TB preventive treatment during COVID-19 pandemic

Background

The global COVID-19 outbreak, caused by the SARS-CoV-2 virus, has disrupted health systems worldwide. This has resulted in changes to health services related to other diseases such as tuberculosis (TB). For persons at high risk of TB and other diseases, access to the health services they need is likely to become more difficult. The WHO has stressed the importance of continuing essential services to protect the affected persons and those at risk. Therefore, it is crucial that national programmes continue to provide TB services while at the same time maintaining their response to the COVID-19 outbreak.

The symptoms of COVID-19 disease (see table) are similar to those of TB disease, however there is an important difference in onset: being sudden with COVID-19 in comparison to the slower onset of symptoms for TB. Patients with suspected COVID-19 disease often present with cough, fever and shortness of breath, they might have a history of contact with a person that is infected with SARS-CoV-2. Patients with TB often present with cough, fever, loss of weight and night sweats, with or without history of contact with a TB patient. Both diseases affect the lungs and are transmitted through close contact and in crowded areas. Current guidelines recommend that any person with a cough of any duration needs to be screened for TB. Therefore, symptoms of TB and COVID-19 directly overlap in this population.

There are several reasons why TB services might be affected by the COVID-19 outbreak:

- **Stigma and discrimination:** The COVID-19 pandemic has provoked social stigma and discriminatory behaviours against people perceived to have been in contact with the virus or at the origin of the epidemic. Stigma contributes to groups being isolated, which can increase spread of TB. Likewise, stigma and fear around TB in communities can hamper the response to COVID-19.

- **Reduced health care seeking behaviour:** Due to stigma and understandable fear of being infected with SARS-CoV-2, people are driven to hide illness, not seek healthcare and be discouraged from adopting healthy behaviours. This may mean that some people with TB wait longer to seek care, and therefore become sicker.

- **Increased risk of severe COVID-19 disease:** Although experience with these concomitant illnesses is limited, there is increasing evidence that people with existing lung diseases suffer more from COVID-19. There is good reason to believe that this will be true also for people with lung disease from TB. Treating and preventing TB appropriately in this setting is crucial to reducing the risk of severe COVID-19 disease.
Overlap of early symptoms during screening procedures:
Because of the overlap of symptoms between the two diseases, it might be difficult to rule out TB in the setting of COVID-19. This could lead to confusion and missed diagnoses of both diseases during routine screening.

Pressure on existing diagnostic resources:
Testing platforms used for TB (and especially ruling out TB) can also be used for COVID-19 testing. This includes nucleic acid-based testing resources such as the GeneXpert platform, as well as other diagnostic modalities such as X-ray. This could lead to increased demand and reduced availability of these services for both diseases.

Pressure on contact tracing workforces:
The COVID-19 outbreak has resulted in considerable pressure on health workforces around the world. Contact tracing is a human resource-intensive activity that is essential for both TB and COVID-19 control. Teams used for finding household contacts of persons with TB might be diverted to provide COVID-19 services instead, impacting the contact tracing of TB exposed persons.

Many countries affected by COVID-19 will not have the resources to conduct widespread testing, contact tracing and follow-up in this context, and it is unclear how the triple epidemics of TB, HIV and COVID-19 will be handled in resource-limited settings.

Comparison of Covid-19 and TB

<table>
<thead>
<tr>
<th></th>
<th>COVID-19</th>
<th>Tuberculosis</th>
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</thead>
<tbody>
<tr>
<td>How is it spread?</td>
<td>Droplets and contaminated surfaces.</td>
<td>Airborne.</td>
</tr>
<tr>
<td>How is it diagnosed?</td>
<td>Nasal swabs and/or sputum tests.</td>
<td>Sputum tests for those with cough. Other samples depending on symptoms.</td>
</tr>
<tr>
<td>What is the causative agent?</td>
<td>Virus- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).</td>
<td>Bacteria-Mycobacterium tuberculosis complex.</td>
</tr>
<tr>
<td>How infectious is it?</td>
<td>Currently average of 2-2.5 people infected per one person with COVID-19.</td>
<td>Range from 0-4 people infected per one person with TB.</td>
</tr>
<tr>
<td>How do we prevent it?</td>
<td>Social distancing; good respiratory hygiene measures; handwashing with soap for at least 20 seconds, administrative and environmental controls.</td>
<td>TB preventive treatment (like 3HP) for those with known exposure; good respiratory hygiene measures; administrative and environmental controls.</td>
</tr>
<tr>
<td>How do we treat it?</td>
<td>Trials are ongoing for the use of several antivirals, supportive care and medications to prevent complications.</td>
<td>Antibiotics (usually 4 drugs for 6 months, although longer may be needed for some forms of extra-pulmonary TB and for drug resistant TB).</td>
</tr>
<tr>
<td>Is there a vaccine?</td>
<td>Not yet. Promising results from vaccine trials suggest there may be a final product in the near future.</td>
<td>BCG has some protective effects, particularly for children.</td>
</tr>
</tbody>
</table>

