Consensus Document on the control of Tuberculosis in Spanish Prisons (summary)

Working group for the creation of the document*

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INTRODUCTION

Tuberculosis (TB) still remains a main concern for public healthcare due to cases of multi drug resistance(MDR), amongst others, which involve an adverse prognosis because if their difficult treatment and the exponential increase in the resources needed for each patient.

People housed in Spanish detention facilities answer to a demographic profile which includes almost all risk factors related to TB. Since the permeability between the penitentiary and the general populations is high, an appropriate control of TB is obviously beneficial for everyone.

This document complements the 2001 TB prevention and control program in Spanish prisons as far as it compiles the consensus among the groups with a greater implication in TB in our country.

The grades of recommendation followed have been:

A: strongly recommended

B: favourable recommendation

C: favourable recommendation but inconclusive.

The degrees of evidence have been classified as follows:

I: Randomized, controlled and properly designed trials and meta-analysis.

II: Properly designed controlled trials, cohort or case control studies preferably from more than one centre or research group.

III: Opinions based on clinical experience, descriptive studies, clinical observations and expert opinions.

DIAGNOSIS OF TUBERCULOSIS DISEASE

Early diagnosis of tuberculosis, especially of the pulmonary forms, is essential for its control [2]. Approximately 14% of Tuberculosis (TB) cases are negative for cultures[3], in which case the diagnosis criterion and the therapeutic attitude will be based

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on clinical, radiologic and laboratory data (including anatomopathologic information when necessary).

The identification of cases will greatly depend on the suspicion degree and, therefore, of the awareness of the problem among the healthcare professionals and the population.

IDENTIFICATION OF TUBERCULOSIS CASES

The diagnosis and early detection of tuberculosis are based on:

A. Diagnostic suspicion: Pulmonary tuberculosis (PTB) must be suspected before any person spontaneously consulting for coughing and/or expectorating, with no other identified cause, during two or more consecutive weeks. Suspicion must be even more if the symptoms are accompanied by haemoptysis and/or systemic manifestations[4] (AIII).

B. Active search of TB cases: Upon admission, all inmates will be assessed by means of a directed clinical questionnaire [1] on respiratory or constitutional symptoms, history of tuberculosis infection (TI), contact with people with TB, active TB or the treatment on any of them, as well as for risk factors for resistance (AIII).

Research must be done on social, demographic and clinical factors related to the risk of tuberculosis infection (TI) which lead towards an increased development of the active disease. Within the penitentiary setting, the most important factors are: HIV infection, illicit drug or alcohol consumption, immigration from areas with high rates for TB, undernourishment, homelessness, immunosuppressive treatments, gastrectomy, diabetes mellitus, chronic renal insufficiency and malignant hematologic diseases which also increase the risk.

People belonging to risk groups must be informed about the symptoms of the disease and specific appointments must be periodically arranged for them (medical or nursing consultation) (BIII). If it was a nursery consultation and any symptoms were detected, the patient would be immediately transferred to medical consultation.

We must always take into account the possibility of presentation forms other than the pulmonary, which represent 25% of all the TB forms.

C. Contact studies: Active search of cases among the contacts of TB patients. This will be developed in a specific section.

DIAGNOSTIC TESTS

All those patients suspected from TB must undergo these tests in less than 48 hours [4] after their immediate airborne infection isolation and immediately if possible (AIII).

A. Chest Radiograph in two views; if it is normal it rules out pulmonary tuberculosis in over 95% of immunocompetent adults. It must be read as soon as possible, preferably within the first 24 hours [4, 5] (BIII). There is no pathognomonic pattern for TB; the radiograph doesn't allow differentiating the activity of lesions [6].

B. Microbiology; it is the base for the certain diagnosis of TB. Its sensitivity depends of the quality of samples and its processing. Therefore, efforts must be made to get the appropriate samples and all of them must be processed for microbiologic study (AIII).

It must include: sputum smears series: at least three samples must be taken in three different days, obtained early in the morning and on an empty stomach; these have a moderate sensitivity (22-80%) and are highly specific: a positive result practically confirms over 95% of the cases and is an indication for therapy [8,9] (AIII). Sputum culture: it's more sensitive and specific and it allows identifying and testing antimicrobial drug susceptibility. Antimicrobial susceptibility: it must be specifically required. It has to be done in all positive cultures and it must be done at least for all 1st line medications (AIII). Antimicrobial susceptibility must be repeated when cultures remain positive after three months of TB therapy or if once negative they convert to positive [10, 11].

All biologic samples affected must undergo these tests in case of suspicion of TB forms other than pulmonary.

C. Tuberculin Skin Test (TST), it plays a secondary role in the diagnosis of TB but it can be useful when there is a previously negative TST.

