	1000	—	2	—	—	1323	—	—	—	—	745	—	—	1	—
15-	985	—	1	—	—	507	—	1	3	—	739	—	—	—	—	336	—	—	—	—
20-	1917	—	—	—	—	965	1	—	2	3	2135	1	—	1	—	991	—	1	1	1
30-	1618	—	—	—	—	765	1	4	3	—	1586	—	—	—	—	860	—	1	3	—
40-	1150	1	1	—	1	574	1	4	6	—	1039	—	—	—	1	522	2	4	2	—
50-	871	—	1	—	—	428	—	5	4	1	552	—	—	—	—	272	—	2	3	—
60+	553	—	—	—	—	245	1	2	2	1	251	—	—	—	—	105	—	—	2	—
?	13	—	—	—	—	—	—	1	—	—	5	—	—	—	—	—	—	—	—	—
Total	10962	2	3	—	3	5788	4	20	21	5	9477	1	—	1	1	5044	2	10	12	1
II. Normal X-ray at Round I, second X-ray at Round III (average observation period: 33.7 months):																				
	Rd. I					*Rd. III*					*Rd. I*					*Rd. III*				
0-	118	—	—	—	—	36	—	—	—	—	90	—	—	—	—	36	—	—	—	—
5-	577	—	—	—	—	192	—	—	—	—	544	—	—	—	—	178	—	—	—	—
10-	856	—	—	—	1	234	—	—	2	—	578	—	—	—	—	156	—	2	—	—
15-	478	1	—	—	—	125	1	—	1	—	403	1	—	—	—	96	—	1	1	1
20-	952	1	1	1	—	248	—	1	2	—	1144	—	—	—	—	311	—	2	1	—
30-	853	—	—	—	—	230	—	1	1	—	726	—	—	—	—	193	1	—	—	1
40-	576	—	—	—	—	161	—	1	1	—	517	—	—	—	—	142	—	—	1	—
50-	443	—	1	—	—	120	—	2	—	2	280	—	—	—	—	72	—	—	—	—
60+	308	—	—	—	—	63	—	1	2	—	146	—	—	—	—	36	—	—	—	—
?	13	—	—	—	—	1	—	—	—	—	5	—	—	—	—	—	—	—	—	—
Total	5174	2	2	1	1	1410	1	6	9	2	4433	1	—	—	—	1220	1	5	3	2
III. Normal X-ray at Round I, second X-ray at Round IV (average observation period: 42.3 months):																				
	Rd. I					*Rd. IV*					*Rd. I*					*Rd. IV*				
0-	82	—	—	—	—	16	—	—	—	—	54	—	—	—	—	10	—	—	—	—
5-	388	—	—	—	—	68	—	—	—	—	368	—	—	—	—	42	—	—	—	—
10-	624	—	1	—	—	72	—	—	—	—	425	—	—	—	—	25	—	—	—	—
15-	356	1	—	—	—	55	—	—	—	—	310	—	1	—	—	28	—	—	—	—
20-	730	—	—	—	—	97	—	1	—	—	847	—	—	—	—	92	—	—	2	—
30-	646	—	—	—	—	87	—	—	—	—	542	—	—	1	—	65	—	—	—	—
40-	443	—	—	—	—	69	—	—	—	—	384	—	—	—	—	39	—	1	—	—
50-	342	—	—	—	—	37	—	—	1	—	227	—	—	—	—	11	—	—	—	—
60+	275	—	1	—	—	28	—	2	—	1	118	—	—	—	—	5	—	—	—	—
?	12	—	—	—	—	—	—	—	—	—	5	—	—	—	—	1	—	—	—	—
Total	3898	1	2	—	—	529	—	3	1	1	3280	—	1	1	—	318	—	1	2	—

[a] For X-ray categories, see footnote [a] to Table 22, page 110.

