

Diagnosis of tuberculosis in individuals with respiratory symptoms. Commentary on the II Guidelines of the Brazilian Society of Pulmonology and Phthisiology and the Ministry of Health*

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Recently, the Brazilian Society of Pulmonology and Phthisiology, together with the Ministry of Health, held a meeting in the city of Brasilia in order to establish general guidelines for the management of tuberculosis. The resulting *II Diretrizes Brasileiras para a Tuberculose* (II Brazilian Guidelines for the Management of Tuberculosis), as well as *Tuberculose. Guia de Vigilância Epidemiológica* (Tuberculosis - A Guide to Epidemiological Surveillance), issued by the Centro Nacional de Epidemiologia (Cenepil, National Center for Epidemiology)/Fundação Nacional de Saúde (FUNASA, National Health Foundation), were published in this journal in 2004.⁽¹⁾

The initiative to hold the meeting deserves to be highly commended since this meeting brought together great experts on the subject, who discussed one of the major Brazilian public health problems.

However, by reaffirming concepts previously established in official Brazilian government documents,⁽²⁻⁵⁾ the Guidelines, in my view, are in conflict with the opinion of the vast majority of pulmonologists in various aspects. In this commentary, I intend to demonstrate the irrationality regarding the diagnosis of individuals with respiratory symptoms.

After stating that "Bacteriological investigation is recognized as the method of choice, either for diagnosis or for tuberculosis control", the Guidelines affirm that "Conventional chest X-ray investigation is indicated always as an auxiliary method, and, especially in the following cases: individuals with respiratory symptoms and presenting negative spontaneous sputum smear microscopy results; household or institutional contact with active-TB patients, of all ages, with or without respiratory

symptoms; individuals suspected of having extrapulmonary tuberculosis; individuals infected with human immunodeficiency virus or individuals with acquired immunodeficiency syndrome." However, in another passage, the document recognizes that "radiology is a relevant diagnostic tool" and that "cavitation probably occurs as a result of late diagnosis." In the "Norms", sputum smear microscopy is also considered fundamental, but the use of radiology is justifiable in individuals presenting positive sputum smear microscopy results in order to exclude accompanying diseases and allow the evaluation of the evolution.

This preference for sputum smear microscopy was previously advocated by Prof. Hélio Fraga in the 1960s and is still endorsed by the World Health Organization for use in developing countries.⁽⁶⁻⁷⁾

This belief certainly derives from some conceptions or preconceptions. Although chest X-ray sensitivity is much higher than is that of sputum smear microscopy, specificity is much more important since many physicians would misinterpret chest X-rays, thereby, on the one hand, negatively affecting patients suffering from other diseases that would remain undiagnosed and, on the other hand, failing to diagnose the principal vectors of the disease, which would consequently remain untreated. Therefore, the typical physician would be considered almost totally incapable of integrating various aspects such as age, race, gender, clinical profile, personal/family history, etiology, social aspects, physical examination, adjunct exams and evolution, which are taken into account in the diagnosis of any disease. In summary, for the

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advocates of this norm, sputum smear microscopy is the ideal initial exam for use in individuals with respiratory symptoms since it makes it possible to identify the principal vectors of the disease. Let us examine some important aspects.

In 2004, the World Health Organization emphasized, among the measures to control tuberculosis, the identification of cases through the use of sputum smear microscopy.⁽⁷⁾

The Plano Nacional de Combate à Tuberculose (National Plan to Combat Tuberculosis) and Edict 1474/GM, issued August 19, 2002, emphasize that disease control necessarily presupposes early diagnosis.⁽⁵⁾

Tuberculosis-related mortality is mainly attributable to late diagnosis or no diagnosis, as well as to inappropriate chemotherapy. In developing countries, it is estimated that it takes at least two or three months to diagnose a patient with active-TB. In developing countries, it takes much longer, and this would, consequently, result in a greater number of infected individuals and new cases of active-TB.

The official documents issued by the Ministry of Health⁽²⁻⁵⁾ always emphasize that individuals who have had respiratory symptoms for more than three weeks should be submitted to sputum smear microscopy, assuming that at least 1% to 5% of the population is symptomatic, and that 4% of those would present positive sputum smears, and that sputum smear microscopy must be repeated both for individuals presenting positive sputum smears and for those presenting negative sputum smears.^(3,8) However, Farga assumes higher percentages since he considers that between 5% and 10% of adult individuals have respiratory symptoms, 1% to 10% of which present positive sputum smears.⁽⁹⁾

