

# Editorial

## Recurrence of tuberculosis

Antonio Ruffino-Netto

The performance of activities in the area of public health care depends a great deal on the combination of various factors, starting with the political decision of implementing such activities. However, the planning phase of such activities certainly implies the existence or discovery of appropriate indicators that can translate the magnitude of the problem in question. Planning without an epidemiological diagnosis of the current situation of the problem could result in a significant waste of time and in a waste of financial resources.

In the area of tuberculosis (TB), various indicators that translate the magnitude of each stage of the disease and the rate at which individuals change from one state to another are used to analyze the epidemiological situation. There are also operational indicators that portray how the activities are being performed (assessing their effectiveness, cost, benefits, etc.)

Historically, it is worthwhile to recall that the mere occurrence of tuberculous meningitis was, some time ago, an important indicator (for epidemiologists) of the recent existence of sources of infection (patients with active tuberculosis) in the community. Similarly, recurrence of TB is an important indicator: what information can this indicator provide? A very important (and well-written) article on the theme is presented in this issue of the Brazilian Journal of Pulmonology. It is the study conducted by Picon et al.<sup>(1)</sup> on 'Risk factors for recurrence of tuberculosis'.

Just for the sake of a theoretical reflection on the problem, I will resort to a historical formula for the pathogenicity of TB proposed by Rich,<sup>(2)</sup> (a formula that does not have mathematical significance, but that is rather a way of expressing the problem):

$$P \cong \frac{N.V.H}{R(n+a)} \quad (1)$$

where P is the pathogenicity of the process, N is the number of bacilli that penetrate the organism, V is the virulence of the bacillus, H is the allergy or hypersensitivity of the organism, Rn is the natural resistance, and Ra is the acquired resistance. Evidently, the current knowledge about immunology might have incorporated/modified the formula above. However, it is a historical element that will be used just for the sake of reasoning. The numerator of this formula shows various aspects: the number of bacilli that penetrate the organism depends on the number of sources of active TB; on the conditions of transmissibility; on the existence of a *Programa de Controle da Tuberculose* (PCT, Tuberculosis Control Program); on the efficacy of this PCT; on the efficacy of the medication; on

the cultural aspects involved in the demand for *serviços de saúde* (SS, health care facilities) by the patient (source of infection); on the health policies implementing (nor not) the SS in the appropriate areas, and on the level of qualification of the health professionals who work at the SS. In other words, the numerator of the expression is associated with the social and economic conditions (which determine the conditions of living, housing, transportation, working, etc) as well as with the health policies and the policies of qualification of human resources. All these elements will direct or indirectly catalyze the progression of primary TB and the occurrence of reinfection TB (also designated exogenous TB).

In contrast, the denominator, which is restricted to the aspect of resistance (natural or acquired) of the organism, is associated with all the elements that are likely to interfere with immunity, such as vaccination status; coinfection (such as TB/HIV); comorbidities (diabetes mellitus or others); age; intake of immunosuppressive agents; nutritional status; etc. Having interfered with resistance (that is, having caused it to decrease), such factors, per se, will cause pathogenicity to increase regardless of new re-infections. This promotes both the progression of primary TB and the endogenous reactivation of TB.

Therefore, it is clear that recidivism (or recurrence) of TB can be associated with a large number of variables, being an important indicator that merits study. Evidently, this is a specific indicator at a historical moment of each community, thus precluding external generalizations.

The objective of the abovementioned study was to identify risk factors for TB recurrence. A retrospective study was conducted using a database containing information about patients who were enrolled for treatment in an outpatient clinic, which belongs to the Rio Grande do Sul State PCT, in the city of Porto Alegre between 1989 and 1994. A total of 610 patients were included. The variables considered likely exposure factors (age, gender, race, duration of symptoms, extent of disease, cavitation on chest X-ray, noncompliance, delayed negative sputum conversion, diabetes mellitus, alcoholism, medication doses, and HIV testing) were studied, as was the detection of recurrence of TB in those patients for 7.7 years after cure. In the period studied, the recurrence rate was found to be 4.5% (or 0.55/100 person-years). Of the variables studied (in a multivariate analysis), only HIV infection and noncompliance proved to be independently associated with recurrence. In other words, only these two variables had predictive value for recurrence in those circumstances.

