PULMONARY PARAGONIMIASIS AND TUBERCULOSIS IN SORSOGON, PHILIPPINES

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Abstract. The clinical epidemiology of pulmonary paragonimiasis and tuberculosis was investigated in a known endemic municipality of Sorsogon, Philippines. Records of diagnosed tuberculosis patients on treatment and follow up at the local Rural Health Unit over a two year period from 1993 to 1994 were reviewed to provide an overview of pulmonary tuberculosis in the area, specifically to describe the population at risk, the basis for diagnosis and the proportion of case notification who were sputum negative. Patients from the same group of individuals as well as undiagnosed tuberculosis patients with productive cough, fever with chest and/or back pain, or hemoptysis were examined to look into clinical manifestations, duration of symptoms, history of crab-eating and sputum examination results for acid-fast bacilli and Paragonimus. There was difficulty in determining the number of non-responders as the records did not have any provision for the recording of such.

Annual tuberculosis case notification rates for the two years (374 and 401 per 100,000 population) were higher than the national figure in 1991 (325 per 100,000 population) indicating that tuberculosis is still a major health problem in the area and tuberculosis control efforts may have to be more aggressive to better contain the disease. Twenty-six out of 160 individuals surveyed were sputum smear positive for Paragonimus. Paragonimiasis rates were not significantly different in the two groups (15.6% vs 16.9%, respectively) indicating that there is a need for routine sputum examination for Paragonimus which is not available at present. Only six patients surveyed were sputum smear positive for acid-fast bacilli.

A high index of suspicion is necessary to diagnose paragonimiasis and to be able to differentiate it from tuberculosis. The diagnosis may be suggested by a patient’s place of origin being a known endemic area, a long period of chronic cough and the habit of eating raw or insufficiently cooked crabs or crayfish.

Laboratories in endemic areas should have the capacity to differentiate between the two infections by being able to provide the routine laboratory procedures necessary for definitive diagnosis and treatment.

INTRODUCTION

Paragonimiasis and tuberculosis are public health problems which overlap in many countries in the world. Paragonimiasis is generally considered of little significance especially with limited information available resulting in the continuing lack of awareness and inability to properly diagnose and manage affected individuals (Toscano et al, 1995). In contrast, tuberculosis remains as an important public health issue which is known to have a considerable impact on the health and productivity of affected people and their families. The focal distribution of paragonimiasis is closely related to the cultural habits of different groups of people who eat raw or insufficiently cooked crabs or crayfish. About 22 million people around the world are estimated to be infected with Paragonimus. (WHO, 1993) On the other hand, the geographical distribution of tuberculosis is global with about 1.7 billion people affected.

Paragonimiasis, or lung fluke reported to be endemic in the Philippines by Musgrave in 1907. Human disease is known to be caused by 2 species: Paragonimus westermani, which is present in all endemic areas of the country; and, P. philippinensis, which was described as a new species by Miyazaki in 1978 and is known to be present in Jaro, Leyte.

Results of limited surveys to determine the prevalence rates of paragonimiasis are available and
provide a limited picture of the extent of the problem. From 1973 to 1975, in three municipalities in Leyte, Cabrera et al. found 22 infected persons (0.57%) in 3,866 individuals examined by sputum examination. In 1974, using both sputum and stool examination, 21 persons (12.5%) out of 168 individuals examined were found positive for Paragonimus eggs. In a survey in 1977-1978 covering 9 municipalities in Sorsogon Province, 13 sputum positive persons (0.15%) were found among 8,779 individuals examined (Cabrera, 1979).

The provinces of Sorsogon and Leyte are considered to be the main endemic areas. Based upon place of origin of individual cases, other areas, including areas in Mindanao, have also been considered endemic, although no surveys have been reported (Micozzi and Ongchangco, 1980). Individual cases of paragonimiasis have been reported from Batanes, Camarines Norte, Camarines Sur, Albay, Samar, Mindoro, Cebu, Negros, Cavite and Metro Manila (Cabrera, 1979). A recently reported endemic area is Basilan (Jueco et al., 1992).