DERIVATION FOR THE DIAGNOSIS OF THE DISEASE

An expert should be consulted whenever any disagreement between clinical manifestations and different diagnostic test should arise; if any specialised resources were needed or were not available within the facility; this is, if there were any doubts concerning the diagnosis of the disease (AIII).

TREATMENT OF TUBERCULOSIS

The treatment of TB implies an appropriate use of medication during a proper period of time. This converts patients from contagious to non-contagious in a short period of time [11]. Monotherapy should never be used and active medications should always be administered (AI).

An incorrect prescription and/or fulfilment can encourage the emergence of drug resistances. Within detention facilities, all conditions lead to an appropriate directly observed therapy (DOT) which must COMPULSORILY BE CARRIED OUT[1] (AII).

Basis for the treatment of TB

The treatment for TB is divided into two different phases: an Initial Phase, with a daily regimen [4, 8 13] (AI) and a Continuation Phase during which the sterilising effect eliminates bacilli and prevents relapse with intermittent administration. The latter should only be used in prisons under extraordinary circumstances.

Medications against TB

Anti-TB drugs are classified in two different groups according to their efficiency, power, toxicity and tolerance.

a. First line drugs [14-17]: Isoniazid (H), Rifampin (R), Pyrazinamide (Z), Ethambutol (E) and Streptomycin (S): see Table 2 for dosing and routes of administration. There are other drugs within the rifamycin group with anti-TB activity: Rifampentin and Rifabutin.

b. Second line drugs: Quinolones (moxifloxacin, gatifloxacin, levofloxacin, ofloxacin), aminoglycosides, capreomycin, ethionamide, prothionamide, cycloserine, PAS, linezolid.

Treatment Regimens

Within detention facilities it is recommended an Initial Regimen with 4 drugs, so that the standard regimen will be 2HRZE/4HR[1, 10](AI). If cavitation is developed or the culture reveals a positive result two months later and the patient is HIV positive with < 200 CD4/ml, the regimen administered should be 2HRZE/7HR (AI).

In order to encourage adherence and prevent monotherapy related risks, standard regimens should be administered as combined preparations (BIII): see Table 2 for the main pharmaceutical combined preparations available in the Spanish market.

Table 1. First line anti TB drugs

		DOSING mg/kg (maximum daily)		
DRUG	ROUTE	DAILY	3 TIMES/WEEK	2 TIMES /WEEK
Rifampin	Oral IV	10mg/kg. Max. 600mg	10mg/kg Max. 600mg	10mg/kg Max. 600mg
Isoniazid	Oral IV IM	5mg/kg Max. 300mg	10mg/kg Max. 900mg	15mg/kg Max. 900mg
Pyrazinamide	Oral	25-30mg/kg (2,5g)*	30-40mg/kg Max. 3g	50mg/kg Max. 4g
Ethambutol	Oral	25-30 mg/kg (Initial Phase) 15mg/kg (Continuation Phase)	25-30mg/kg (4g)	50mg/kg (2,4g)
Streptomycin	IM	15mg/kg Max. 1g >60 years old max. 0.75 g	25 mg/kg Max.1.5g >60 years old 1g	25-30mg/kg Max. 1.5g >60 years old 1g

*If <50 kg: 1.5g; from 50 to 75 kg: 2g; >75 kg: 2.5g.

Table 2: Anti-TB Combined Presentations

Composition	Dosing (mg)	Commercial Name
H+R	150/300	Rifinah® Rimactacid®
H+R+vit.B6	300/600/50	Tisobrif®
H+R+Z	50/120/300	Rifater®
H+R+Z	75/150/400	Rimcure®
H+R+Z+E	75/150/400/275	Rimstar®

TREATMENT OF SPECIAL SITUATIONS

A. HIV+ Patients:

In view of the complications derived from TB in a patient infected by HIV, if the situation concerning HIV infection is unknown, the relevant serology will be carried out except in case of flat refusal.

Priority will be given to the treatment for TB because Highly Active Antiretroviral Therapy (HAART) allows more flexibility.

Special attention must be paid when both treatments are jointly administered (CIII) because of drug interactions, shared toxicity and the immune reconstitution inflammatory syndrome (IRIS); the latter leading to paradoxical worsening of TB.

STRATEGIES:

1. Patients with no HAART and CD4 cell count >350/ml: anti TB therapy should be completed before starting antiretroviral therapy [17-20].
2. If HAART must be administered: it should be deferred 4 to 8 weeks so that potential side effects can be attributed to one or another, to improve adherence and prevent paradoxical reactions such as IRIS.
3. Patients already carrying out HAART: relevant adjustments should be made in order to suit both treatments trying to keep within the regimen a rifamycin [17]. If this was not possible regimens such as 2HEZ/16HE or 2HZE/16HE and fluoroquinolones (moxifloxacin or levofloxacin) can be used (BIII). In this case, it is recommended to consult an expert because of relapse risk associated to regimens without a rifamycin.

