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Editorial

Surveillance of tuberculosis contacts: How can the strategy be improved?☆



Vigilancia de los contactos en la tuberculosis: ¿cómo podemos mejorar la estrategia?

Pere Godoy^{a,b,c,d,*}, Miquel Alsedà^{a,b,c}

^a Agencia de Salud Pública de Cataluña, Catalunya, Spain

^b Institut de Recerca Biomèdica de Lleida (IRBLleida), Lleida, Spain

^c Facultat de Medicina, Universidad de Lleida, Lleida, Spain

^d CIBER de Epidemiología y Salud Pública CIBERESP, Spain

Tuberculosis remains one of the world's main public health problems. The World Health Organisation (WHO) estimated that, in 2017, tuberculosis caused 1.6 million deaths and that 10 million new cases were diagnosed.¹ In the European Union/European Economic Area (EU/EEA) as a whole, mortality was 0.8/100,000 (4300 deaths) and the incidence rate was 12.3/100,000.² In recent years, there has been a reduction in Spain in the incidence from 17.93 cases/100,000 in 2007 to 9.43 cases/100,000 in 2017.³ In low-incidence countries, defined as those with an incidence below 10/100,000 inhabitants, most cases of tuberculosis are concentrated in a vulnerable population and some of the cases are produced by reactivation of a latent tuberculosis infection (LTI).

At the 67th World Health Assembly, in May 2014, the WHO adopted the “End TB” strategy with the aim of achieving the elimination of the disease.⁴ Currently, 24% of the world's population has a LTI⁵ and it is estimated that these individuals have a reactivation risk of tuberculosis throughout life of 5–10%; greater in the first five years after the initial infection. People with LTI are the reservoir of *Mycobacterium tuberculosis*, and it is believed that while this reservoir persists the elimination of tuberculosis will not be feasible.⁶

The approach to LTI requires a complex array of consistent interventions in the selection of people to study, the diagnosis of LTI and the administration of a safe and effective treatment in such a way that most of those who start treatment complete it with a minimum of adverse effects. The follow-up and assessment of the whole process is also recommended.

Within the global “End TB” strategy, the detection of LTI among the contacts of tuberculosis patients is one of the main priorities.⁴ There is considerable evidence that the contacts of tuberculosis

patients present very high incidences of the disease. Therefore, Saunders et al.⁷ in a cohort study with more than 10 years of follow-up, estimated a tuberculosis incidence of 0.93 per 100 person-years. Similarly, in an evaluation of 108 contact tracing studies performed in countries with high admissions, Fox et al.⁸ estimated that the prevalence of tuberculosis cases among contacts was 1.4% (95% CI: 1.1–1.8%) and that the prevalence of LTI was 28.1% (95% CI: 24.2–32.4).

There are risk factors and environmental conditions that, in very specific situations, can increase these very high risks even further. Therefore, this risk can be much higher in exposures to index cases with positive bacilloscopy of the sputum and with a long diagnostic delay, which involves cavernous lesions that facilitate the elimination of a large number of bacilli.⁹ These patients, in particular in rooms with poor ventilation, can generate outbreaks of tuberculosis with very high incidence rates of tuberculosis and prevalences of LTI. These outbreaks are real challenges for health systems due to the difficulty in identifying the true index case which generated the transmission, tracing all those exposed, diagnosing and recording all the cases of tuberculosis and LTI, prescribing preventive treatments and ensuring compliance with them.¹⁰ In addition, they are situations which require strong coordination of public health teams with care services to manage the outbreak and tackle the potential social alarm and media impact that they can generate.

Therefore, in the study by Castells et al.¹¹ which was published in this issue of the journal, an outbreak was reported in which in one of the affected rooms, an incidence of tuberculosis of 10.4% and a prevalence of LTI of 88.1% was reached, much higher than those found in a conventional contact tracing study. This study gathered a good part of the characteristics which the outbreaks published in the literature tend to present¹⁰: difficulty identifying the case which generated the transmission, long diagnostic delay, positive sputum bacilloscopy and repeated exposures in environments with incorrect ventilation.

Exposure in places with deficient ventilation enables very high concentrations of aerosols of *M. tuberculosis*, which facilitate the new LTIs among those exposed. In a cohort study with more than 10 years of follow-up, it was estimated that the cohabitants of

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* Corresponding author.

E-mail address: Pere.godoy@gencat.cat (P. Godoy).

homes with fewer windows presented a greater risk of LTI.⁷ In an environmental study, Escombe et al.¹² revealed that natural ventilation by means of opening doors and windows provides high air exchange rates per hour, even higher than those supplied by negative-pressure isolation rooms.