In an editorial of the World Health Organization in 2002, Perkins and Kristki stated that the adequate control of tuberculosis requires a balance between detection and treatment.⁽¹⁰⁾ The latter is practically resolved using the Directly Observed Treatment, Short-course (DOTS), but the authors assert, "we fail dismally in diagnosis." The authors recognize that sputum smear microscopy has low sensitivity, requires multiple visits and is laborious, as well as the fact that it is clearly necessary to use simpler and more sensitive methods. The authors also discuss improvements in microbiological methods, but they recognize that implementation is difficult, and that these methods would be available, at best, within three to five years. They conclude that detection is

Chart 1 - Sputum smear microscopy. General aspects

Lack of ratification by Brazil
Delay in identifying patients with respiratory symptoms
Low incidence of tuberculosis among patients with respiratory symptoms
Low sensitivity
Time-consuming process
Not useful for diagnosing other diseases
Cost comparable to that of Chest X-ray

the Achilles' heel of the DOTS strategy. Surprisingly, the authors do not comment on radiology.

The various criticisms of sputum smear microscopy as an initial diagnosis method for use in individuals with respiratory symptoms are discussed herein (Chart 1).

Ratification

Brazilian studies on this subject are unknown, and the few international studies, cited repeatedly, refer to countries where social and sanitary conditions are much worse than in Brazil and were carried out many years ago. Boyd, Marr, and Parrot et al., as early as the 1970s, demonstrated how mistaken this practice was by proving that sputum smear microscopy without the aid of radiology is quite unreliable.⁽¹¹⁻¹²⁾ Also notable is the absurdity of Etienne Bernard's statement that radiology is indispensable in developed countries, but that substituting sputum smear microscopy for radiology is a significant advancement in developing countries.⁽¹³⁾

Delayed suspicion of tuberculosis in individuals with respiratory symptoms

Many years ago, Nagpaul et al. drew attention to the fact that 42% of active-TB patients had been symptomatic for less than 15 days.⁽¹⁴⁾ A recent study of 252 patients diagnosed in Sanatorinhos demonstrated that 41 (16.3%) had presented symptoms for less than 15 days, 70 (27.8%), between 16 and 30 days, 103 (40.9%), between 30 and 90 days and 38 (15%), for more than 90 days. Therefore, many patients who are currently diagnosed having had symptoms for less than 3 weeks would be diagnosed much later if the proposal that sputum smear microscopy be performed only in individuals who have had respiratory symptoms for more than 3 weeks were adopted.

Tuberculosis in symptomatic individuals

In 1990, the incidence of acute respiratory infection in Algeria was 20,377/100,000, 611 of which were cases of pneumonia, whereas the prevalence of severe forms of asthma was 80/100,000, and the prevalence of chronic obstructive pulmonary disease among adults (> 40 years of age) was 125/100,000.⁽¹⁵⁾ However, the annual incidence of tuberculosis (all forms) was 46/100,000, and the annual incidence of active-TB was 23/100,000. Therefore, it is easy to conclude that sputum smear testing proved useless for nearly all symptomatic individuals.

In our milieu, Palombini et al. examined the cause of chronic cough in 78 patients with normal chest X-rays and found that, in 93.6% of the cases, the cause, isolated or in combination, was asthma, postnasal drip or gastroesophageal reflux. In addition, they reported that, in the USA, 29 million medical appointments per year are scheduled due to chronic cough, which occurs in 14% to 23% of nonsmokers.⁽¹⁶⁾ Again, it is easy to conclude that performing sputum smear microscopy is futile when the number of patients is extremely high.

In a study published in 1980, we demonstrated that, of a total of 1026 diagnosed patients, 679 sought medical assistance due to disease, whereas the others were detected because they were contact cases or because they underwent routine exams.⁽¹⁷⁾ In these two last groups, 150 were asymptomatic and 197, despite being symptomatic, apparently were unaware of the severity of the disease. Sputum smear positivity was 62% among the patients of the first group, 58% among the symptomatic patients who did not recognize the significance of the symptoms and 22% among the asymptomatic patients. Therefore, almost half of the symptomatic patients presented negative sputum smears, whereas many of the symptomatic patients or patients who did not recognize the significance of the symptoms presented positive sputum smears. In addition, sputum smear positivity was found to be strongly correlated with the extent of the disease, being 16% among individuals presenting mild forms, 61% when tuberculosis was moderate and 89% when tuberculosis was advanced. Sputum culture was positive in half of the patients who presented negative sputum smears. Bearing in mind that there is a strong likelihood that individuals presenting mild forms and

negative sputum smears will evolve to severe and symptomatic forms within a few months, it is inexplicable that sputum smear microscopy should be used as a form of triage.

The most convincing evidence of the inconvenience of this procedure is found in the study recently carried out by the Secretaria de Saúde de São Paulo (São Paulo State Department of Health), whose results, with the addition of personal extrapolations, are summarized in Table 1. It is easy to see the enormity of the task of interviewing more than 2 million people, carry out almost 50,000 sputum smear tests and finding 548 positive results, disregarding how many of the patients presenting positive sputum smears already knew they had the disease. This colossal task was carried out by 980 mobile teams, which visited 4210 institutions (*).

