

TUBERCULOSIS CASE INVESTIGATION PROTOCOL

1. Case, case contacts and epidemic investigation aims

1.1 *Single case investigation aims*

The infectiousness of each tuberculosis case is necessarily assessed, i.e. the risk that the patient will transmit (or has transmitted) the disease to other people. For this purpose, apart from collecting information about the characteristics of the patient's disease, information is also collected regarding the patient's activities and social environment. This information itself leads to the next step of the investigation, which is the investigation of the case contacts. For this reason, the continuous aim is to ensure the patient's cooperation and the creation of a climate of trust.

1.2 *Case contacts investigation aims*

The contacts have to be investigated in all instances of tuberculosis cases, which entail a risk of transmitting the disease to other people. The aim is to actively search for all the people who have had high-risk contacts (regular, close and prolonged) with the patient, and to examine them in order to detect latent tuberculosis infection or active tuberculosis and administer chemoprevention or full anti-tuberculosis treatment. This aims at protecting these people's health, but also at breaking the tuberculosis transmission chain, so that public health is protected.

1.3 *Epidemic investigation aims*

A tuberculosis epidemic is the appearance of two or more cases of the disease, which are not directly related to each other, in the same social, professional or other environment. This fact suggests that tuberculosis has been widely transmitted in a particular place. Therefore, an epidemic investigation primarily aims at **breaking the transmission chain**, and, if possible, **detecting the original source of infection** in order to prevent a new transmission in the future. As for the remainder, the same principles that govern the contacts investigation are applied on a greater scale and by taking into consideration the special characteristics of every environment.

Some places possess characteristics that favor the spread and the infection of *M. tuberculosis*, sometimes in combination with the presence of susceptible people who are more likely to become ill with active tuberculosis. These cases require special handling, even in the instance of a single case, in order to prevent an epidemic outbreak.

2. Case, case contacts and epidemic investigation

2.1 *Single case investigation*

In order to fully assess the infectiousness of a tuberculosis case, information on the characteristics of the disease is required:

- Anatomic detection of the disease (pulmonary / extrapulmonary)
- The patient's symptoms (e.g. cough, haemoptysis) and their start date
- Imaging test results (mainly chest X-ray)
- Laboratory test results (and information on the samples which have been sent to the laboratory and whose results are expected to be received)
- Anamnesis of previous tuberculosis disease and previous administration of anti-tuberculosis treatment
- Anamnesis of a chronic disease or other chronic health problems (e.g. alcoholism, substance use)
- Anamnesis of infection of the HIV virus

The physician can gather most of this information.

In the case that the characteristics of the disease do not suggest a risk of transmission to other people (extrapulmonary tuberculosis), no further investigation is required. Exceptionally, investigation may be recommended in some cases in order to detect the source of infection, especially when the patient is a child, who has probably been recently infected by an adult (see 4.2 'Investigation of the source of infection').

Contrarily, when there is a risk of transmission to other people (in all the cases of pulmonary or laryngeal detection, or tuberculous pleural effusion), the **transmission period** has to be defined. This usually begins when the patient's first symptoms occur or three months before diagnosis.

Moreover, further information has to be collected so that, contacts are subsequently investigated:

- Contact details (address, telephone number) of the patient and possibly of their immediate family;
information about the environment in which the patient was active (working, social, familial), where there are probably people who have come into close contact with the patient;
- An initial list of the people who came into close contact with the patient during the estimated transmission period, including their contact details.

This information is collected by patients themselves and is very important, especially with regard to the symptoms and the patients' environment. Therefore, it is necessary to create a climate of trust and cooperation, in order for the obtained information to be trustworthy.

In this framework, the public health official should give the patient the opportunity to ask any questions they have about the disease and the subsequent investigation steps, and these questions should be clearly answered. Discretion and respect for the patient's wishes are required, as tuberculosis is a disease that still carries a social stigma. Moreover, the patient has to be ensured regarding confidentiality, which is always in balance with the need for public health protection.

References:

1. Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of Persons with Infectious Tuberculosis - Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR 2005;54(No. RR-15)
2. Public Health Agency of Canada. Canadian Tuberculosis Standards, 2007.

2.1 Case contacts investigation

Contacts investigation is a main tool for the protection of public health against tuberculosis. Contacts must be investigated in *all* instances of tuberculosis cases when there is a risk of transmission to other people, i.e. in all instances of pulmonary or laryngeal tuberculosis cases. Priority is given to the investigations of contacts in which:

1. The case presents increased contagiousness (i.e. with positive microscopic examination of sputum, positive sputum culture or a cavern in the chest X-ray).
2. The case was not diagnosed for a long period of time (long period of contagiousness).
3. A big number of contacts or quite vulnerable people are involved (who are more likely to become ill with active tuberculosis if they are infected, such as children and immunosuppressed people).