APPENDIX TABLE 7 (*continued*)

Age	Males									Females								
	Number X-rayed	"Spontaneous" cases				Number X-rayed	Cases detected by X-ray				Number X-rayed	"Spontaneous" cases				Number X-rayed	Cases detected by X-ray			
		A	B	C	D [a]		A	B	C	D [a]		A	B	C	D [a]		A	B	C	D [a]
IV. Normal X-ray at Rounds I and II, third X-ray at Round III (average observation period between Rounds II and III: 18.9 months):																				
	Rd. II					*Rd. III*					*Rd. II*					*Rd. III*				
0-	159	—	—	—	—	102	—	—	—	—	128	—	—	—	—	92	—	—	—	—
5-	1143	—	—	—	—	677	—	—	—	1	1083	—	—	—	—	686	—	2	—	—
10-	998	—	—	—	—	593	—	—	—	—	744	—	—	—	—	415	—	—	—	—
15-	503	—	—	—	—	258	—	—	—	—	366	—	1	—	—	183	—	2	—	—
20-	959	1	—	—	—	513	—	1	—	—	988	—	—	1	—	497	1	1	—	—
30-	757	—	—	—	—	390	—	2	—	1	856	1	—	—	—	487	—	1	—	—
40-	563	—	—	—	—	302	—	3	—	—	514	—	1	—	—	286	—	—	—	—
50-	418	—	1	—	—	223	—	1	2	—	267	—	—	—	—	135	1	—	—	—
60 +	239	1	—	—	—	109	—	—	1	—	103	—	—	—	—	47	—	—	—	—
Total	5739	2	1	—	—	3167	—	7	3	2	5049	1	2	1	—	2828	2	6	—	—
V. Normal X-ray at Rounds I, II and III, fourth and last X-ray at Round IV (average observation period between Rounds III and IV: 8.6 months):																				
	Rd. III					*Rd. IV*					*Rd. III*					*Rd. IV*				
0-	102	—	—	—	—	55	—	—	—	—	92	—	—	—	—	52	—	—	—	—
5-	676	—	—	—	—	399	—	—	—	—	684	—	—	—	—	386	—	—	—	—
10-	593	—	—	—	—	344	—	1	—	—	415	—	—	—	—	211	—	—	—	—
15-	258	—	—	—	—	140	1	1	1	—	181	—	1	—	—	90	—	1	—	—
20-	512	—	—	—	—	273	—	—	—	—	495	—	—	—	—	248	—	—	—	—
30-	387	—	—	—	—	218	—	—	2	—	486	—	—	—	—	249	1	2	2	—
40-	299	—	—	—	—	169	—	—	—	—	286	—	—	—	—	131	—	1	—	—
50-	220	—	—	—	—	117	1	—	—	—	134	—	—	—	—	61	—	—	—	—
60 +	108	—	—	—	—	53	—	—	—	—	47	—	—	—	—	20	—	—	—	—
Total	3155	—	—	—	—	1768	2	2	3	—	2820	—	1	—	—	1448	1	4	2	—
VI. Normal X-ray at Rounds I and II, third and last X-ray at Round IV (average observation period between Rounds II and IV: 27.5 months):																				
	Rd. II					*Rd. IV*					*Rd. II*					*Rd. IV*				
0-	58	—	—	—	—	14	—	—	—	—	35	—	—	—	—	11	—	—	—	—
5-	465	—	—	—	—	111	—	1	—	—	390	—	—	—	—	116	—	—	—	—
10-	408	—	—	—	—	116	—	—	—	—	325	—	—	—	—	59	—	—	—	—
15-	244	—	—	—	—	66	—	—	—	—	150	—	—	—	—	28	—	—	—	—
20-	441	—	—	—	—	132	—	1	1	—	483	—	—	—	—	94	—	—	—	—
30-	379	—	—	—	—	102	—	—	—	—	355	—	—	—	—	82	—	—	—	1
40-	275	—	—	—	—	70	—	1	—	—	209	—	—	—	—	44	—	—	1	—
50-	203	—	—	—	—	44	—	—	—	—	120	—	—	—	—	13	—	—	—	—
60 +	149	—	—	—	—	35	—	—	1	1	48	—	—	—	—	11	—	—	—	—
Total	2622	—	—	—	—	690	—	3	2	1	2115	—	—	—	—	458	—	—	1	1
VII. Normal X-ray at Rounds I and III, third and last X-ray at Round IV (average observation period between Rounds III and IV: 8.6 months):																				
	Rd. III					*Rd. IV*					*Rd. III*					*Rd. IV*				
0-	36	—	—	—	—	18	—	—	—	—	36	—	—	—	—	17	—	—	—	—
5-	192	—	—	—	—	91	—	—	—	—	178	—	—	—	—	53	—	—	—	—
10-	232	—	—	—	—	87	—	2	—	—	154	—	—	—	—	44	—	—	—	—
15-	123	—	—	—	—	53	—	1	—	—	93	—	—	—	—	28	—	—	—	—
20-	245	—	—	—	—	85	—	—	—	—	308	—	—	—	—	102	—	—	—	—
30-	228	—	—	—	—	89	—	—	1	—	191	—	—	—	—	75	—	—	—	—
40-	159	—	—	—	—	59	—	—	2	—	141	—	—	—	—	49	—	1	—	1
50-	116	—	—	—	—	43	—	2	1	—	72	—	—	—	—	18	—	—	—	—
60 +	60	—	—	—	—	19	—	—	—	—	36	—	—	—	—	9	—	—	—	—
?	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	1392	—	—	—	—	544	—	5	4	—	1209	—	—	—	—	395	—	1	—	1