Some points of the abovementioned study are noteworthy. Firstly, the study cited presents a rate of recurrence of TB (4.5%) in treated cases. Only a few studies in Brazil have actually addressed this issue. The Brazilian National Ministry of Health, in the programming of the PCT activities, estimates the rate of re-entry into the system (due to recurrence or abandonment) to be 10%.<sup>(3)</sup> Looking for an example in the state of Rio de Janeiro, where the epidemiological situation of TB is extremely serious, we have found data<sup>(4)</sup> revealing that the rate of recurrence in the city of São Gonçalo is 8%. As previously mentioned, none of the findings of the studies cited, either those by Picon et al.<sup>(1)</sup> or those by Guedes et al.,<sup>(4)</sup> can be generalized: the rates were obtained for the populations studied at the time. For the city of Rio de Janeiro (Personal communication by Afrânio Lineu Kritski, Adjunct Professor at the Federal University of Rio de Janeiro and Vice Coordinator of the Brazilian Tuberculosis Research Network), the rate of recurrence is estimated to be from 5 to 6% (in a follow-up period of 5 years after cure); for the state of São Paulo (Personal communication by Vera Galesi, Coordinator of the São Paulo State PCT), this rate is approximately 5%. Another noteworthy point of the study conducted by Picon et al.<sup>(1)</sup> is that the 26 cases of recurrence detected occurred within 2 to 96 months. In 6 patients (6/26 = 19.2%), recurrence occurred within the first 6 months. Of those 6, 4 were noncompliant, and 2 had delayed negative sputum conversion. Those 6 patients tested negative for HIV.

In general, early recurrence is associated with the endogenous reactivation of the process. Current diagnostic tests using polymerase chain reaction could elucidate the nature of the process (reinfection or reactivation). However, it is of note that the data found refer to the population of an area where the test cited was not available at the time. Later recurrence would be more commonly associated with exogenous reinfection. It is important to remember that the city of Porto Alegre is an area of high prevalence of TB and HIV infection. The authors conclude that, in order to prevent treatment noncompliance in the city studied, it would be important that supervised treatment be used. This conclusion is extremely important since the mobilization for the implementation of the directly observed therapy, short-course strategy in the city of Porto Alegre was too slow until recently.<sup>(5)</sup>

The study in question leads to an important reflection on recurrence and on the epidemiology of TB in Brazil and around the world. Mirta Roses, in a

recent visit to Brazil, stated that social inequality and poverty pose challenges for the achievement of the Millennium Development Goals and advocated the need for more agile and efficient responses to problems such as maternal health, infant survival, malnutrition, tuberculosis, and malaria (2007; Mirta Roses, director of the Pan-American Health Organization – <http://www.opas.org.br/mostrant.cfm?codigodest=230>). Roses points out that “in Latin America and the Caribbean, 230 million inhabitants (46%) do not have health insurance; 125 million (27%) lack regular access to basic health care; 152 million do not have access to drinking water or sanitation; and 17% of the births do not receive personal, qualified health care. The rate of immunization is 90%. However, the remaining 10% represents 82 million children.”

The study on recurrence is one more contribution to enriching our knowledge about the dynamics of TB, which is one of the problems mentioned above by Roses.

#### **Antonio Ruffino-Netto**

**Full Professor of Social Medicine at the Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo – FMRP/USP, University of São Paulo at Ribeirão Preto School of Medicine – Ribeirão Preto, Brazil**  
**Coordinator of the Rede Brasileira de Pesquisas em Tuberculose – REDE TB, Brazilian Tuberculosis Research Network – Ribeirão Preto, Brazil**

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