B. Patients on methadone

Methadone dosing must be readjusted because of the effect of rifamycins, especially R, due to its interaction, both at the beginning (withdrawal) and at the end of the treatment (overdose) (AI), affecting methadone levels. It can be useful to split up daily dosing in two to achieve more stable blood levels throughout the day [6]. These interactions can also take place if an R intake is missed out; therefore, intermittent administrations are contraindicated. The first day not taking R, methadone dosing will be reduced by 50% with strict monitoring of the appearance of any overdose symptoms.

Patients must be informed about such risk before initiating therapy and reminded in case of discharge. The outer facility where the patient will continue methadone therapy must also be informed [6].

C. Extrapulmonary tuberculosis

Usually diagnosis will be made by the expert and we will follow the regimen established by him/her. Combination therapy used is the same as in pulmonary TB and most commonly periods are also the same, except in the case of central nervous system or meningeal involvement, which require longer periods[4].

D. Pregnancy and Lactation

Regardless of the gestational status, therapy must be initiated as soon as the disease is diagnosed; the standard regimen is recommended.

During breast feeding, first line agents do not entail any problems, since only minimum concentrations reach breast milk. Anyway, women who breast feed must take pyridoxine supplements [1, 10].

E. Hepatopathy

Patients suffering from acute hepatitis or chronic hepatopathy (especially cirrhosis) are at risk of worsening because of iatrogenesis. Therefore, the reference expert must be consulted [1, 10].

These patients must be closely monitored so that any abnormal results in liver function tests or clinical symptoms suggesting toxicity are diagnosed as soon as possible to prevent hepatopathy worsening [20].

TOXICITY AND INTOLERANCE

Special attention must be paid to interactions between anti TB agents, especially R, and other medications because of the potential appearance of serious interactions.

If any serious toxicity or intolerance cases occur, the reference expert must ALWAYS be consulted.

Adherence to tuberculosis treatment

TB treatment has to be specifically monitored in order to detect adverse effects and assess clinical and microbiological response (CIII); patients must be informed about symptoms indicating iatrogenesis so that they consult. It is recommended that a fixed number of appointments is established so that clinical revision takes place and blood tests are reviewed (complete blood count and biochemical analysis). Therefore appointments have to be set at least 15 days, one month and on months 2, 4 and 6 after initiation of therapy [6], radiograph on months 2 and 6 and upon completion if therapy is prolonged.

If S is used, monthly audiometry, renal function tests and electrolytic determinations must also me done. Whenever Rifabutin is used, monthly complete blood count and platelet count have to be done [1].

Multi Drug Resistant (MDR) TB implies that minimum follow-up must be done up to 24 months after completing therapy (C).

Management of Adverse Effects

The appearance of dermatological, hepatic, gastrointestinal and/or hematologic manifestations do not always entail systematic discontinuation of therapy.

Because of the particular circumstances of the penitentiary setting, with high hepatopathy rates, special attention is paid to hepatic abnormalities; in case of appearance of jaundice all drugs have to be discontinued because of the high risk of severe cases of liver failure.

It also has to be taken into account that therapy should never be discontinued for over a week and monotherapy should never be used (AI): regimens must always include three active anti TB agents during the initial phase and two during continuation [21] (AI).

Interrupting Therapy

Discontinuation highly depends on the phase of therapy but generally speaking the situation is more serious if discontinuation occurs on early stages and for a long period of time. Continuation of therapy is more important at the beginning, when both the bacillary load and the risk of developing resistance are higher [10]. An expert must always be consulted in these cases and if therapy is retaken, four drugs must be used.

MANAGEMENT OF TREATMENT FAILURE AND RELAPSE

A. Treatment Failure

Treatment failure is defined as recurrently positive cultures after four months of treatment or the appearance of two new positive cultures after previous conversion. The possibility of drug resistance must be considered and must be empirically managed with at least four anti-TB agents which have not been used before. A single drug should never be added to a failing regime (AII). For patients infected by HIV on HAART, IRIS should also be considered. Anyway, in prison, early consultation with an expert should always be pursued (AIII) so that a new regimen is established.

Drug susceptibility testing for both first and second line agents should be done (BIII) in all cases.

