

## TECHNICAL AND OPERATIONAL APPRAISAL OF TUBERCULOSIS CASE-FINDING METHODS<sup>1</sup>

Stefan Grzybowski, M.D., F.R.C.P.(C), F.R.C.P. (London)<sup>2</sup>

77

*Programs for detecting cases of tuberculosis employ the following diagnostic methods: chest X-rays, tuberculin tests, and sputum smear or sputum culture examinations. The methods selected by public health authorities for case-finding programs should be closely tailored to local circumstances, especially the severity of the TB problem and economic considerations. In many developing areas, programs using direct sputum smear examinations will yield the best results at the lowest cost.*

### Introduction

Public-health-oriented tuberculosis control programs are aimed primarily at reducing the tuberculosis problem in the community. The underlying strategy of these programs, which is really quite simple, is based on two independent approaches.

The first approach (see Table 1) has the goal of increasing acquired resistance by widespread use of BCG vaccination; the second aims at reducing the incidence of tuberculosis infection by discovering sources of infection and curing them with appropriate chemotherapy.

It must be emphasized that the two latter activities (discovery of cases of tuberculosis and provision of treatment leading to cure) are two integral parts of the same basic activity—elimination of sources of infection—and they must be closely coordinated. Discovery of cases of tuberculosis through excellent case-finding programs is useless if the cases are not given appropriate chemotherapy; furthermore, such chemotherapy must be well-prescribed, taking into account existing resistance patterns in the community. A case-finding program without chemotherapy obviously makes no sense, while

case-finding with poor chemotherapy may even lead to an increase in the prevalence of sources of infection.

### Case-Finding Methods

Let us first consider the diagnostic tools available, namely, chest X-ray, the tuberculin test, and bacteriologic examination.

#### *Radiology*

The chest X-ray is the traditional tool for diagnosing tuberculosis. The introduction of miniature radiography in South America some 40 years ago constituted a giant step forward in control of tuberculosis by mass case-finding. There seems little doubt, however, that both in diagnosing tuberculosis and in assessment of response to treatment we have in the past overemphasized the importance of radiological findings to the detriment of more important bacteriologic findings. Furthermore, mass radiography of the whole community is costly and is unsuitable for countries with severe economic constraints. The technical quality of the films must be excellent, and they must be interpreted by well-trained physicians. Even then, as shown by several studies, there is tremendous reader-to-reader variation.

The International Union Against Tuberculosis has conducted studies of radiological

<sup>1</sup>Paper presented at the II PAHO/WHO Regional Seminar on Tuberculosis. Also appearing in Spanish in *Boletín de la Oficina Sanitaria Panamericana*.

<sup>2</sup>Associate Professor, Department of Medicine, University of British Columbia, Vancouver General Hospital, Vancouver, Canada.

TABLE 1—Aims and methods of tuberculosis control programs.

Aim	Methods for achieving aim
(1) Increase in acquired resistance	BCG vaccination
(2) Reduction of intensity of tuberculosis infection	Case-finding; appropriate chemotherapy; cure

interpretation. In one of them, 20 expert readers from several countries read the same 205 chest X-ray films. The degree of variation in their interpretations is really astonishing. The main differences related to the etiology (tuberculous or non-tuberculous) and to the clinical status (active or inactive) of the disease. In all, 29 per cent of those giving a negative response to the tuberculin test were wrongly diagnosed as having active tuberculosis. On the other hand, 13 per cent of the sputum-positive cases were not diagnosed as tuberculous (1).

Obviously, suspect cases revealed by X-ray must be examined bacteriologically and should be tuberculin-tested. Most cases diagnosed by mass radiography as active should be confirmed bacteriologically; if too high a proportion of such cases are bacteriologically negative, "over-reading" of the X-ray shadows is taking place. Advantages and disadvantages of the chest X-ray technique are shown in Table 2.

TABLE 2—Usefulness of the chest X-ray.

Advantage	Disadvantages
Early diagnosis is possible	High cost
	Non-tuberculous disease may masquerade as tuberculosis
	It is hard to distinguish between active and inactive tuberculosis
	Reader variation

TABLE 3—Usefulness of the tuberculin test.

Advantages	Disadvantages
Useful as an initial screening test in groups with low prevalence of infection	Two appointments 48 or 72 hours apart are necessary
	Non-specific sensitivity confuses the results

### *Tuberculin Testing*

In countries with very low tuberculosis infection rates and little non-specific sensitivity, tuberculin testing may be of value as an initial screening test to select persons needing X-ray examinations. In addition, the test is obviously valuable for testing suspects. (Table 3 shows the major advantages and disadvantages of this tool.)