In Sorsogon Province, insufficiently cooked freshwater mountain crabs, the known intermediate host of Paragonimus westermani are eaten as a delicacy called kinagang, which is prepared by wrapping the crabs with banana leaves and quickly boiling the preparation in coconut milk. The crabs are not boiled for a prolonged period of time to avoid drying up the natural juices.

Paragonimiasis has been masked and confused with the diagnosis of tuberculosis for many years. It is important to note that many countries which are endemic for paragonimiasis are among those with the highest incidence rates of tuberculosis. In the Western Pacific Region, where many countries are endemic for paragonimiasis, the total case notification was 65 per 100,000 in 1992. In the Philippines alone, the notification rate was 324.9 in 1991, well above the other countries in the region like China (32.1 in 1991) (Zhong et al., 1981), Laos (45.0 in 1991 and 6.5 in 1992) and Republic of Korea (108.8 in 1992) (Shim et al., 1991). The rates of notification of active tuberculosis cited earlier are generally underestimated due to the poor health service coverage.

To demonstrate the overlap of pulmonary paragonimiasis and to determine the status of the two entities in the Philippines, a municipality in Sorsogon Province was the site of a study involving “TB patients”, who are diagnosed patients by the Rural Health Unit (RHU) according to the National Tuberculosis Control Programme (NTP) and who are on follow up at the RHU, and “non-TB patients”, who presented with productive cough for two weeks or more, fever for two weeks or more with chest or back pain, or hemoptysis at the time of the survey and who have not been labeled as having tuberculosis by the RHU.

The following were the objectives of the study:

1. To prepare a general overview of pulmonary tuberculosis in Irosin, Sorsogon.
   1.1 To determine the current number of TB patients registered or annual number of case notification.
   1.2 To describe the population at risk.
   1.3 To determine the basis for diagnosis.
   1.4 To determine the proportion of case notification who are sputum negative.

2. To compare a group of “TB patients” with a group of “non-TB patients”.
   2.1 To compare the clinical manifestations of the two groups.
   2.2 To compare the duration of symptoms of the two groups.
   2.3 To compare the history of crab-eating habits of the two groups.
   2.4 To compare the sputum examination results for acid-fast bacilli and Paragonimus in the two groups.

**MATERIALS AND METHODS**

**Study site**

The municipality of Irosin, in Sorsogon Province, is an agricultural community some 630 km southeast of Manila. It is surrounded by rolling hills and mountains with numerous rivers and streams cutting across its terrain. It has a mild tropical climate with abundant rainfall all year round. The main agricultural products are rice, copra and abaca. Administratively and geographically, the municipality is divided into 28 barangays. In 1990, Irosin had a population of 37,887.
Pulmonary tuberculosis was the third leading cause of mortality in the municipality of Irosin and the province of Sorsogon in 1993. The National Tuberculosis Control Program (NTP) is implemented in the province with the local RHUs responsible for case finding, treatment and surveillance. Symptomatic patients consult the RHU and are defined as patients with one or more of the following symptoms: productive cough for 2 weeks or more with chest or back pain; and, hemoptysis. Sputum collection and smear examination are done at the RHU, but RHU midwives may collect sputum from the field as well and forward specimens to the RHU for processing and examination. Patients found to be positive for tubercle bacilli are started on short course chemotherapy (SCC). Those who have negative smears are generally given symptomatic non-TB treatment for 10 days. With persistence of symptoms, they are advised repeat smear examination. Positives are likewise started on SCC, while negatives are advised to undergo chest x-ray examination. Those found to have cavitary lesions are started on SCC, while those with infiltrative lesions are given standard regimen (SR). The Clinical Treatment Card is used to keep track of all "TB patients".

Although there has never been any note of paragonimiasis in Irosin, the province of Sorsogon is known to be endemic for paragonimiasis having been of several epidemiologic surveys in the 1970s. In spite of many reported cases in the past, sputum examination for Paragonimus is unavailable in the whole province.

Patients and survey

Record of "TB patients" entered into the TB registry over a two year period from January 1993 to December 1994 were reviewed at the Irosin RHU. The same patients as well as wellas "non-TB patients" or individuals presenting with productive cough for two weeks or more, fever for two weeks or more with chest or back pain or hemoptysis but are not included in the registry were invited to participate in the survey which was conducted at the RHU and all nine peripheral health facilities or barangay health stations (BHS).