We should remember that photofluorography was abandoned because it detected only 1% to 2% of abnormalities in the general population, including tuberculosis and other diseases. If it were used exclusively in symptomatic patients, its efficiency would be much greater and with considerable economic advantages over the indiscriminate use of sputum smear microscopy in symptomatic patients.

Low sensitivity

In general, the diagnostic yield of sputum smear microscopy is approximately 50%. The World Health Organization estimates that, in 2004, there will be approximately 8.5 million new cases of tuberculosis worldwide, of which 46% will present positive sputum smears, this positivity rate being the same

TABLE 1

Sputum smear microscopy. Expectations and reality

Population studied	2.441.661		
	Expected	Observed	Difference
Respiratory symptoms	24.166	81.757	340%
Tests performed	48.337		
Positive results	1.855(4%)	548(1,2%)	71,5%
Transposed for Brazil			
Population		160.000.000	
Respiratory symptoms (3,4%)		5.440.000	
Tests performed (2x)		10.880.000	
Cost (SUS)*		R\$ 47.110.400	
Positive sputum (1,2%)		65.280	

*SUS: Sistema Único de Saúde (Unified Health System)

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in the various regions of the world.⁽⁷⁾ In a study involving direct cooperation between Mexico and the USA, for example, it was demonstrated that, on the border between these two countries, 3,456 (51.3%) of the 6572 Mexican patients diagnosed with pulmonary tuberculosis presented positive sputum smears, whereas the exam was positive in 6684 (46%) of the 14,800 American patients tested.⁽¹⁸⁾ It is estimated that, in Brazil, only 55.07% of the patients diagnosed with tuberculosis present positive sputum smears.⁽³⁾ If this were the only method used, half of the cases would go undiagnosed. Therefore, it is impossible to achieve one of the objectives of the previously mentioned government directive, which is to detect 90% of the estimated cases using sputum smear microscopy.

Performing a second sputum smear microscopy when the first one is negative is unpractical since, in our experience, 89% of the positive results are so in the first exam, whereas only 6% are negative in the first exam and positive in the second, dropping to 5% when three or more exams are carried out.⁽¹⁷⁾

Assuming that 1% of the population in Brazil has respiratory symptoms and considering the need to carry out two sputum smear tests, it would be necessary to carry out 3,200,000 sputum smear tests in order to diagnose approximately 64,000 patients, that is, nearly two thirds of the annual incidence, or half of it, according to some speculations.

In São Paulo, the prevalence of the disease in prisons is astounding and can only be reduced by, among other measures, making immediate diagnoses, which is only rationally feasible by carrying out X-rays of all prisoners.⁽¹⁹⁾ The numbers are simply terrifying since 7.5% of the cases of tuberculosis in the state occur among prisoners, the incidence being 2650/100,000, (50 times greater than among the general population), and the index of infection being 71%. Therefore, if sputum smear microscopy were used in isolation, half of the prisoners would remain undiagnosed, and this, as well as perpetuating the problem, would magnify it.

Costs

It is totally unacceptable to justify the preference for sputum smear microscopy based on cost since it is established in the cost table of the Sistema Único de Saúde (Unified Health System) that sputum smear microscopy costs R\$ 4.20, anterior-posterior chest X-ray costs R\$ 4.91, culture costs R\$ 4.91 and

tuberculin test costs R\$ 2.83. In addition, we should bear in mind that a country that provides the general population with free (at a high cost to the taxpayers) treatment and medication, such as hemodialysis (65,534 patients) and treatment for the acquired immunodeficiency syndrome (11,383 new cases in 2000), has no right to deny chest X-rays by claiming that the cost is too high.⁽²⁰⁾ Furthermore, the number of patients who seek our health services after having already been diagnosed and submitted to computed tomography, fiberoptic bronchoscopy, transbronchial biopsy and even open-lung biopsy is significant and, evidently, the respective expenditures are high. However, many of these patients could be initially oriented without the need for these procedures. Clinical and radiological integration, carried out properly, would suffice.

Returning to the data in Table 1, we can see that extrapolations for Brazil make it possible to conclude that approximately 11 million sputum smear tests should be carried out at an estimated cost of approximately 50 million Brazilian Reals according to the cost table of the Unified Health System, a significant amount for any health program in any country. In addition, X-rays account for less than 2% of the expenditures in facilities that treat tuberculosis.⁽²¹⁾

Time required to perform the exam

In addition to the considerable amount of time devoted to preparing a sputum smear microscopy slide, a trained technician must examine that slide for at least ten minutes. Considering that many patients are diagnosed or suspected in emergency rooms where there are general technicians who perform numerous other exams, we can infer that it takes several hours to obtain the result of a sputum smear microscopy and, during this time, the suspect is in close contact with many patients who are temporarily or permanently immunosuppressed. Obviously, these patients should be immediately submitted to radiographic examination and, in case of suspicion, be referred to a health clinic for sputum smear microscopy, or oriented, or hospitalized if suspected of having other lung diseases.