### *Bacteriology*

*Smear examination.* Several studies have shown that patients who excrete enough tubercle bacilli to be visible on smear examination are the most potent sources of infection in the community. Those patients whose sputum is positive only on culture, or whose disease is considered active but bacteriologically negative, are of much less epidemiologic importance.

TABLE 4—Usefulness of the microscopic sputum smear examination.

Advantages	Disadvantages
Low cost	Positive and negative errors
Discovery of the most important sources of infection	Early cases are missed
	Cases with more advanced disease are diagnosed, but these are more difficult to cure and more commonly show residual respiratory damage

TABLE 5—Examination of a single collection specimen of sputum from newly diagnosed patients, by smear and culture.

Laboratory <sup>1</sup>	Total positive by smear or culture	Culture positive		Smear positive		Positive only on culture	
		No.	%	No.	%	No.	%
London, 1954-1962	776	773	99.6	275	35.4	501	64.6
Madras, 1956-1968	324	324	100.0	267	82.4	57	17.6

<sup>1</sup>Sputum collection conditions and methods of examination by smear and culture were similar at the two laboratories.

Source: *Bulletin of the International Union against Tuberculosis*, Vol. 41, p. 139, 1968.

TABLE 6—Usefulness of sputum culture examination.

Advantages	Disadvantages
Greater accuracy	More costly
Larger proportion of earlier (smear negative) cases diagnosed	Requires laboratory facilities
	Longer period (six weeks) is needed before results are available

(Table 4 shows the advantages and disadvantages of sputum smear examination.)

*Sputum culture.* When does it become worthwhile to carry out culture examination in addition to other diagnostic methods? Mitchison (2), in an excellent paper on case-finding by sputum examination, shows an interesting difference between findings in London, England, and in Madras, India (see Table 5).

In London, 64.6 per cent of 776 bacteriologically proven cases were positive on culture only, while in Madras the corresponding figure for 324 cases was 17.6 per cent. Obviously, patients in Madras reported at more advanced

stages of their disease. Thus, if Madras is representative of developing countries, in many of them the additional benefit from culture examination done on sputum of the patients reporting to clinics or health centers with symptoms would be rather small. On the other hand, in surveys performing bacteriologic examination on all persons able to produce sputum, the value of culture examination is much greater. Nagpaul *et al.* (3) estimated in 1968 that one-third of the bacteriologically proven cases in rural India would be diagnosed by culture only. (Table 6 shows the advantages and disadvantages of adding culture examination to microscopy.)

## Types of Case-Finding

It is customary to consider case-finding as either active or passive. Active case-finding can be defined as a specific program organized by health authorities to detect tuberculosis cases in the community. Mass community surveys, examinations of contacts of active cases, and surveys of special groups (for instance, miners or persons with certain known radiological abnormalities) are all examples of active case-finding.

Passive case-finding means diagnosing tuberculosis cases that were not uncovered by the active efforts of health authorities. For example, passive case-finding occurs when a patient comes to his doctor with hemoptysis and is then diagnosed as having active tuberculosis. The distinction between these two categories of case-finding is not always clear-cut; for instance, persons with chronic cough and sputum may be taught by health educators that these symptoms signify tuberculosis. Some of them may go to their private physicians, while others will go to official clinics or community surveys for diagnosis.

It is often tempting to compare the proportion of cases diagnosed by each type of case-finding. However, it must be realized that such a comparison will reflect a large variety of factors—such as the availability of general medical services, cultural patterns and population habits, and general physicians' knowledge of tuberculosis—in addition to the availability and frequency of general surveys.

### *Active Case-Finding*

The choice of specific case-finding techniques must depend on the size of the tuberculosis problem and the financial resources of the country concerned. Priorities must be established, and any program must be based on the needs of the whole population.

*Low-cost program for high-incidence areas.* In countries where tuberculosis rates are high and where there are considerable economic constraints, case-finding programs based on

sputum microscopy are the obvious choice. Through such surveys, cases which are epidemiologically most important are diagnosed. The examination is cheap, and treatment can be started immediately after the diagnosis has been made.