The survey was conducted in January 1995 and attempted to look into the patients' history, clinical manifestations, crab-eating habits, physical examination findings, results of sputum examination for acid-fast bacilli and Paragonimus. Patients consenting to participate in the study were interviewed, examined and asked to submit early morning sputum for acid fast staining and sputum examination for Paragonimus.

Laboratory examination for Paragonimus

Sputum examination for Paragonimus was performed by the research team from the Department of Parasitology, University of the Philippines, College of Public Health (UP-CPH) at the Health Research Field Station of the UP-CPH in Monbon, Irosin. An equal volume of 3% sodium hydroxide was added to the sputum specimen, after which the mixture was centrifuged, and the sediment was examined by light microscopy for Paragonimus eggs. Sputum smear examination by light microscopy following staining with the Ziehl-Neelsen method was done at the Department of Medical Microbiology, UP-CPH in Manila.

Data analysis

All data and information in the questionnaires and result forms were encoded in the computer with the use of Dbase version 3.0, and descriptive and analytical statistics were derived using Epi-Info version 5.0.

RESULTS

Records review

A total of 302 Clinical Treatment Cards were retrieved by the RHU and represented the same number of patients in the TB registry over a two year period. There were more cases entered into the registry in 1994 than in 1993 resulting in a higher case notification rate in 1994. The annual rates in Irosin are higher than the national figure in 1991 (Table 1).

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of patients in TB registry</th>
<th>Population</th>
<th>Case notification rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>145</td>
<td>38,806</td>
<td>374</td>
</tr>
<tr>
<td>1994</td>
<td>157</td>
<td>39,118</td>
<td>401</td>
</tr>
</tbody>
</table>
Patients' ages ranged from 4 to 80 with a mean age of 43.5 years (SD = 16.0). Majority of the patients (88.4%) were between the ages of 21 and 70 years. There were more males than females (63.6% vs 36.4%, respectively) (Fig 1). Forty one percent (42%) of the patients were engaged in economic activity at the time of enlistment, while 46% were unemployed and 11% were housewives. The rest had no information on occupation. Ninety-two percent (92%) of the patients were classified as new patients, while the rest had suffered from relapse (2%). The rest had resumed treatment, had transferred from another site, or had no information available.

**Fig 1 - Age and sex distribution of patients in TB registry Irosin RHU, 1993-1994. (n = 302)**

Patients included in the registry were from almost all barangays except Liang where no patient was reported over the two year period. The top 5 barangays with the most number of patients were Gabao, Bacolod, San Julian, Macawayan and Gulang-Gulang (Fig 2a and 2b).

![Map showing distribution of TB cases Irosin, Sorsogon, 1993.](attachment:map1.png)

**Fig 2a - Map showing distribution of TB cases Irosin, Sorsogon, 1993.**

Before treatment, sputum positives made up 33.4% of the patients in the registry, while majority (64.6%) of cases were chest x-ray positive. Among the chest x-ray positives, cavitary lesions were about twice as common as the infiltrative lesions. Sputum negatives made up 45.7% of cases (Table 2).

**Table 2**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>1993</th>
<th>1994</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum positive (+)</td>
<td>59</td>
<td>42</td>
<td>101 (33.4)</td>
</tr>
<tr>
<td>negative (-)</td>
<td>53</td>
<td>85</td>
<td>138 (45.7)</td>
</tr>
<tr>
<td>Chest x-ray cavitary</td>
<td>51</td>
<td>81</td>
<td>132 (43.7)</td>
</tr>
<tr>
<td>infiltrative</td>
<td>33</td>
<td>30</td>
<td>63 (20.9)</td>
</tr>
<tr>
<td>no information</td>
<td>0</td>
<td>2</td>
<td>2 (0.7)</td>
</tr>
</tbody>
</table>

**Field survey**

A total of 160 individuals consented to participate in the survey. Of these, 77 (48%) were “TB patients” earlier diagnosed by the RRU in the past two year period and had Clinical Treatment Cards reviewed.
by the study team. The rest (83 or 52%) were not diagnosed to have TB by the RHU but had a history of productive cough for two weeks or more, fever for two weeks or more with chest or back pain, or hemoptysis, and were therefore referred to as “non-TB patients”.