[a] For X-ray categories, see footnote [a] to Table 22, page 110.

APPENDIX TABLE 7 (*concluded*)

Age	Males									Females								
	Number X-rayed	"Spontaneous" cases				Number X-rayed	Cases detected by X-ray				Number X-rayed	"Spontaneous" cases				Number X-rayed	Cases detected by X-ray			
		A	B	C	D[a]		A	B	C	D[a]		A	B	C	D[a]		A	B	C	D[a]
VIII. Normal X-ray at Round II, second X-ray at Round III (average observation period: 18.9 months):																				
	Rd. II					*Rd. III*					*Rd. II*					*Rd. III*				
0-	93	—	—	—	—	55	—	—	—	—	54	—	—	—	—	29	—	—	—	—
5-	670	—	—	—	—	314	—	—	1	—	560	—	—	—	—	320	—	—	—	—
10-	458	—	—	—	—	190	—	—	—	—	296	—	—	—	—	138	—	—	—	—
15-	174	—	—	—	—	57	—	—	—	—	183	—	—	—	—	67	—	—	—	—
20-	396	1	—	—	—	146	—	—	1	—	482	—	—	—	—	180	1	—	—	—
30-	300	—	—	—	1	105	—	1	1	1	277	—	—	—	—	116	—	—	—	—
40-	227	—	—	—	—	71	—	1	—	1	148	—	—	—	—	71	—	—	—	—
50-	144	—	—	—	—	60	—	—	—	—	142	—	—	—	—	60	—	—	—	—
60+	140	—	—	—	—	46	—	—	—	—	96	—	—	—	—	22	—	—	2	—
?	3	—	—	—	—	—	—	—	—	—	2	—	—	—	—	—	—	—	—	—
Total	2605	1	—	—	1	1044	—	2	3	2	2240	—	—	—	—	1003	1	—	2	—
IX. Normal X-ray at Rounds II and III, third and last X-ray at Round IV (average observations period: 8.6 months):																				
	Rd. III					*Rd. IV*					*Rd. III*					*Rd. IV*				
0-	55	—	—	—	—	28	—	1	—	—	29	—	—	—	—	20	—	—	—	—
5-	313	—	—	—	—	173	—	—	—	—	320	—	—	—	—	179	—	—	—	—
10-	190	—	—	—	—	94	—	—	—	—	138	—	—	—	—	51	—	—	—	—
15-	57	—	—	—	—	25	—	—	—	—	67	—	—	—	—	24	—	—	—	—
20-	145	—	—	—	1	64	—	—	—	—	179	—	—	—	—	92	—	—	1	—
30-	102	—	—	—	—	52	—	—	—	—	116	—	—	—	—	35	—	—	—	—
40-	69	—	—	—	—	26	—	—	—	—	71	—	—	—	—	28	—	—	—	—
50-	60	—	—	—	—	20	—	—	—	—	60	—	—	—	—	28	—	—	1	—
60+	46	—	1	—	—	21	—	1	—	—	20	—	—	—	—	4	—	—	—	—
Total	1037	—	1	—	1	503	—	2	—	—	1000	—	—	—	—	461	—	—	2	—
X. Normal X-ray at Round II, second and last X-ray at Round IV (average observation period: 27.5 months):																				
	Rd. II					*Rd. IV*					*Rd. II*					*Rd. IV*				
0-	38	—	—	—	—	10	—	—	—	—	25	—	—	—	—	4	—	—	—	—
5-	356	—	—	—	—	72	—	—	—	—	240	—	—	—	—	56	—	—	—	—
10-	268	—	—	—	—	43	—	—	—	1	158	—	—	—	—	21	—	—	—	—
15-	117	—	—	—	—	19	—	—	—	—	116	—	—	—	—	12	—	—	—	—
20-	250	—	—	—	—	36	—	—	—	—	302	—	—	—	—	41	—	—	—	—
30-	195	1	—	—	—	40	—	—	—	—	161	—	—	—	—	23	—	1	—	—
40-	156	—	—	—	—	35	1	1	1	—	77	—	—	—	—	14	—	—	—	—
50-	84	—	—	1	—	11	—	—	—	—	82	—	—	—	—	6	—	—	—	—
60+	94	—	—	—	—	16	—	—	—	—	74	—	—	—	—	15	—	—	—	—
?	3	—	—	—	—	—	—	—	—	—	2	—	—	—	—	—	—	—	—	—
Total	1561	1	—	1	—	282	1	1	1	1	1237	—	—	—	—	192	—	1	—	—
XI. Normal X-ray at Round III, second and last X-ray at Round IV (average observation period: 8.6 months):																				
	Rd. III					*Rd. IV*					*Rd. III*					*Rd. IV*				
0-	131	—	—	—	—	52	—	—	—	—	129	—	—	—	—	45	—	—	—	—
5-	585	—	1	—	—	254	—	1	1	—	492	—	—	—	—	209	—	—	—	1
10-	325	—	—	—	—	148	—	1	—	—	232	—	—	—	—	92	—	1	—	—
15-	147	—	—	—	—	56	—	—	—	—	165	—	—	—	—	43	—	—	—	—
20-	288	—	—	—	—	88	—	1	—	—	356	—	—	—	—	119	—	—	—	—
30-	239	—	—	—	—	104	—	—	1	—	182	—	—	—	—	63	—	—	—	—
40-	161	—	1	—	—	53	—	—	1	1	93	—	—	—	—	23	—	—	1	—
50-	102	—	—	—	—	30	—	—	—	—	94	—	—	—	—	26	—	1	—	—
60+	85	—	—	—	—	25	—	—	—	—	76	—	—	—	—	22	—	—	1	—
?	8	—	—	—	—	—	—	—	—	—	6	—	—	—	—	—	—	—	—	—
Total	2071	—	2	—	—	810	—	3	3	1	1825	—	—	—	—	642	—	2	2	1