B. Relapse

Relapse is defined as recurrent positive smears and cultures, or clinical worsening suggesting active TB, at any time after completion of treatment and apparent cure. Most relapses occur within the first 6 to 12 months following completion of therapy and are mainly due to a relapsed infection due to the same M. Tuberculosis strain. Exogenous reinfection with a new strain is more unusual. Factors suggesting potential relapse risk are: initial resistance to H and/or R, positive cultures after two months of effective treatment, self administered treatments and no rifampin-containing regimens. The latter entails a high risk of acquired resistance. An expert should promptly be consulted.

DRUG RESISTANT TUBERCULOSIS

The appearance of drug resistance is mainly due to improper management of the disease, something which can make us somewhat responsible for it [16]. It can also occur because of non adherence to therapy by the patient. The management of patients with resistant disease should ONLY be done by, or in very close consultation with, experts in this area (AIII).

Apart from primary or secondary, the different types of drug resistant tuberculosis are defined as follows:

a. Poly drug resistance is defined as resistance to more that one of the first line drugs but not to both R and H simultaneously.
b. Multidrug-resistant tuberculosis (MDR-TB) refers to resistance to at least H and R simultaneously aside from additional resistance to other chemotherapeutic agents.
c. Extensively drug resistant tuberculosis (XDR-TB) refers to resistance to H and R as well as to fluoroquinolones and either aminoglycosides or capreomycin, or both.

PREVENTION OF TRANSMISSION

a. Airborne Infection Isolation

The protection of the general population must sometimes prevail over individual rights; in prison any inmate suspected from active TB must be isolated until contagiousness is ruled out.

Negative pressure rooms are employed whenever feasible and inmates must undergo isolation until AFB smears become negative. All detention facilities are recommended to build negative pressure rooms but anyhow, recirculation to general ventilation should be avoided.

During isolation, AFB smears must be repeatedly tested once a week if previous results were positive after two weeks therapy. If no negative pressure rooms are available the patient will be placed in a cell alone and will be told to close the window and use a protection mask whenever the door is going to be opened, clean the room frequently, wash the floor and cover his/her mouth when coughing.

Surveillance staff will also be informed about these measures in order to ensure fulfilment.

b. Personal Protection

Patients will be given surgical masks to prevent respiratory secretions from entering the environment, when having contact with other people in any circumstances. Any person having contact with TB patients will be given respiratory protection masks such as FFP2 or FFP3.

The patient will be allowed to have contact with his/her relatives in the Nursing Room of the facility with the aforementioned protection measures.

The patient under isolation will not be transferred to any other detention facility. If required to leave the facility, the patient will be transferred alone by means of an ambulance and both the patient and custody staff will be given appropriate protection measures and will be informed about their importance.

DIAGNOSIS AND TREATMENT OF TUBERCULOSIS

The Tuberculin Skin Test (TST) is the most extended and accepted for the diagnosis of tuberculosis infection (TBI). It is performed by means of the Mantoux technique y must be done on any inmate upon admission with no previous documented positive TST (TST+) (BIII). Booster response must be considered when performing a TST for the first time with a negative result.

Positivity criteria for tuberculin skin test

Induration values of 5mm or more are considered positive aside from vaccination as well as the appearance of vesicles or necrosis.

Conversion criteria for TST within detention facilities

Conversion is defined as any expansion of TST induration of over 5mm. As far as patients previously vaccinated, it can not be reliably established whether the response is due to *M. tuberculosis* infection or to a reaction caused by vaccination. Anyway, when dealing with groups at high risk of infection, a history of previous vaccination must not be taken into account. For those with previous vaccination it is established that a TST reaction of 5 mm or more indicates infection by *M. tuberculosis*. Interferon Gamma Release Assays (IGRA) have proven suitable for people living with, or in close contact with active TB patients, patients with a chest radiograph suggesting inactive TB, HIV infected patients or at HIV related risk factors and patients with silicosis [9]. IGRAs measure T cell release of interferon-gamma following stimulation by antigens unique to *M. tuberculosis*.

Conversion entails a higher risk for developing the disease and therefore, a priority for instituting treatment of TB infection.

Latent TB Infection Treatment and chemoprevention

Prevention can be either primary or secondary. Primary prevention is designed for patients with a negative TST in order to avoid infection and Secondary prevention is for patients with positive TST as to avoid the development of the disease. The latter consists of therapy for latent TB infection so currently the term LTBI Treatment is used.

Candidates for LTBI treatment within detention facilities

Three levels for LTBI treatment are defined regarding the presence of risk factors for developing the disease: very high risk, medium risk and low risk (see Table 3).

Rationale for Primary Prevention

Primary Prevention is indicated for people at high risk of exposure to TB patients without a documented infection, in the following cases: children under 5, HIV infection, severely immunosuppressed or anergic patients, as well as in the case of microepidemics. TB disease must be excluded; therefore, the TST is repeated 2-3 months later and if conversion occurs therapy is continued upon completion. If TST remains negative discontinuation of therapy is therefore indicated except if there is concern about any risk situation.