Fig 3 shows the age and sex distribution of those seen during the survey. The youngest patient was 6 years old, while the oldest was 83 years old. The mean age was 48.6 years (SD = 15.9). Majority of the patients (87.5%) were between the ages of 21 and 70 years. There were more males than females as in the cases in the TB registry (53.8% vs 46.2%, respectively). Fifty-three percent (53%) of those surveyed were engaged in productive activity, while housewives comprised 31% and the unemployed made up 17% of those surveyed. The distribution of patients seen during the survey according to barangay of origin are shown in Fig 4. All barangays were represented in the survey except for Bolos, Liang and Salvacion.

Productive cough for at least two weeks was reported by 83% of individuals surveyed. Cough was the most common clinical manifestation reported. Mean duration of cough among “TB patients” was 53.7 months (range: <1 - 408 months; SD = 94.4), while mean duration among “non-TB patients” was 31.8 months (range <1 - 528 months; SD = 76.6). There was no significant difference between the mean duration of the two groups (p > 0.05). Over all, the mean duration of cough among all patients surveyed was 42.0 months (SD = 85.7) or 3.5 years.

Hemoptysis was reported by 42% of those surveyed with a mean duration of 47.9 months (range: <1 - 288 months; SD = 74.6) among the “TB group and a mean duration of 21.6 (range: <1 - 144; SD = 35.0). There was no significant difference between the mean duration of the two groups (p > 0.05).
Among all patients surveyed, the mean duration of hemoptysis was 34.7 months (SD = 59.3) or 2.9 years. All patients with hemoptysis also had concomitant cough.

Clinical manifestation and their corresponding frequencies are listed in Table 3. Both groups of patients reported similar signs and symptoms with easy fatigability, chest and/or back pain, dyspnea, headache as more common manifestations.

Table 3
Clinical manifestations reported by patients surveyed Irosin, Sorsogon, 1995.
(n = 160)

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>133 (83.1)</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>67 (41.9)</td>
</tr>
<tr>
<td>Fever</td>
<td>63 (39.4)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>65 (40.6)</td>
</tr>
<tr>
<td>Headache</td>
<td>88 (55.0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>125 (78.1)</td>
</tr>
<tr>
<td>Chest/back pain</td>
<td>123 (76.9)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>102 (63.8)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>88 (55.0)</td>
</tr>
</tbody>
</table>

On physical examination, 42.5% of those surveyed were found to have poor nutritional status, while 33.1% had abnormal chest findings notably rales or coarse breath sounds. Twenty-four percent (24%) or about one out of four patients seen had poor nutritional status and abnormal breath sounds.

An overwhelming majority (93.8%) or patients included in the survey admitted having the habit of eating crabs. Most crab-eaters (91.3%) readily admitted consuming well-cooked crabs, while only a few (6.0%) admitted eating raw or medium cooked crabs.

Laboratory findings

Twenty-six (26) individuals were found to be sputum positive for *Paragonimus* ova on single early morning sputum examination, giving a rate of 16.3%. Twelve patients were known "TB patients" (15.6%), while the other 14 were "non-TB patients" (16.9%).

The prevalence of paragonimiasis in both groups were not significantly different (p > 0.05).

There was variation in the color of the sputum collected from the paragonimiasis patients. Most specimens had a whitish to yellowish color (16), some were greenish (5), while only a few had a reddish to brownish color (3). There was no note of color of two sputum specimens positive for *Paragonimus* ova.

There were more males with paragonimiasis than females (17 vs 9, respectively), with patients distributed among all age groups more than 10 years old (Fig 6). The youngest case was 12 years old, while the oldest was 79 years old. More than half (15 out of 26) of the patients were engaged in productive activity, either attending school or doing economic activity.

