Guidance on logistical arrangement for targeted screening and treatment of latent tuberculosis infection among immunocompetent household contacts of smear-positive pulmonary tuberculosis patients in TB and Chest Service

(1/4/2013; updated 1/11/2013 and 1/7/2018)

Internal Guidance Notes of the Tuberculosis & Chest Service of the Department of Health of the Government of the Hong Kong SAR
Introduction

The internal “Guidelines on targeted tuberculin testing and treatment of latent tuberculosis infection” for the Tuberculosis and Chest Service (TB&CS) has been updated on 12/12/2012 to strengthen the targeted screening and treatment of latent tuberculosis infection (LTBI) in Hong Kong. In the current set of guidance notes, general guidance is provided to assist individual chest clinics to put in place suitable logistical arrangement for effective implementation of this public health function.

General Principles

1. With the increasing proportion of active tuberculosis (TB) being attributable to endogenous reactivation of LTBI in Hong Kong, targeted screening and treatment of LTBI is required to complement the prompt identification and active treatment of TB under directly observed therapy (DOT).

2. While each clinic should work out the detailed logistical arrangement suitable for the particular setting, the clinic protocol must be designed to allow the effective implementation of this important public health activity in a way conforming to the “Guidelines on targeted tuberculin testing and treatment of latent tuberculosis infection”.

3. As the control of tuberculosis is a major mission area of the TB&CS, priority should accordingly be given to patients with active TB or LTBI in the quota allocation or booking system to facilitate their access to care. In particular, for patients who are called to attend the clinic at a pre-scheduled session / time-slot should be attended to as quickly as feasible to minimize the chance of defaulting, and no quota should apply to those who arrive punctually as instructed.

4. Like the treatment of active TB, follow-up action should be arranged for patients who refused screening and / or treatment of LTBI, and defaulters of follow-up and treatment should also be traced accordingly.

5. Streamlining of the logistical arrangement is strongly encouraged to avoid the proliferation of different protocols for similar patient groups. In particular, it will be desirable to have a single protocol for household contacts (of smear-positive source) aged from 1 to 64 (<65) years inclusive.

Outline of Screening Arrangement (subject to modification where appropriate)

All household contacts of smear-positive index tuberculosis patients should be identified during contact tracing and asked to come to the clinic on a particular date / session / time-slot (preferably after rush-hours) with a special public health appointment slip. All of them should be registered as a new case (or old case for patients who have previously attended). Fast track arrangement should then be made for medical consultation, followed
by chest x-ray examination. For close contacts without evidence of active TB and past history of TB treatment (for at least two or more months), screening of LTBI by tuberculin skin test (TST) (or Interferon Gamma Release Assay (IGRA) where appropriate) should be considered for those aged below 65 unless there is definite contraindication for treatment of LTBI. Figure 1 summarizes the screening arrangement in accordance with the current local guidelines. Special arrangement is required for neonates and infants (< 1 year old) because of possible immaturity of the immune system and heightened disease risk (Figure 2).

Reasonable efforts should be made to contact the contacts through the index patient, phone and / or mail at 2 weeks and 1 month after contact listing. Health education should be provided to all contacts and/or their parents, covering, among other things, the risk for developing TB, common symptoms for TB and the need for seeking early medical consultation should such symptoms develop. For contacts who refuse chest x-ray examination or TST (if offered) after explanation, the refusal and the above advice on passive symptom surveillance should be documented in the nursing and / or clinical record. They should not be asked to sign any DAMA form as such form is neither necessary nor appropriate.

After the administering of TST, arrangement should be made for follow up in two to three days (48 to 72 hours) for reading of the tuberculin reaction size (maximum transverse diameter of the indurated area). All household contacts (and/or their parents) with tuberculin reaction ≥ 15 mm (≥ 5 mm for those aged under 1 year) should be interviewed by the public health unit. They will be told that they are likely to have been infected by TB and the life-time risk of developing TB disease later is approximately 10% (higher for those aged below 5 years or with compromised immunity). Fast track arrangement should be made for them to see a doctor within the same session. Active TB should be excluded through clinical and radiological assessment, followed, if necessary, by sputum examination and other investigations. Care should also be exercised to exclude extrapulmonary TB, especially TB lymphadenopathy commonly occurring in neck area. The decision to screen normally implies an intention to treat if screened positive. Unless there are contraindications to such treatment, treatment of LTBI should normally be recommended. For test-positive, previously untreated AND asymptomatic contacts with old fibrotic lung scars (which are stable for 6 or more months) and 2 or more negative sputum culture, treatment for LTBI can be similarly offered. Those who refuse treatment after proper explanation, the refusal and relevant advice on passive symptom surveillance should be documented in the clinical record. Suitable follow-up may be arranged if considered necessary. Latently infected contacts with contraindication for treatment of LTBI should be reminded of the need to seek early medical consultation should symptoms suggestive of TB develop. Defaulters at any stage should be traced by the public health unit in accordance with the usual defaulter tracing mechanism. Patients who have completed the full course of preventive treatment should be advised to return for follow-up when they develop symptoms suggestive of TB.