There are some errors in microscopic examination of sputum smears, and in certain areas the frequency of false positive smears is quite high (10-15 per cent). Because of the importance of the diagnosis to the individual and the effort involved in treatment, false diagnosis must be avoided. Before a definite diagnosis is made, a single positive smear should always be confirmed by another positive smear, by a positive culture, or by X-ray abnormality. Treatment, however, may be started whenever a smear is found to be positive.

False negative smears may also be fairly common; thorough training of personnel and checking of a sizable sample of the smears read as negative by sputum technicians is essential in order to diminish this error. Examination of more than one smear may be indicated, since it increases the number of positive findings by at least 10 per cent (2).

*Moderate-cost program for moderate-incidence areas.* In countries with moderate tuberculosis rates and moderate economic constraints, miniature chest X-ray followed by thorough bacteriologic examination of suspected cases may become the method of choice; however, surveys based primarily on bacteriologic examination (microscopy and culture) have not been performed enough to compare their value with those of X-ray surveys. As emphasized before, when mass radiography is chosen, a high rate of bacteriologic confirmation of the majority of cases considered active is essential, lest limited resources be squandered on treatment of persons with no tuberculosis or on those with inactive disease.

*Higher-cost program for low-incidence areas.* In countries with low rates of tuberculosis and considerable financial resources, widespread community surveys are often not justified. In the past, tuberculin surveys of such countries' school populations has been advocated in hopes

that examining contacts of tuberculin-positive children would uncover sources of infection in adults. These expectations have not been realized, possibly because many tuberculin-positive children have been infected with atypical mycobacteria and not with tubercle bacilli. As a result, tuberculin surveys of school-children are being abandoned in many places.

Surveys of high-risk groups are more worthwhile. Examination of the contacts of active cases, follow-up examination of inactive cases and persons with fibrotic lesions, as well as surveys of populations living in poor conditions (e.g., city slums) constitute rewarding case-finding methods.

In some countries with low tuberculosis rates, the availability of large numbers of miniature mass X-ray units seems the primary reason why mass surveys are continued, since very few active cases are found. The surveys are often officially justified on the basis of their educational potential and their value in diagnosing non-tuberculous diseases. I am skeptical about the educational value of these surveys; their real place, if any, in the diagnosis of other chest conditions is yet to be firmly established. However, it is true that in some countries the mass survey organization is so well developed that it would be a pity to dismantle it—if it can be used to effectively screen the population for other diseases.

#### *Passive Case-Finding*

The majority of tuberculosis cases in most countries are diagnosed by practicing physicians or at general hospitals. It is therefore essential that official and voluntary agencies devote considerable effort to education and re-education of the medical profession on the subject of tuberculosis. Specifically, the value of bacteriologic examination in diagnosing the disease should be stressed, since (at least in the countries with which I am more familiar) this method of examination is frequently neglected.

#### *Examination of "Symptomatic" Patients*

Examination of sputum smears from indi-

viduals with respiratory symptoms has been shown to yield a high rate of positive diagnoses in some countries. In a rural district of India, for instance, 11 per cent of the patients complaining of cough and sputum lasting over two weeks were found to yield a positive sputum smear for tubercle bacilli (3).

On the other hand, in many countries chronic productive cough is a very common symptom and is due mainly to chronic bronchitis. In Canada a quarter of the older men suffer from chronic bronchitis; as there is also a generally low rate of tuberculosis, sputum smear examination of such "symptomatics" would obviously be quite unrewarding. As this illustrates, in planning case-finding programs that deal with "symptomatic" patients one needs to know not only about the prevalence of tuberculosis in the region, but also about other common diseases causing respiratory problems.

#### **Assessment of Case-Finding Programs**

Case-finding programs should be assessed in several ways. Technical assessments (e.g., evaluating the quality of sputum smears, X-ray films, and their interpretations) is, of course, most important. They should be performed in an unhurried fashion, on unselected but relatively large samples, by experts in the particular field involved.

However, the yield of a case-finding program, expressed as the rate of bacteriologically proven tuberculosis cases discovered in the population surveys, provides the best yardstick for determining the program's value. This yield should be related to an analysis of the program's true costs. Such costs may be expressed in terms of the cost of one examination or that of diagnosing one case. Table 7 provides an example of cost estimates cited by Nagpaul *et al.* (3).

These findings show that in one rural district of southern India the most economical way of diagnosing tuberculosis cases is by direct microscopy and by taking chest X-rays at fixed sites. However, the district in question has only one static unit, which is readily accessible only

TABLE 7—Cost of diagnosing one tuberculosis case by different methods in a rural district of southern India.