Cough was manifested by 21 (80.8%) out of 26 cases, while hemoptysis was experienced by only 12 (46.2%). Mean duration of cough was 39.6 months (range: 1 - 348 months; SD = 75.1) or 3.3 years, while that of hemoptysis was 13.7 months (range: <1 - 36 months; SD = 14.2) or 1.1 years. All 12 patients had cough and hemoptysis concurrently. Other signs and symptoms in the order of frequency among the paragonimiasis patients were: chest and/or back pains (23), easy fatigability (21), dyspnea (17), headache (13), fever (10), weight loss (9) and anorexia (5).

On physical examination, only 9 (34.6%) out of the 26 paragonimiasis patients were noted to have poor nutritional status, while only 8 (30.8%) had
abnormal chest auscultatory (rales or coarse breath sounds). Furthermore, only 5 (19.2%) patients had both poor nutritional state and abnormal breath sounds.

As for crab-eating, 24 (92.3%) out of the 26 reported having such a history. The two remaining patients denied consumption of crabs.

Among “TB patients”, sputum examination results for *Paragonimus* were correlated with sputum examination results for tubercle bacilli before the start of treatment for TB or upon entry into the registry. Only 4 (33.3%) of the 12 patients were recorded by the RHU as sputum positive for tubercle bacilli, while 5 patients (41.7%) were actually sputum negative for tubercle bacilli. Of the 12 “TB patients” shown to have paragonimiasis, only 8 were noted to be chest x-ray positive in the registry records. Of these 8 positives, 2 had cavitory lesions, while 6 had infiltrative lesions. Only 6 patients out of 160 were found to be sputum smear positive for tubercle bacilli on single early morning sputum examination. This gives a rate of 3.8%. Both “TB” and “non-TB” groups each had 3 patients who were sputum positive with more males than females (5 vs 1, respectively). Four out of the 6 were engaged in economic activity.

One patient, a 34 year old male, unemployed, from Gulang-Gulang, who belonged to the “non-TB” group, was found positive for both *Paragonimus* eggs and tubercle bacilli during the survey. Clinically, he manifested with productive cough (4 years) with a recent onset of hemoptysis associated with chest and back pains and easy fatigability. He admitted consuming medium cooked crabs. On physical examination, he was poorly nourished with coarse breath sounds and rales all over both lung fields.

**DISCUSSION**

From local RHU data, it is clear that pulmonary tuberculosis remains as one of the more important causes of morbidity in Irosin. Annual case notification rates in 1993 and 1994 have shown higher rates in the municipality compared with the national figures. With the consideration that these available data are actually underestimates because of limited case finding especially in the more peripheral areas and that the actual status is actually worse, it may be said that tuberculosis control efforts may have to be more aggressive to better contain the disease.

The algorithm for the diagnosis of TB in this review made use of two main methods utilized for the epidemiologic study of the disease: chest X-ray and bacteriological examination of sputum for tubercle bacilli.

It is important to note that several pulmonary diseases can mimic tuberculosis in its radiologic appearance and especially paragonimiasis (Ogakwu and Nwokolo, 1967). In general, X-ray evidence of clinically active tuberculosis is generally unreliable. This study further confirms that chest X-ray findings alone cannot differentiate paragonimiasis from pulmonary TB. This finding has been concluded by Wang in China more than half a century ago (Wang and Hsieh, 1987). In general, the chest X-ray findings in paragonimiasis are not pathognomonic (Jung-Gi, et al., 1993). Pulmonary infiltrates in paragonimiasis are usually poorly defined densities that change rapidly with time, while tuberculosis infiltrates are nodular lesions that change slowly. Cysts in paragonimiasis usually have a smooth inner margin and a thin wall with a typical ring shadow. Sub-pleural linear opacities are common in paragonimiasis, especially in the early stage, but are unusual in tuberculosis (Wang and Hsieh, 1987). Diagnosis of tuberculosis therefore should not be solely based on chest X-ray findings but on sputum smear for acid-fast bacilli or sputum culture if facilities permit, and parasitologic sputum smear examination for *Paragonimus*.

Microscopic sputum examination to demonstrate the presence of tubercle bacilli is one of two definitive means for diagnosis of pulmonary tuberculosis. Direct smear examination is an essential in epidemiological studies, and classification of patients into smear-positive and smear-negative groups enables the study of the transmission of tubercle bacilli from host to host and their treatment outcomes. Sputum culture may also demonstrate the bacilli and also offers a means for definitive diagnosis.