Situations in which chest X-ray is indicated

Chart 2 shows some of the situations in which chest X-ray is currently indicated.

We can clearly perceive the irrationality of the

Chart 2 - Some situations in which a chest X-ray is indicated

Pneumonia - Consenso Brasileiro
 Pneumonia - Brazilian Consensus
 Chronic obstructive pulmonary disease - Brazilian Consensus
 PPD-positive contacts - II Guidelines
 Patients with respiratory symptoms and negative sputum smears - II Guidelines
 Suspected extrapulmonary tuberculosis - II Guidelines
 Patients with respiratory symptoms in New York and Caribbean candidates for entry into the USA presenting respiratory symptoms

diagnostic procedure recommended by the II Guidelines. The USA demands that all individuals intending to live there be submitted to chest X-ray regardless of whether or not they have respiratory symptoms or come from areas where prevalence of the disease is high.⁽²²⁾ It could be argued that the USA is a rich country and that these X-rays are paid for by the individual concerned, but the key role played by this exam in the diagnoses of the disease is undeniable since indiscriminate use of X-rays detects approximately 90% of cases.⁽²³⁾ Therefore, it is not surprising that, in New York (USA), chest X-ray is used as triage, although it is curious to observe that, in the Caribbean, the norms are the same.⁽²⁴⁻²⁵⁾

It even more curious that the current II Guidelines recommend chest X-ray for individuals suspected of having extrapulmonary tuberculosis and not for those suspected of having the pulmonary form, and that our Society recommends X-ray for individuals suspected of having pneumonia (800,000 annual hospitalizations under the Unified Health System) and for individuals with chronic obstructive pulmonary disease (10% to 15% of individuals older than 40

years of age).

In conclusion, we doubt that any pulmonologists follow the diagnostic proposal of the Guidelines in dealing with individuals who have respiratory symptoms, suspected of having tuberculosis or not, in their daily activities. On the contrary, experience shows that the first complementary test in these cases is invariably chest X-ray, which will serve as a guide to complement diagnosis.

Proposal

We propose that, rather than continuing to defend illogical norms, our Society reformulate the recommendations for the investigation of individuals with respiratory symptoms, emphasizing chest X-ray as the main method of triage. In cases of suspected tuberculosis, sputum smear microscopy should be performed, although it is very important to bear in mind that positivity is closely correlated with the extent of the disease and the presence of cavities.

Therefore, spending time and money on campaigns to demonstrate the excellence of sputum smear microscopy in the investigation of individuals suspected of having tuberculosis is not worthwhile. It is much more important to properly equip health centers located in areas where the prevalence of tuberculosis is high. In addition, we should bear in mind that 47% of all cases of tuberculosis occur in nine metropolitan areas (Belém, PA; Fortaleza, CE; Recife, PE; Salvador, BA; Rio de Janeiro, RJ; São Paulo, SP; and Porto Alegre, RS), and that 28% occur in two of those cities (São Paulo and Rio de Janeiro). If we cannot accept that, in these locations, it is difficult to submit an individual suspected of having tuberculosis to chest X-ray, what is the rationale for establishing, as a nationwide priority, the use of a method devised for deprived areas?

It is also obvious that the physicians who are responsible for the treatment of individuals with

Chart 3 - Proposal for the investigation of respiratory symptoms

1. All patients suspected of having severe or acute chronic lung disease with bronchial involvement should be submitted to chest X-ray; in accordance with the clinical and radiological suspicion, subsidiary exams should be performed, bacteriology being fundamental in suspected cases of tuberculosis.
2. In locales where chest X-ray is unavailable, sputum smear microscopy should be performed as the initial test.
3. In rare instances, the diagnosis of tuberculosis can be made exclusively on clinical grounds

respiratory symptoms should be properly trained to, for example, not confuse cavitated carcinoma with tuberculous cavitation, as the advocates of bacteriology like to exemplify. A summary of this proposal is shown in Chart 3.

In addition to being mandatory for individuals who have respiratory symptoms, chest X-ray should be provided to potential carriers of tuberculosis belonging to special groups, such as health professionals (especially those who treat particularly susceptible patients, including nursery workers and those who work in dialysis and with immunosuppressed patients in general), day-care center workers and convicts entering the prison system.

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