Pretreatment evaluation

LTBI treatment is only instituted when the risk for developing the disease is clearly higher than that of hepatic toxicity derived from therapy. Therefore, it must be a priority for high-risk patients (AI), for whom DOT is highly recommended, and a suggestion for medium-risk patients (BIII).

TB disease and medical contraindications must be previously excluded. People who have previously completed treatment for LTBI do not need to be treated again unless contact with active TB patients has occurred and if they meet the aforementioned primary prevention conditions.

Monitoring of patients during LTBI treatment

All patients should undergo clinical monitoring at least monthly, considering both compliance and adverse reactions. Hepatic function tests should be carried out monthly and every 1 or 2 month at a later stage, especially for patients with previous hepatic test abnormalities, HIV infection, pregnancy, active illegal drug consumption or a reported history for HBV and/or HCV. Proper compliance must be checked and the patient must be motivated to adherence.

Discontinuing LTBI treatment

Discontinuation of therapy is indicated for clinical signs suggesting toxicity such as either of the transaminases being greater than 5 times the upper limit of normal without symptoms, or greater than 3 times the upper limit with simultaneous presence of clinical symptoms or clinical hepatitis signs.

Treatment regimes for TB infection

A lot of inmates stay for less than a year within detention facilities. Therefore, short regimes are preferred in order to ensure completion of therapy. Recommended regimes (see Table 4) are the following:

A. Isoniazid (H) daily or interruptedly.

It is the most studied and efficient drug [4]. It is administered once a day (300mg/day) or twice weekly (900mg/day), and so DOT is used, during 6 to 9 months [23-25].

B. Rifampin (R).

The regimen includes 600mg/ day during 4 months [4]. It is an alternative regimen indicated for patients who do not tolerate R or who have had contact with isoniazid resistant tuberculosis with susceptibility to R (BIII). It can be recommended within detention facilities for its shorter duration.

Special care must be taken with patients under methadone treatment or HAART for HIV including protease inhibitors except Ritonavir, or non-nucleoside reverse transcriptase inhibitors (NNRTI).

C. Alternative regimens for LTBI treatment with short regimens.

C1. Regimen including 3HR: 3 months of H (5mg/kg/day with a maximum dose of 300mg/day) and R (10mg/kg/day, maximum 600 mg/day), with a similar efficiency and security degree to the standard regime [1, 24-26]. Due to its shorter duration and to the fact that commercial combined preparations are available, this regimen enhances adherence and therefore, is the regimen chosen within correctional and detention facilities (AIII).

C2. Regimen including 2RZ: 2 months of R and Z. It is considered contraindicated, especially for HIV seronegative patients [27, 28] due to its high toxicity [25, 27, 29].

Short and intermittent regimens are always administered by DOT (AIII) and in a daily basis.

Table 3: Priority rate for instituting LTBI treatment

RISK	PATIENTS
VERY HIGH	Close contact with TB patient Frequent contact with TB patient and risk factors HIV+ Recent conversion< 2 years Rx with fibrotic lesion suggesting old untreated TB with no activity signs
MEDIUM	With medical conditions or under treatments which increase TB risk Low risk contact with no previous TST
LOW	No risk factors People under 35 at no risk of hepatic toxicity

Table 4: Recommended LTBI treatment regimens

			Evidence	
Drug	Duration	Interval	HIV-	HIV+
H	9 months	Daily	AII	AII
H	9 months	Intermittent	BII	BII
H	6 months	Daily	AI	CI
H	6 months	Intermittent	BII	CI
HR	3 months	Daily	AIII	AI
R	4 months	Daily	BII	BIII

Discontinuation of LTBI treatment or incomplete therapy

If LTBI treatment is discontinued, in order for it to be retaken, the number of completed doses has to be considered [21]; as for the 6H regimen, the 180 doses must be completed in a maximum period of 9 months, in the case of 9H, the indicated doses (270) have to be completed in 12 months, the 120 doses of the 4R regimen must be taken within 6 months and the 3HR (90 doses) within 4 months.

If discontinuation lasts longer a new LTBI treatment will be instituted regardless of the doses previously taken.

Special Situations

A. Pregnancy and lactation: the H regimen is recommended, along with pyridoxine (25mg/day).
B. Children: the 9H regimen is preferred (also with 300 mg/day) [22]. For children under 5, primary prevention is indicated. 8-12 weeks after contact, TST will be repeated and if it is negative therapy is discontinued, while if the result is positive therapy is continued up to 9 months.
C. Contact with MDR-TB. Consultation with an expert should be pursued before initiating LTBI treatment.
D. Patients with fibrotic lesions. Although any of the aforementioned regimens can be used, the 9H regimen is recommended, especially under DOT.