The first step of the investigation is the examination of the case environment and the detection of the people with whom the patient came into contact during the period of contagiousness (case contacts). A person's environment can be divided in three parts: the familial environment, the school or working environment and the wider social environment. In these places, the case comes into regular, close and prolonged contact with some people, and it comes into less close contact with other people. These are depicted in image 1.

The investigation is led by the information given by the patient regarding their environment and contacts. Subsequently, the public health official thoroughly researches all the case contacts in these three directions. The places where the infection possibly occurred are also important; often, a visit to these places (e.g. to the patient's house) may reveal characteristics of theirs, which favor transmission, as well as contacts that were not initially detected.



Then, each contact undergoes a test in order to assess whether they suffer from active tuberculosis (in which case they have to receive full anti-tuberculosis treatment), or if they have latent tuberculosis infection (in which case they have to receive chemoprevention treatment). Unfortunately, up to now there is no single, simple and reliable screening test that separates the people who have been recently infected with *M. tuberculosis* from the people who have not been infected.

The initial risk assessment of each contact is *probabilistic*, and takes into consideration:

1. The **possibilities of infection**, based on exposure to the case.
2. A person's **vulnerability** to the infection and to the disease, i.e. the possibility of becoming ill with active tuberculosis after infection.

In this way, the case contacts are categorized into **high-risk, medium-risk and low-risk** contacts and priority is accordingly given to their investigation. The following characteristics increase a contact's risk:

Exposure to the case: This is a factor, which is difficult to quantify. The frequency and duration of contacts between the contact and the case plays an important role. Moreover, the place where

the two people came into contact is significant; the more confined, closed and poorly ventilated a space, the greater the possibility of transmission.

Age: Children up to 5 years of age have a significantly higher risk of becoming ill with active tuberculosis if they are infected, with a shorter incubation period. Moreover, they are more likely to suffer from more serious forms of the disease (such as tubercular meningitis), even though they do not usually transmit the disease themselves, but, on the contrary, are infected by adults who are in their environment.

Immunosuppression: The administration of cortisone, immunosuppressants (such as anti-TNF α agents) or chemotherapeutic substances, and the infection with the HIV virus, significantly increase the risk of active tuberculosis outbreak after an infection with *M. tuberculosis*. HIV-infected people, in particular, may become ill with active tuberculosis very quickly, with an atypical clinical and radiological appearance; therefore they require special attention. HIV testing should be provided to all those who are suspected of being infected.

Other conditions: Malnutrition and low body weight, alcoholism, diabetes mellitus, chronic renal insufficiency and intestinal malabsorption syndromes are conditions, which, increase a contact's vulnerability to the infection and to the disease.

The process of testing each case contact includes the following:

1. Medical history taking:
 - Assessment of the risk (possibility of infection and vulnerability to the infection)
 - Questions about tuberculosis symptoms (cough, haemoptysis, weight loss)
2. Mantoux test (or IGRA)
3. Chest X-ray (if necessary)

The Mantoux test is done during the initial assessment. If the result is negative and if less than 8 weeks have passed since the person's last contact with the case, the test is repeated when the period of 8 weeks has elapsed. This is the maximum time required for the Mantoux test to produce positive results after an infection with *M. tuberculosis*. The test result is assessed according to the possibility of infection and the person's vulnerability to the infection, by using different boundaries for the reaction diameter, measured in millimeters (see table 1). The test is also taken in order to cover the possibility of alteration (increase >10mm) in comparison to a previous Mantoux test.

IGRA testing, if available, can be used alternatively or additionally, especially in cases where the positive result of the Mantoux test is doubtful, for example due to previous vaccination with BCG. However, it is highlighted that there is not wide experience regarding the use of IGRA in children, immunosuppressed people and people who have been recently exposed to the mycobacterium.

If the result of the Mantoux test (or of the IGRA) is positive, or if there are any suspicious symptoms (cough, haemoptysis, weight loss), a chest X-ray must be taken in order to exclude the possibility of active tuberculosis. Full anti-tuberculosis treatment is administered to those who become ill with the disease. If the X-ray is negative, the possibility of chemoprevention is

considered (see section 5.2 'Precautionary measures'). Under no circumstances should chemoprevention be administered if there is any clinical, radiographic or microbiological indication of active tuberculosis.