Six months of isoniazid is therefore recommended for the treatment of LTBI, but 9 months of isoniazid may also be considered, especially among HIV-infected subjects and
other immunocompromised persons. The drug is usually given as self-administered therapy at the following daily doses:
- Children aged 5 - <16 years: 5mg/kg daily (max. 300mg)
- Children aged <5 years: 10mg/kg daily (max. 300mg)
- Adults: 300mg daily

Pyridoxine supplementation at 10 mg daily should be considered for those with malnutrition or at risk of neuropathy, e.g. diabetes mellitus, habitual alcohol use, chronic renal failure, and HIV infection.

The efficacy of weekly rifapentine plus isoniazid for 12 doses (3HP regimen) has been established in clinical trials among both non-HIV-infected and HIV-infected individuals (adults and children aged 2 years or above).

Rifapentine dosage:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dose</th>
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<tbody>
<tr>
<td>10.0-14.0 kg</td>
<td>300 mg</td>
</tr>
<tr>
<td>14.1-25.0 kg</td>
<td>450 mg</td>
</tr>
<tr>
<td>25.1-32.0 kg</td>
<td>600 mg</td>
</tr>
<tr>
<td>32.1-49.9 kg</td>
<td>750 mg</td>
</tr>
<tr>
<td>&gt; =50.0 kg</td>
<td>900mg</td>
</tr>
</tbody>
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PLUS
- Isoniazid 15 mg/kg (round up to nearest 50 or 100 mg; 900 mg max) once weekly x 12 doses if aged 12 years or above. Isoniazid 25 mg/kg (round up to nearest 50 or 100 mg; 900 mg max) if 2—11 years old.

Before availability of more convenient paediatric preparations for dosing of rifapentine, the 3HP regimen will be used as an alternative regimen mainly in persons aged 12 years or above.

Rifampicin alone for 4 months should be considered in the following situations:
1. Past intolerance of, or contraindication to use of, isoniazid
2. Mycobacterium tuberculosis cultured from index patient already known to be resistant to isoniazid

If bacillary isoniazid mono-resistance is discovered in the index patient after LTBI treatment with isoniazid is initiated in an infected contact, switching to rifampicin therapy should be considered, subject to a continuing need for LTBI treatment. A similar consideration applies to isoniazid intolerance necessitating withdrawal of isoniazid in an infected contact, but caution should be exercised in case of significant drug-induced hepatotoxicity as rifampicin is also potentially hepatotoxic (see Management of hepatotoxicity in the “Guidelines on targeted tuberculin testing and treatment of latent tuberculosis infection”). Careful balance of risks and benefits would be required, and expert consultation should be sought where necessary.
For contacts of patients with multidrug-resistant TB, expert opinions differ on whether to treat, with at least two drugs or just a fluoroquinolone, and for how long, despite some encouraging preliminary results on the use of fluoroquinolone-containing regimens recently. Close clinical observation for two years is normally recommended locally, except when specific clinical circumstances require otherwise.

If bacillary resistance to isoniazid PLUS rifampicin is discovered in the index patient after LTBI treatment with isoniazid is initiated in an infected contact, it would be appropriate to discuss with the patient as to whether to complete the remaining course of isoniazid treatment. As about half of the active tuberculosis diseases to be observed among such contacts are caused by drug-susceptible tubercle bacilli locally, isoniazid treatment is likely to offer some degree of protection, mainly against the development of drug-susceptible TB. Careful balance of risks and benefits would be required, and expert consultation should be sought where necessary.
Index case with smear +ve pulmonary TB

Household or other similar contacts

Arrange for medical consultation at a suitable time slot

Active TB

CXR examination

No evidence of active TB

No history of past anti-TB treatment

History of past anti-TB treatment

TST with 2 unit of PPD-RT23 (TTa)

Aged < 1 year

Aged 1-64, unless contraindication

Aged 65 or above

Observe

TSTa ≤ 14 mm

Repeat TST at 3 m (Skip 2nd TST & observe if last contact > 8 wk ago) (TTb)

TTb ≤ 14 mm, and TTb - TTa ≤ 9 mm)

observe

TTa or TTb ≥ 15 mm, or documented TST conversion (TTb - TTa ≥ 10 mm)