[a] For X-ray categories, see footnote [a] to Table 22, page 110.

APPENDIX TABLE 8

CASES WITH NON-TUBERCULOUS PATHOLOGY FOUND AT FIRST MASS MINIATURE X-RAY SURVEY AND ENTERED UNDER CATEGORIES D AND E IN TABLE 22*

	Males						Females					
	0-9	10-19	20-29	30-49	50 +	Total	0-9	10-19	20-29	30-49	50 +	Total
Category D:												
Pneumonia	—	—	2	1	—	3	—	2	1	1	—	4
Lung abscess	—	—	—	2	3	5	—	—	—	—	—	—
Bronchiectases	1	1	4	4	4	13	2	1	1	6	7	17
Atelectasis	—	1	—	—	—	1	—	—	—	—	—	—
Cystic disease (including hydatid cyst)	1	—	—	1	1	3	1	—	1	1	—	3
Eosinophilia, tropical	—	—	—	—	1	1	—	—	—	—	—	—
Empyema, pleural	—	1	—	—	1	2	—	—	—	—	—	—
Total	2	3	6	8	10	29	3	3	3	8	7	24
Category E:												
Heart disease	3	6	3	2	7	21	2	7	6	10	12	37
Liver abscess	—	—	—	—	—	—	—	—	—	1	—	1
Abnormal diaphragm	—	1	—	—	—	1	—	—	—	—	—	—
Tumour, mediastinal	1	—	—	—	—	1	—	—	—	—	—	—
Fluorosis, costal	—	—	—	3	—	3	—	—	—	—	—	—
Total	4	7	3	5	7	26	2	7	6	11	12	38

* Page 110.