Examination	Approximate cost of one examination	Approximate cost of diagnosing one case
Direct microscopy	US\$0.21	US\$3.4
Culture examination	0.49	12.1
70-mm X-ray film (stationary unit)	0.26	3.5
70-mm X-ray film (mobile unit)	0.50	73.0

Source: *Bulletin of the International Union Against Tuberculosis*, Vol. 41, pg. 150, 1968.

to people living in the immediate neighborhood; therefore, the most economical way of diagnosing tuberculosis in the majority of the inhabitants is through sputum microscopy.

The planner in India may be justified in deciding that both of these economical methods should be the first ones utilized and developed, and that culture examination should be introduced to supplement microscopy once these initial methods have achieved 70 or 80 per cent of their potential. A wise planner will also maintain constant supervision of treatment program results, remembering that effort is being wasted if discovered cases are not cured. He will therefore not allow the case-finding program to outstrip the potential of the treatment program.

In assessing a particular case-finding program, one must also know the number of cases found by the program relative to the total number of cases diagnosed (or estimated) in the country. For instance, a case-finding program among miners exposed to silica dust may show a very high yield; yet the program's contribution to solving the national tuberculosis problem may be negligible if only a tiny fraction of the population is employed in the mines.

The proportion of people examined among the population eligible for examination is less important than the program's case yield and the number of cases diagnosed. The proportion of the population covered should always be broken down by age and sex, or the results may be misleading; for example, the overall coverage may seem satisfactory (80 per cent), but the program may cover 100 per cent of the

schoolchildren (with little tuberculosis) and only 30 per cent of the older men (with high rates of disease).

In some countries there is a tendency to set targets, such as the number of sputums to be examined or the number of X-rays to be taken in one year. These targets must be carefully devised, for otherwise they may prove a handicap rather than a stimulus to tuberculosis control.

### Conclusions

One of the great recent achievements in tuberculosis control has simply been the realization that bacteriology has so much to contribute to diagnosis and assessment of treatment. Bacteriology has been kept in the dark for almost a generation by the shadow of the chest X-ray, which received overwhelming but often undue attention. The reinstatement of bacteriology to its rightful place is largely due to the work done in the developing countries.

Tradition plays an important role in treating a chronic disease like tuberculosis. It is thus difficult for many of us to break with established approaches and accept new technology and new ways of conducting our programs. However, if we are to achieve our goals of first controlling and then eradicating the disease, we must somehow demonstrate the ability to modify old approaches and adopt new ones.

How can a person best select the case-finding programs to adopt in one's own country? It is necessary first to consider the size of the tuberculosis problem and the financial resources which the country can devote to controlling the disease. After that, laboratory

facilities, X-ray equipment, and especially the medical and para-medical personnel which are available must be taken into account.

While the needs of the total population must be considered, the programs may assume different forms in rural areas and in cities. For example, in rural areas the case-finding programs of choice may be examination of sputum smears from patients with symptoms; but if mass X-ray units are available in the cities it may be more profitable to use X-rays as an initial screening procedure for selecting patients requiring bacteriologic examination. The latter

may consist of microscopic and culture examination of two or three specimens.

In certain groups, such as students, it may be best to use tuberculin testing for the initial screening, followed by X-ray screening of positive reactors, and finally by bacteriologic examination of those with X-Ray shadows. In essence, what is advocated for countries that already have well-established tuberculosis control programs is appropriate use of new technology and new approaches in existing programs.

### SUMMARY

Tuberculosis case-finding and treatment programs, designed to reduce the incidence of disease by detecting and curing sources of infection, constitute one of two general methods used by public health authorities to control the disease (the other is large-scale BCG vaccination). The various case-finding techniques used are based on examination of chest X-rays, tuberculin tests, and sputum smear and sputum culture examinations.

The main advantage of the X-ray method is that it permits early diagnosis; on the other hand, it tends to be expensive and poses major interpretation problems. The tuberculin test is useful for screening groups where the incidence of tuberculosis is low; but each patient screened must go to the clinic twice, and the test's lack of specificity tends to confuse the results. Smear examinations are relatively cheap and detect the most infectious cases; on the other hand, they are subject to error and tend to detect cases late. Sputum culture examinations are more accurate than direct smear examinations and detect more early cases; but they are more costly, need laboratory facilities, and require waiting six weeks for the results.