Fit for treatment of LTBI

Yes

Treatment of LTBI with 6H (or other regimens where appropriate, e.g., index case with resistance to H)

Advice on passive symptom surveillance

No

Arrange suitable follow-up if necessary

See Fig. 2

Aged ≤ 64, unless contraindication

Aged 65 or above

Aged < 1 year
Targeted screening for active TB and latent TB infection is regularly offered to subjects exposed to smear-positive pulmonary TB patients in the same household or other similar scenarios. Medical consultation is arranged at a suitable time slot, when chest X-ray examination will first be done to exclude active TB for which treatment will be given. Contacts with no evidence of active TB but a history of past anti-TB treatment will be observed, whereas those with no history of past anti-TB treatment will be managed according to their age group. For contacts aged below 1, please refer to Figure 2. For contacts aged 1 to 64, tuberculin skin test (TST) is routinely offered, unless there are contraindications. For those aged 65 or above, just observe. TST is done using 2 units of PPD-RT23. If the induration measured after 48 to 72 hours is no more than 14 mm, repeat TST 3 months later, unless the contact has had no further contact with the index case for more than 8 weeks. If the test response of either the first or the second TST is at least 15 mm, or if the difference between the two test responses is at least 10 mm, consider treatment of latent TB infection with daily isoniazid for 6 months (or other regimens where appropriate, for example, when the index case has TB with isoniazid resistance). If treatment of latent TB infection is indicated but the contact case is medically not fit, provide advice on passive symptom surveillance and arrange suitable follow-up if necessary.
Index case with smear +ve pulmonary TB

Household or other similar contacts aged below 1 year

Arrange for medical consultation at a suitable time slot

Active TB

CXR examination

No evidence of active TB

No history of past anti-TB treatment

History of past anti-TB treatment

TT ≤ 4 mm

TT ≥ 5 mm

TST with 2 unit of PPD-RT23

TT ≥ 5 mm

Complete full course of 6H (or other regimen)

TT ≤ 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)

TT ≤ 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)

TT > 4 mm

TST with 2 unit of PPD-RT23

TT > 5 mm

Fit for treatment of LTBI

Yes

No

Advice on passive symptom surveillance

Arrange suitable follow up if necessary

TT > 4 mm

TST with 2 unit of PPD-RT23

TT > 5 mm

Complete full course of 6H (or other regimen)

TT > 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)

TT > 4 mm

TST with 2 unit of PPD-RT23

TT > 5 mm

Complete full course of 6H (or other regimen)

TT > 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)

TT > 4 mm

TST with 2 unit of PPD-RT23

TT > 5 mm

Complete full course of 6H (or other regimen)

TT > 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)

TT > 4 mm

TST with 2 unit of PPD-RT23

TT > 5 mm

Complete full course of 6H (or other regimen)

TT > 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)

TT > 4 mm

TST with 2 unit of PPD-RT23

TT > 5 mm

Complete full course of 6H (or other regimen)

TT > 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)

TT > 4 mm

TST with 2 unit of PPD-RT23

TT > 5 mm

Complete full course of 6H (or other regimen)

TT > 4 mm

Observe + BCG if not yet done (or BCG < 2 months before LTBI treatment)
Targeted screening for active TB and latent TB infection is regularly offered to subjects aged below 1 year and exposed to smear-positive pulmonary TB patients in the same household or other similar scenarios. Medical consultation is arranged at a suitable time slot, when chest X-ray examination will first be done to exclude active TB for which treatment will be given. For contacts with no evidence of active TB but a history of past anti-TB treatment, the need for retreatment of latent TB infection versus observation will be assessed. For those with neither active TB nor a history of past anti-TB treatment, further management is stratified by their age group. For contacts aged below 3 months, withhold BCG if possible, and treat with isoniazid daily (or other regimens) for 3 months. This is followed by tuberculin skin test (TST) using 2 units of PPD-RT23. If the test response is at least 5 mm, complete a full course of 6-month isoniazid preventive treatment (or other regimens). If the test response is no more than 4 mm, observe and give BCG if it has not yet been given or given less than 2 months before starting treatment for latent TB infection.

For contacts aged 3 months or above, TST is done using 2 units of PPD-RT23. If the test response is no more than 4 mm, repeat TST 3 months later, unless the contact has had no further contact with the index case for more than 8 weeks. If the test response of either the first or second TST is at least 5 mm, consider treatment of latent TB infection with daily isoniazid for 6 months (or other regimens where appropriate). If treatment of latent TB infection is indicated but the contact case is medically not fit, provide advice on passive symptom surveillance and arrange suitable follow-up if judged necessary. If the test response of the second TST (or the single TST done more than 8 weeks ago after last contact) is no more than 4 mm, observe and give BCG if it has not yet been given.