This and other studies¹³ indicate that, despite the importance of transmission in homes and the significant risk for cohabitants, the transmission of tuberculosis also occurs outside homes. Therefore, Yates et al.¹⁴ estimate that the majority of transmissions occur at a community level, outside the normal residences of infected individuals.^{13,14} In this context, the approach to individuals exposed using the concentric circles technique can have certain limitations and new techniques and strategies which help in the routine contact tracing studies should be incorporated. It has been suggested that the incorporation of the analysis of social networks that enable risk situations to be identified outside homes could improve the comprehensiveness of contact tracing studies. Therefore, in Japan, in a retrospective study of an outbreak, Kawatsu et al.¹⁵ reveal the greater risk of LTI in contacts who have a high score in social contacts. These techniques, along with the incorporation of genotyping techniques, could facilitate the detection of infected cases that may escape conventional investigations. Thus, in a survey conducted in Germany¹⁶ the usefulness of molecular epidemiology techniques in routine contact tracing studies performed by public health officials who had this test available, in comparison to those who did not have access to this technique, was shown.

The improvement in the effectiveness of contact tracing studies should be assessed in the overall context of the so-called “cascade” of the contact tracing study. In a review of 58 studies with 748,572 people, Alsdurf et al.¹⁷ identified the “cascade” stages in which the greatest number of contact losses occurred. In this review, they estimate that the initial screening is completed by 71.9% of the candidates, subsequently the medical assessment is completed by 43.7%, LTI treatment (LTIT) is started in 35.0% and, in the end, the LTIT is completed in 18.8%. The same authors recommend that each health system investigates the stages of the process and identifies the factors responsible for the greatest number of contact losses. In the study by Castells et al.¹¹ the compliance of LTIT with superior results to those published is described, but the problems that should be subject to reflection for our health system are also pointed out.

The reduction in diagnostic delay attributed to patients and to the health system itself should be a priority to reduce transmission and the probability of outbreaks occurring. This delay should not be longer than 30 days, and, for this, it is key to reduce the stigma of the disease in the population, normalise its approach and manage to make tuberculosis a priority for the health system. In a context of low incidence such as the current incidence, it is key for professionals to consider tuberculosis when faced with patients with symptoms of persistent cough which started two or more weeks ago.

To prevent contact losses in the first stages of the process, it is key to have public health units in all territories that have adequate resources for the tracing and study of contacts in coordination with the care services. Some studies indicate the usefulness of case management public health nurses and of community health agents to complete the concentric circle techniques. The availability of molecular biology techniques for all territorial units would help to detect groups of cases that can go unnoticed in the conventional contact tracing studies. The creation of clinical tuberculosis units which facilitate access and the timely study of contacts, coordinated with the public health services, could also improve the diagnosis and follow-up of contacts with LTI and LTIT.¹⁸

The test that continues to be recommended for the study of LTI in the future Plan for the Prevention and Control of Tuberculosis in

Spain is the tuberculin skin test with positivity for values ≥ 5 mm in the case of contacts. In the same Plan, it is also indicated that the interferon gamma release assays (IGRA) should also be made available for positive reactions in those vaccinated with BCG or with negative results in immunosuppressed individuals or those under 5 years of age.

Effective compliance with the LTIT is the key element to manage to prevent cases among contacts. This is one of the most deficient steps in the entire “cascade” and, therefore, it is subject to improvement in Spain. Existing studies point to compliance rates that, in general, do not exceed 70%. Among the international studies on acceptance factors and compliance with LTIT,^{19,20} there is high variability in elements associated with different health systems, the profile of contacts, the types of factors studied and the treatment regimens used. The classic treatment for LTI has been isoniazid in a regimen for six or nine months for the general population and 12 months for patients co-infected with HIV. However, shorter regimens have also proven to be effective, such as rifampicin for three or four months, isoniazid plus rifampicin for three months and isoniazid plus rifapentine once a week for three months. Some studies have suggested higher compliance rates for the shorter regimens and fewer side effects. The efficacy of these regimens has been established in clinical trials, but its effectiveness in real situations of the tuberculosis control programmes is unknown.²⁰ Therefore, the recording and supervision of LTIT by clinical and public health services are key to assess LTIT and improve these outcomes. The follow-up of these by health agents and public health nurses may also be useful. Some studies also suggest the usefulness of directly observed treatment (DOT) in subgroups of patients, and there are also initiatives which will be subject to assessment in the future, such as DOT by video via the telephone which can be particularly useful in rural and dispersed areas.

The “End TB” strategy is going to involve placing emphasis on the detection and treatment of LTI, as a matter of high priority (although not exclusively) on the contacts of tuberculosis patients over the next few years. This should involve prioritising the prevention and control of tuberculosis from the health services and strengthening the coordination of the different clinical and public health services. The new plan for the prevention and control of tuberculosis in Spain may help this process provided that it facilitates the allocation of the necessary resources and the prioritisation of the research lines which provide practical knowledge to contribute to this considerable international public health goal which is the elimination of tuberculosis.

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