Contraindications of LTBI treatment

LTBI treatment is contraindicated whenever there is: active TB disease, a previous history of toxicity to employed drugs, severe hepatic disease or hepatic decompensation, previous anti-TB treatment, both for latent TB and TB disease, except for exceptional cases of high-risk exposure to active patients and whenever treatment compliance and control are not feasible.

In case of pregnancy, therapy must be personalised. HIV+ pregnant patients must certainly undergo anti-TB therapy, as well as those who have had contact with pulmonary TB patients or those who have recently converted in TST.

Although it is not a contraindication, ALT or AST baseline values over 3 to 5 times the upper limits of normal require strict monitoring of hepatic function.

Follow-up upon completion of LTBI treatment

Neither medical nor radiographic follow-up is required. Patients must be educated about the need of pursuing consultation whenever TB suggesting symptoms occur[1].

Adherence to LTBI treatment and DOT criteria

Treatment adherence is of paramount importance to ensure preventive efficiency. In view of the risk concerning acquired resistance and its correlation with both short and intermittent regimens, treatment will be administered by means of directly observed therapy (DOT).

CONTACT INVESTIGATION

The identification of a potentially infectious case of TB in a correctional facility should always provoke immediate contact investigation. The overall goal for contact investigation is to interrupt transmission of *Mycobacterium tuberculosis* [1, 22], by means of early diagnosis, isolation and treatment of infected contacts, providing LTBI treatment whenever indicated.

The index case is defined as the first diagnosed case of latent TB infection (either pulmonary or laryngeal). Exposed contacts are those who have had any relationship with TB patients and therefore at risk of infection.

Decision to initiate a contact investigation

Contact investigation should be carried out before: any inmates exposed to pulmonary or laryngeal TB patients, with AFB smear-positive respiratory specimens, positive cultures for both sputum or bronchial lavage specimens (AIII) or cavitation without microbiological confirmation. Contact investigation is also recommended for TB forms other than pulmonary or laryngeal (C).

Who and When?

The physician diagnosing a case of TB must carry out contact investigation reports due to the assumption that among the patient's environment there can be other infected or diseased cases. Contact Investigation must be carried out within 15 days following the identification of the index case.

How must contact investigation be conducted?

The different stages of contact investigation are the following:

A. Medical and epidemiologic characteristics of the index case. Source patients who have either cavitation on chest radiograph or AFB smear-positive respiratory specimens are substantially more likely to transmit TB than persons who have neither characteristic.
B. Contact census. Data must be collected on the following items: previous TB or LTBI treatment, presence of clinical manifestations or risk factors suggesting the development of TB disease, duration of exposure (hours of daily contact), intensity of exposure (where contact took place; cell, dining-room, school, workshop). Contact census will be reported to correctional healthcare officials, healthcare departments of those facilities where the source patient might have been and both to public health care services and outer contacts (AIII).
C. Diagnosing contacts. To decide upon the contacts which must undergo diagnostic tests, the concentric circle [1] system is applied (AIII). Investigation is therefore initiated with those contacts which have had a greater exposure rate (first circle) and is eventually extended to the rest of the circles according to the results of the investigation. The first circle includes all those contacts in close relationship with the source patient, during more than 6 hours every day or in reduced spaces (inmates sharing cell, and work mates if working times and spaces entail close contact). Second circle: it includes inmates with frequent contact: less than 6 hours every day and/or larger locations (workshop, school, gym, common rooms). Third circle: it includes sporadic contacts; exposure has not lasted long enough, or hasn't been intense enough, to entail an important transmission risk (dining-room, grounds, TV room).

INITIAL CLASSIFICATION

According to the characteristics of the source patient, of the exposed contacts and the intensity of the exposure, the following classification can be done: Group A: high risk of transmission, including those contacts who have been closely exposed to an AFM smear-positive patient (circle 1) as well as frequent contacts (circle 2) at risk. Group B: low risk of transmission; the rest of the contacts.

Management of symptomatic cases

All contacts with symptoms suggesting TB are the priority investigation group. These will under-

go TST, chest radiograph and sputum analysis. Airborne Infection Isolation must be set up until infectiousness is ruled out (AII).

Management of asymptomatic cases

TST is conducted to all contacts, except in the case of previous documented positive TST. Closer contacts must also undergo this test within a week and the rest of contacts, within 15 days.

Contact investigation considers positive TST all induration ≥5mm, and conversion, any expansion> 5mm, regardless of the vaccination status and risk factors (AIII).