During the contacts investigation of a tuberculosis case, medium-priority and high-priority contacts are investigated first, according to their proximity to the case and their vulnerability. It may be decided to **extend the investigation** to cases of lower priority in one of the following cases:

- If an unexpectedly high percentage of tuberculosis infection or active tuberculosis is detected in the investigated contacts. This depends on the type of the investigated population and on its transfection rate, which should be normally defined by prevalence studies.
- If there are indications of secondary transmission, i.e. transmission from diseased case contacts to other (secondary) contacts.
- If there are indications of transmission or disease among contacts of lower priority.

In any case, high-priority contacts must be investigated before it is decided to extend the contacts investigation. In other words, the investigation follows the logic of concentric circles, as shown in image 1. The decision to extend the investigation to the next circle always takes into consideration the expected benefit (detection of contacts with latent tuberculosis infection or active tuberculosis) in relation to the available resources. Additionally, the more we walk away from the initial case, the higher the possibility of a false-positive Mantoux test result among the people who are investigated. In the case of a lack of resources, both human and material, assistance is sought from a larger health organization.

The case investigation is completed when there are no more reasons to extend it, when all the suspicious case contacts have been detected and investigated, and when the treatment of the people who suffer from active tuberculosis or latent tuberculosis infection is underway.

Investigation of the source of infection

Children up to 10 years of age do not usually transmit tuberculosis to other people, and they are infected by diseased adults who are in their environment (usually in the familial environment). Therefore, there is no point in investigating the contacts of a child who is ill with the disease, but it is important to search for the adult who constituted the source of infection, in order to investigate their contacts. This reverse process is called *investigation of the source of infection*: people who display tuberculosis symptoms are sought in the environment of the case (i.e. of the child), and they take a Mantoux test and a chest X-ray. The relevant information is usually obtained from the child's parents or guardians.

The success of an investigation of the infection source depends on the time when a person was infected. A diseased adult may have been infected with *M. tuberculosis* many years ago, therefore it is practically impossible to detect the source of the infection. Children, however, and especially very young children (up to 5 years of age), have been recently infected; usually, the adult who constitutes the infection source is still in the child's environment and therefore he or she can be identified and receive anti-tuberculosis treatment in order for the transmission chain to break.

However, the investigations of an infection source are generally not very effective in comparison to the effort they require; therefore in most cases they are recommended only when there are large resources and when the high-priority contacts investigations are successfully conducted.

2.3 Epidemic investigation

In the event of an outbreak of more than one cases of tuberculosis on the same site, the same process of contact investigation applies, but on a larger scale. A very large number of individuals to be checked may be involved, an undertaking that involves difficulties in terms of organization and limited availability of resources. The assistance of numerous bodies and the cooperation of numerous interested parties are often needed.

The contacts of each case are investigated while focusing on the epidemiological connections between the cases and between the contacts. At this point, techniques of molecular typing of mycobacterium (genotyping) implemented over the last years may help. Contact search is carried out aggressively and thoroughly, as, if diseased individuals elude, the epidemic will continue and there will be new cases. At the same time, the initial patient who served as a source of contamination is searched for between the contacts.

However, apart from the outbreak of several tuberculosis cases on one site, some sites have specific characteristics that favor the spread of *M. tuberculosis* and contamination. In view of many specificities in these sites, special action is required even when a case occurs.

Schools and educational institutions

This category includes crèches and childcare facilities, kindergartens, primary and secondary schools, and universities.

The investigation of tuberculosis case contacts on these sites has many specificities and difficulties:

- Large number of contacts, with indefinite duration and proximity.
- Presence of individuals with particular vulnerability, because of young age and/or ongoing health problems.
- Particular sensibility to children of families and society.
- Possible interest by the Media

An absolute prerequisite for the success of the investigation is the establishment of a climate of trust. All actions are taking place in direct consultation with the officials responsible in the school, and parents are provided with full information. This looks particularly complicated: parents often have difficulty understanding the reasoning behind the contact investigation, sometimes reveal mistrust and suspicion, and may object to both the administration of chemoprophylaxis to their child and non-administration. The public health official should have patience and communicative skills, respond to all questions and, as far as possible, prevent them by informing in advance of the actions required.

At the same time, the social status of the case should be protected, whether it involves a child or an adult. This is not so much about the -self-explanatory- effort to protect the private data· it is more about preventing the social stigma of the case, which depends on a more complete public information and enlightenment of the disease.