It is essential that TPT services be maintained wherever possible to decrease the risk to PLHIV and household contacts in the setting of this pandemic.
The following algorithm is proposed to assist programs in deciding when to start TPT in the setting of COVID-19:

**Adult or adolescent >15 years requiring TB preventive treatment**

**Screen for active respiratory disease**

- **No symptom suggestive of COVID-19 or TB**
  - Assess for contra-indications to 3HP
    - **No contra-indications**
      - Initiate 3HP
    - **Contra-indications to 3HP**
      - Eligible for other TPT regimens
        - **No**
          - Defer preventive treatment
        - **Yes**
          - Initiate alternative regimen (6H, 9H, 12H or 4R)

- **Any one symptom suggestive of COVID-19 or TB**
  - Current cough, Any fever, Unintentional weight loss, Any night sweats
  - Assess for contra-indications to 3HP
    - **No contra-indications**
      - Initiate 3HP
    - **Contra-indications to 3HP**
      - Eligible for other TPT regimens
        - **No**
          - Defer preventive treatment
        - **Yes**
          - Initiate alternative regimen (6H, 9H, 12H or 4R)

**COVID-19 Testing available?**

- **No**
  - Test for TB only
  - TB diagnosed
    - Supportive treatment as appropriate
  - COVID-19 Diagnosed
    - Supportive treatment as appropriate
  - Follow up and consider TPT once illness resolved

- **Yes**
  - Test for COVID-19 and TB (check national guidelines)
  - Symptomatic suggestive of Covid-19 and TB negative
    - Supportive treatment as appropriate
  - TB diagnosed
    - TB Treatment
  - COVID-19 Diagnosed
    - Supportive treatment as appropriate

*Differentiating symptoms of Covid-19 and active Tuberculosis*

<table>
<thead>
<tr>
<th>COVID-19</th>
<th>Tuberculosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden onset of symptoms</td>
<td>Slow onset over several weeks/months</td>
</tr>
<tr>
<td>Night sweats</td>
<td>Night sweats</td>
</tr>
<tr>
<td>Cyclical fevers</td>
<td>Cyclical fevers</td>
</tr>
<tr>
<td>Dry cough</td>
<td>Productive or dry cough</td>
</tr>
<tr>
<td>No immediate weight loss</td>
<td>Weight loss over a long period</td>
</tr>
<tr>
<td>Loss of taste and smell</td>
<td>Taste and smell preserved</td>
</tr>
<tr>
<td>Acute development of shortness of breath/difficulty breathing</td>
<td>Late onset of difficulty breathing or shortness of breath</td>
</tr>
<tr>
<td>Sore throat</td>
<td>Sore throat not typical</td>
</tr>
<tr>
<td>Extreme fatigue, rapid onset</td>
<td>Fatigue is typical, but slower onset</td>
</tr>
</tbody>
</table>

**KEY:**

- H = isoniazid
- 3HP = 3 months of isoniazid and rifapentine
- 6H = 6 months isoniazid
- 9H = 9 months isoniazid
- 12H = 12 months isoniazid
- 4R = 4 months rifampicin
• PLHIV, people exposed to TB and others at high risk need TPT to be provided to decrease mortality and morbidity from Tuberculosis.

• Symptoms of COVID-19 are similar to those used to rule out active TB.

• People being evaluated for COVID should also be assessed for TB risk (PLHIV, contacts, others as per national guidelines).

• Where testing for COVID-19 is available, both TB and COVID-19 testing should be performed to rule out both diseases in high-risk patients presenting with fever/cough.

• COVID-19 and TB can occur at the same time. Where testing for COVID-19 is not available, symptom-based diagnosis and supportive care for COVID-19 should be offered, while also proceeding with diagnosis and treatment for TB or other underlying disease as appropriate.

• TPT can be offered after COVID-19 disease symptoms have resolved in persons who are at high risk of TB. Patients should be actively engaged so as not to miss the opportunity to provide TPT.

• COVID-19 requires quarantine or isolation for the patients and also for those who are contacts. All efforts should be made to rule out TB rapidly in persons who are going to be quarantined or isolated due to the risk of TB transmission to other members of the household.

• Persons who are already on TPT should not interrupt their treatment due to COVID-19 illness, except in cases where they are asked to do so by their health care provider.

• The algorithm on the previous page is proposed to assist programs in deciding when to start TPT in the setting of COVID-19.