Besides selecting from among these methods and combinations of them, public health authorities can choose between an active approach or a passive one. The active approach uses specific programs specially designed to detect cases, while the passive approach depends solely on detection of cases without these special efforts.

Active case-finding programs should be tailored to the availability of financial resources

and the rate of tuberculosis in the country involved. For example, countries with very limited resources and a high rate of tuberculosis would probably find that a program based on direct sputum smear examination would yield the best results. On the other hand, countries with moderate resources and a moderate rate of tuberculosis may prefer to use chest X-rays supported by thorough bacteriologic examinations, while countries with extensive resources and a low rate of disease may find it best to limit their screening activities to high-risk groups. Regardless of the techniques used, education and re-education of the medical community concerning tuberculosis is an important feature of any campaign against the disease.

The proportion of "symptomatic" patients actually having tuberculosis can vary greatly from country to country. Therefore, both the incidence of the disease and the prevalence of other conditions with similar symptoms must be kept in mind when planning programs that deal with such patients.

Both the value and the technical proficiency of case-finding programs should be periodically assessed. Technical assessments (such as evaluation of X-ray quality) should be made by experts who are given enough time and relatively large samples to work with. Value assessments should be based on the costs incurred in screening each person and in finding each case of tuberculosis.

Growing attention has been drawn in recent years to the great contributions that can be made by bacteriology in detecting tuberculosis,

despite the fact that the bacteriologic approach has experienced decades of relative neglect. In planning case-finding programs, it is thus extremely important to be willing to modify old

approaches and adopt new ones, while continuing to give due consideration to all the relevant factors involved.

#### REFERENCES

- (1) *Ad Hoc* Committee for the Study of Classification and Terminology in Tuberculosis. "Complementary Document 2: Results of the Multiple Radiophotography Reading Trial Performed in 1963." *Bull Int Un Tuberc* 36: 61-72, 1965.
- (2) Mitchison, D. A. "Examination of Sputum by Smear and Culture in Case-Finding." *Bull Int Un Tuberc* 41: 139-147, 1968.
- (3) Nagpaul, D. R., et al. "Case-Finding by Microscopy." *Bull Int Un Tuberc* 41: 148-158, 1968.

#### DENGUE-2 IN PUERTO RICO

An increase in the incidence of febrile illness with rash was reported in the Guánica-Ensenada area of Puerto Rico in July 1972. An investigation to define the extent and etiology of the illness was subsequently begun.

Two house-to-house surveys in the Guánica-Ensenada area were conducted on 22-24 August and 12-13 September to determine the incidence of all febrile illness since 1 June 1972 and the presence or absence of *Aedes aegypti* mosquito larvae. Six geographic subdivisions were selected for the studies, and every fifth occupied house was visited. A total of 263 families were interviewed, and data were obtained on 1,156 persons.

The investigation revealed that the overall attack rate for febrile illness during the 15-week period was 245 per 1,000 population. There was no striking predilection for a specific age group, nor were significant differences in sex-specific attack rates noted. No hemorrhagic manifestations were reported.

Blood specimens were obtained from persons who had experienced fever within 10 days of the interview. Of the 39 pairs of acute and convalescent sera collected and tested by complement-fixation, 22 showed evidence of recent dengue-2 infection, five were inconclusive, and 12 were definitely negative for dengue. Of 22 additional sera obtained in July and August as part of serologic dengue surveillance, 18 showed evidence of recent dengue-2 infection.

Further investigation revealed that 20.7 per cent of the houses examined in the first survey were positive for *A. aegypti* larvae and that 17.8 per cent were positive in the second survey. In the first survey, 1.3 *A. aegypti* adults per man/hour were collected, and 2.7 were collected per man/hour in the second. Large water barrels were the most frequent breeding sites. Selective *Aedes* control measures were instituted following the investigation.

In 1963-1964 and 1968-1969, Puerto Rico experienced explosive epidemic activity of dengue-3 and dengue-2 viruses, respectively. There was no evidence of endemic dengue activity during the interepidemic period. However, since 1969 the persistence of dengue-2 transmission in western and southwestern Puerto Rico has been demonstrated serologically and by virus isolation. Foci of dengue-2 activity were recognized in 1971-1972. [*Morbidity and Mortality Weekly Report*. Center for Disease Control, Atlanta, Georgia, Vol. 21, No. 44, November 1972.]