TB was apparently present in almost all age groups except in the less than one year old group with most cases belonging to the productive age groups. The distribution was simulated a normal one. The number of cases began to rise in the first and second decades of life with the highest numbers during the third to the fifth decades, decreasing in the sixth and seventh decades of life. Males were almost twice as much affected as females. This noted sex difference may need further elucidation in the future.
It is notable that less cases are identified the more remote the barangay is from the center of activity or the farther it is from the main roads. This is clearly seen in Liang where no cases have been detected over the two year follow up period even if TB seems to be widely distributed geographically. The lack of participation in the survey of people from the far flung areas was not unexpected but may indicate the need for more efforts to better reach out to these areas to be able to offer a chance for the prevention and control of disease and the betterment of health.

Cough was the most common clinical manifestation reported by patients surveyed. Cough is the most obvious clinical feature of pulmonary tuberculosis. It usually progresses slowly, and may become more frequent with the production of mucoid to mucoid purulent sputum. Cough was seen to be an important clinical sign of paragonimiasis as well. Hemoptysis is a common clinical sign of paragonimiasis and an important sign of tuberculosis as was confirmed in this study. Health workers without laboratory support will generally assume that patients with hemoptysis have tuberculosis. When the disease is more advanced and the sputum is negative for acid-fast bacilli or in culture, only staff with clinical acumen based on epidemiological knowledge would be likely to suspect paragonimiasis as the etiology. In areas where paragonimiasis is endemic and tuberculosis is suspected, sputum examination should be used to excluded paragonimiasis. Other clinical manifestations may be common in both paragonimiasis and tuberculosis but are not essential for diagnosis. Chest and/or back pain, dyspnea and easy fatigability may be common as was seen in this study and may generally be associated with extensive parenchymal involvement or some amount of pleural effusion (Bass et al, 1990).

The proportion of patients surveyed and proven to have Paragonimus ova in their sputum may be difficult to ignore. Results of this study indicate that from one to two out of ten people earlier diagnosed to have tuberculosis, or from one to two symptomatic patients out of ten, even if they have not been diagnosed to have tuberculosis, may harbor the parasite. In the former, it may be considered as a misdiagnosis unless the infection was of recent onset which may unlikely. Misdiagnosis leads to improper treatment, and misdiagnosis leads to classification in epidemiological statistics.

The learning from the experience of the “non-TB patients” exemplifies the possibility of diagnosing paragonimiasis early such that further complication of the disease may be avoided. This experience has also shown how an approach to diagnosis of both TB and paragonimiasis, specifically doing diagnostic tests for both at the time of consult, may work to make possible early treatment and recovery. Since Paragonimus ova are destroyed by Ziehl-Neelsen stain for detecting acid-fast bacilli, and knowing that tuberculosis is also prevalent in endemic areas for paragonimiasis, separate sputum examinations are strongly recommended (Barrett-Connor, 1982). A small amount of sputum examined directly under the microscope may be enough to observe the operculate ova of Paragonimus. They are easily recognized even under low power since they are over ten times bigger than red blood cells (Nwokolo, 1974).

A high index of suspicion is necessary to diagnose paragonimiasis. The diagnosis may be suggested by a person’s place of origin being a known endemic area, a long period of chronic cough and the habit of eating raw or insufficiently cooked crabs or crayfish.

If tuberculosis is suspected in areas where paragonimiasis is known to exist, Paragonimus infection should be ruled out by parasitological examination of the sputum. Where the suspicion of paragonimiasis is high, tuberculosis should be ruled out by doing three direct sputum smears, and if possible, culture of a concentrated sputum specimen. There is a need for improved surveillance and better case definition.

Tuberculosis laboratories should have the capacity to examine sputum for Paragonimus in known endemic areas. This will avoid the consequences of misdiagnosis leading to unnecessary and expensive diagnostic tests and treatment. Clinicians and public health authorities should recognize the consequences of misdiagnosis and realize that the capacity to differentiate paragonimiasis and tuberculosis leads to proper diagnosis, effective treatment and a better quality of life for people in endemic areas.

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