Contacts are classified as not infected, infected or diseased. TST must be repeated 12 weeks after for close contacts with an initially negative TST to rule out the window period (between 8 and 12 weeks) [4], and resolve whether the contact is a converter in order to take decisions and for future TST determinations.

The management of contacts must be personally designed and maximum priority must be given to HIV patients.

Group A Patients

All patients included in group A must undergo chest radiograph, regardless the TST result [1, 21, 30] (AIII).

— HIV+ patients: regardless of previous or current TST results, chest radiograph and AFB smear sputum analysis must be performed in order to exclude extrapulmonary locations (AIII). Chemoprevention must be conducted in negative TST cases that have been in contact with an AFB smear- positive index case. LTBI retreatment may as well be indicated according to the source patient's contagiousness, the intensity of exposure and the immunological status of the patient.
— HIV- patients: chest radiographs and TST, if no previous documented results are available, must be performed to all patients. Chemoprevention will be initiated in those with negative TST results or in case of anergic patients. Those presenting positive TST (before or after contact) must undergo LTBI treatment if not previously done or completed. Some extraordinary cases of patients presenting risk factors and/or very intense exposure (secondary cases or if skin test conversion occurs) will repeat LTBI therapy.

Group B Patients

Chest radiograph will be conducted if skin test conversion occurs or before a positive TST with no previous tuberculin skin testing. HIV patients will also submit sputum for AFB smear analysis.

DECISION TO CLOSE CONTACT INVESTIGATION AND CLINICAL FOLLOW-UP

Data must be collected on the number of contacts included in each group (A and B), TB disease rates, LTBI rates and absence of infection rates. Contact investigation is concluded when all contacts taken census of have been examined and final conclusions have been reached.

All contacts not undergoing LTBI treatment because of refusal will be closely monitored, by means or periodic and scheduled appointments.

SPECIAL CASES

Epidemic Outbreak of TB

It is defined as the appearance of one or more TB cases as of the source patient [31]. If this was to occur, contact investigation should be conducted on an emergency basis and closely supervised by experts. Both correctional and community health care authorities must be informed.

Employees

It is highly recommended that all correctional and detention facilities staff should determine their status concerning *M. tuberculosis* infection. Therefore baseline TST is recommended. Periodic testing will be later conducted following the same recommendations and phases than inmates [1, 30, 32].

SCREENING AND CASE SEARCH STRATEGIES

Screening at entry

Upon entry, TB disease must be excluded (AIII). This is a recommendation by the Council of Europe and United Nations as well as a legal imperative

for most of the countries and correctional systems[32], including the Spanish one [1]. Tuberculin skin testing must be performed within the first month and chest radiographs upon entry for both HIV+ patients and inmates who have recently had contact with tuberculosis patients (BIII).

Detection in demanded consultation

We must be "aware of TB", and suspect it whenever a patient pursues consultation with respiratory symptoms [33]. All diagnostic tests leading to its detection as quickly as possibly must be performed (BIII).

Active search among inmates

This is aimed at detecting asymptomatic patients. With the purpose of doing so, tests are conducted on inmates for whom TB is likelier to occur. The most commonly used strategies include specific and scheduled appointments where TST and chest radiograph are conducted [1, 3, 34] .

During such appointments, patients must be informed about pursuing consultation whenever clinical manifestations occur. These will take place monthly for HIV+ patients, once every two months for patients at risks other than HIV, and once every six months if there are no risk factors (BIII).

Tuberculin Skin Test

It is extremely useful in identifying potential candidates for LTBI treatment upon entry and converters, in enabling contact investigation and in monitoring TB detection and control programmes [33]. It must be conducted if no previous and documented positive TST results are available in the following situations[1]: within the first month of imprisonment, every six months for HIV+ patients and every year for HIV- patients (BIII), pulmonary or laryngeal TB contacts and if Tuberculosis is suspected, although its utility is very limited in the latter.

Chest Radiograph

As well as an indication within tests indicated for diagnosis of symptomatic cases, chest radiographs will be performed upon entry[34] to inmates referring recent contact with TB patients or HIV and always before instituting LTBI treatment.

TUBERCULOSIS RELATED HEALTH PROMOTION STRATEGIES WITHIN DETENTION FACILITIES

The correctional population portrays a lack of healthy habits, mainly due to relevant social and healthcare deficiencies. Moreover, in recent years the number of immigrant inmates has greatly increased (35.5%) [35]; a lot of them come from areas where tuberculosis is highly prevalent. A recent study reveals that immigration and comprehension impairment, together with intravenous drug abuse and housing within closed facilities are leading factors for nonadherence to TB therapy [36]. Inmates are intended to be highly aware so that they can manage and improve their own health. Most commonly used strategies are the following: a) developing individual skills, b) healthy environment and c) community action.