The strategy to be adopted in contact investigation varies according to whether the case is a child or an adult. If the case is a child <5 years old, then all of the adult workers should be included in the investigation with a view to discover the source of contamination (see investigation of contamination source).

During holiday periods, occupations or excursions, the contact investigation is rendered difficult. The health department in partnership with the officials responsible in the school undertake to inform the close contacts of the case.

Reformatory stations

Tuberculosis is a major public health problem for the reformatory stations of the country. Contributing factors are poor hygiene, incorrect ventilation, increased prevalence of HIV infection and frequent movements of prisoners.

The communication and cooperation of the personnel and the public health officials are a prerequisite for the effective investigation of contacts in the reformatory stations. During the contact investigation, the procedure to be followed is the ordinary one, however the information of the competent management employees of the station is required. Particular emphasis is placed on information involving the detention in other reformatory stations during the period of communicability.

All individuals should be offered a check for HIV infection, especially in high risk cases (e.g. because of injecting substances use). Further, the possibility of infection with hepatitis B or C is taken into consideration, which makes it difficult to administer anti-tuberculosis drugs (both for chemoprophylaxis and treatment).

Those suffering from active tuberculosis should be isolated from the rest prisoners until they receive treatment for a period that is sufficient to allow them to become non-communicable. Such is the case with those who manifest suspected disease symptoms, until the completion of the check. If the reformatory stations do not have a suitable space (e.g. infirmary or separate cell), then they should be transferred to another station.

References:

1. Centers for Disease Control and Prevention. Prevention and control of tuberculosis in correctional and detention facilities: Recommendations from CDC. MMWR 2006;55(No. RR-9)
2. World Health Organization: Tuberculosis control in prisons. A manual for programme managers.

Air Travel

An airplane cabin is a closed and restricted space, but has ventilation systems with filters which keep the high quality of air. The risk of tuberculosis contamination in air travel is considered low and involves flights of long duration.

The World Health Organization recommends that the contact investigation be carried out when a tuberculosis case with a contaminating disease has traveled on a flight of over 8 hours long (total time onboard) and a period of three months has not elapsed since that trip. The investigation involves co-passengers sitting on the same row with the case, and those sitting on two rows ahead and two rows behind.

Nevertheless, there are many doubts about the feasibility of this recommendation. Globally, no cases of active tuberculosis due to onboard aircraft contamination have been reported, except for a few incidents of latent tuberculous infection. Such type of investigation has a low efficiency and presents considerable technical difficulties: airlines are difficult to provide the contact details of passengers, often passengers are dispersed in numerous countries, and the public health authorities of each individual country should be notified.

References:

1. World Health Organization. Tuberculosis and air – travel. Guidelines for prevention and control.
2. Abubakar I, Welfare R, Moore J, Watson JM. Surveillance of air-travel-related tuberculosis incidents, England and Wales: 2007-2008. *Euro Surveill.* 2008;13(23):pii=18896.
3. ECDC technical report. Risk assessment guidelines for infectious diseases transmitted on aircraft.

3. Precautionary Measures and Public Health Interventions

3.1 Patient precautionary and control measures

At the level of a single tuberculosis case, the cornerstone for protecting public health is **the effective and complete treatment of each patient with anti-tuberculosis drugs**. The anti-tuberculosis medication, even with the most recent regimen, lasts at least 6 months, and its temporary interruption increases the risk of recurrence and development of solid strains.

For this reason, the access of all patients with tuberculosis, both in urban centers and provinces, to high level health and care services, should be guaranteed. This is complicated even further in cases of special populations (e.g. immigrants, gypsies, homeless), for whom keeping to the anti-tuberculosis medication is often difficult. In such special groups, the Directly Observed Therapy Short-course (DOTS) plays a role. To prevent the spread of disease, the patient should avoid close contacts with other persons for the duration of the transferability period. During this time, the personnel involved in patient care should comply with the respiratory hygiene measures. Both the simple surgery mask and the respirator N95 provide effective protection from the risk of transmission of tuberculosis. The transferability period of patient ends when the patient has no symptoms and the microscopic examination of sputum is negative for acid-fast bacilli: this usually requires receiving anti-tuberculosis medication for a minimum of 2 weeks. From that point onwards, the patient may return to their activities, provided that they receive with due care the administered anti-tuberculosis medication.

References:

1. Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of Persons with Infectious Tuberculosis - Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR 2005;54(No. RR-15)
2. Ministry of Health. 2002. Guidelines for Tuberculosis Control in New Zealand 2003. Wellington: Ministry of Health.
3. Centers for Disease Control and Prevention. Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings. MMWR 2005;54(No. RR-17)