Developing individual skills

A. Healthcare education. The main aim is to achieve inmate collaboration in identifying symptoms suggestive of TB, transmission routes, preventive regimens and motivating them to undergo screening tests and improve LTBI treatment and TB therapy adherence. An effective method is to be careful about not using too much technical language which can be misunderstood.

Both bidirectional and unidirectional methods are commonly used. The first include counselling appointments and health care education workshops designed for small groups, which have proven very useful and allow an active exchange of information. Other unidirectional methods such as speeches, videos, radio messages, journal articles, posters and brochures have proven less effective yet necessary to raise awareness.

Who should conduct healthcare education and when should it be done? Anyone can be an educator as far as he/she has the correct information and is trained on the most effective ways of imparting it, promoting debate and listening to others. Medical and nursing staff must exploit contact with patients during consultation appointments as fully as possible to provide healthcare education by means of counselling. The most appropriate timing for healthcare education is upon entry, during TST interpretation appointments, when LTBI treatment is initiated or whenever the disease is diagnosed by means of explaining the disease itself, the need for isolation, hygiene measures that should be taken and all those issues related to therapy and to the importance of its

compliance. Healthcare professionals should individually train inmates on healthcare issues if imprisonment lasts longer than one month (BII). The message should include the significance of tuberculosis, its transmission, symptoms, prevention and treatment (BII).

B. Healthcare marketing: a means of raising awareness among inmates prior to educational strategies is to involve them in the creation of materials which will be later issued, regarding the prevention and transmission of TB by using their own language and communication means. Each facility must be aware of its possibilities and readjust them to real requirements by giving priority to those which have proven more efficient. In all prisons, health promotion strategies aimed at spreading messages concerning the prevention and control of TB and other related diseases must be available and used (CIII).

Healthier environment

This entails the creation of healthier settings within prisons, as to improve hygiene, healthcare and social conditions (AI). Adopting healthy lifestyles within a physical setting lacking proper hygiene and healthcare conditions is impossible. Therefore, it is of paramount importance to create a suitable environment by raising awareness among inmates about cleanliness and taking care of the facility's settings: grounds, cells, common rooms, etc. It is also key to encourage a social environment of interpersonal relationships, employment of free time and outside communication in conditions as similar as possible to a freedom status making this compatible with security and discipline penitentiary conditions.

Community Action

Healthcare mediation: any action aimed at the community must bear in mind its culture and its requirements. It is recommended that healthcare agents be trained among inmates to help raising awareness among other inmates so that further collaboration concerning screening and diagnosis of TB, as well as LTBI therapy adherence is achieved. In view of the variety of origins, there should be mediators for each culture and/or language. It is a very useful strategy for settings such as detention facilities and it should be implemented to improve the prevention of TB (AI).

General Recommendations

All inmates upon entry should be able to identify the symptoms of tuberculosis in themselves and in other inmates in order to pursue consultation and cooperate in diagnosing the disease. Ideally information should be channelized by all available means: inmate healthcare agents, healthcare marketing or healthcare professionals.

The most effective means of action concerning healthcare promotion are far-reaching strategies which face the needs of the targeted group and are kept in the long term (AI).

INNER AND OUTSIDE PRISON COOPERATION FOR THE CONTROL OF TUBERCULOSIS

The fact that inner outside prison transmission occurs by infection of visitors, employees [34] or by the fact that after discharge many patients discontinue therapy [37, 38] has suggested that for a control program to be efficient, close cooperation between inner and outside stakeholders must be established [4, 39-41]. Therefore, it is highly recommended that cooperation between penitentiary and community TB control programs be ensured, by urgently reporting to the latter any discharge of patients under anti-TB therapy regimens. Access to healthcare services must be ensured for patients upon discharge by especially promoting access to DOT programs with specifically and readjusted resources. This should be especially done for the more prevalent groups: illegal drug consumers, irregular immigrants, alcoholic and homeless patients, so that therapy compliance is ensured. The figures of healthcare mediators and public health nursery need to be enhanced within outside prison programs to improve contact investigation and the follow-up of the patient and his/her contacts after discharge.

CONFLICT OF INTERESTS

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Abbreviations used:

CP: Centro Penitenciario *(Detention Facility)*

SESP: Sociedad Española de Sanidad Penitenciaria: *Spanish Society of Prison Health*

SEPAR: Sociedad Española de Patología del Aparato Respiratorio: *Spanish Society of Respiratory Diseases*

SEIMC: Sociedad de Enfermedades Infecciosas y Microbiología Clínica: *Society of Infectious Diseases and Clinical Microbiology*

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