Updates on 3rd edition TB CPG

Central Zone Tb Updates
Sibu 27-28/7/2013
Conflict of Interest

• I am in the CPG development group and am closely involved in its development.
Content

1. Introduction
2. Key messages
3. Recommendation highlights of TB CPG 3rd Edition
   1. Epidermiology
   2. Investigation
   3. Treatment
   4. Latent TB
   5. TB in special condition: children, pregnancy and HIV
   6. Follow up
   7. Adverse drug reaction
   8. Screening
   9. Referrals
4. Conclusions
Introduction to 3rd edition
Introduction

• Number of Tuberculosis (TB) cases failed to be reduced in the last 10 years
• High mortality and morbidity
• Development of MDR and XDR TB
• Problems:
  – Delayed presentation
  – Inaccurate diagnosis
  – Inappropriate empirical treatment – smear negative
  – High treatment default rates
Introduction

• The management of TB needs to be standardized
  – Improve patient outcomes
  – Assist monitoring and evaluation efforts
  – Prevent the emergence of MDR-TB.
    • Prevention of MDR-TB can be achieved if health care providers manage TB appropriately and ensure optimal adherence to first-line therapy.
3rd Edition TB CPG

• Objective
  – “The aim of the TB CPG is to standardize the management of TB at all levels of care in Malaysia with a view to improving patient care and preventing the emergence of MDR-TB and XDR-TB.”
  – It is mainly aimed at health care providers in primary care but it should also be useful to those in the secondary/tertiary care.
3rd Edition TB CPG

• First evidence-based TB CPG in Malaysia in contrast to the previous TB CPG which was consensus-based

• Development Group (DG) members
  – Ministry of Health (MoH)
  – Ministry of Higher Education
  – Private sector
  – East and West Malaysians

• There was active involvement of a multidisciplinary review committee (RC) during the process
3rd Edition TB CPG

• Development process
  – A total of 42 clinical questions were developed under different sections
  – Databases:
    • Electronic
      – Guidelines International Network (G-I-N)
      – World Health Organization (WHO)
      – Medline via Ovid
      – Pubmed,
      – Cochrane Database of Systemic Reviews (CDSR)
      – International Health Technology Assessment websites
    • Other CPGs
      – National Institute for Health and Clinical Excellence (2011) – Clinical Diagnosis and Management of Tuberculosis, and Measures for Its Prevention and Control
    • Reference lists of all retrieved literature and guidelines were searched to further identify relevant studies
    • Experts in the field were also contacted to identify further studies
  – The search was limited to literature published in the last ten years and in English. If the evidence was insufficient, the period of publication was extended for another ten years
3rd Edition TB CPG

- All searches were conducted between 9 May 2011 - 29 March 2012
- Literature searches were repeated for all clinical questions at the end of the CPG development Process
- The DG members had met 20 times
  - All literature retrieved were appraised by at least two DG members using Critical Appraisal Skill Programme checklist, presented in evidence tables and further discussed in each DG meeting.
- All statements and recommendations formulated after that were agreed upon by both the DG and RC.
- Where evidence was insufficient, the recommendations were made by consensus of the DG and RC.
- The CPG is than reviewed by an External reviewer
- This CPG is based largely on the findings of systematic reviews, meta-analyses and clinical trials, with local practices taken into consideration.
Key messages from 3rd Edition
Key messages

1. Tuberculosis (TB) is a notifiable infectious disease. Timely diagnosis, prompt treatment & adherence to medication are key factors in combating TB.

2. Screening of TB should be done in high risk groups including all close contacts

   HIGH RISK GROUPS

   • Close TB contacts especially infants & children under 5 years of age
   • Immunocompromised patients such as those with diabetes mellitus, HIV infection, end-stage renal disease, malnutrition, use of immunosuppressant drugs, etc.
   • Intravenous drug users
   • People living in overcrowded conditions

3. Patients with symptoms of TB should have sputum smear for acid fast bacilli (AFB), *mycobacterium culture & sensitivity (C&S)*, & chest x-ray (CXR) done. Nucleic Acid Amplification Tests (NAAT) plays a role in rapid detection of *Mycobacterium tuberculosis* & multidrug-resistant TB (MDR-TB).
Key Messages

4. TB serology should not be used to diagnose pulmonary TB (PTB) or extrapulmonary tuberculosis (EPTB).

5. For latent TB infection (LTBI), tuberculin skin test (TST) is the preferred method for diagnosis. Interferon Gamma Release Assay may be used as an alternative. Treatment should be considered for high risk patients.

6. A daily antiTB regimen is recommended for both intensive & maintenance phases. A proper defaulter tracing system should be in place to detect early interruption in treatment and follow-up. Poorly managed TB will lead to drug-resistant TB.

7. Fixed-Dose Combinations are preferred to separate-drugs combination for the treatment of TB.
Key Messages

8. Infants & children under 5 years of age with close contact are at high risk of developing active TB.

9. Active TB should be ruled out in all HIV-positive patients.

10. Preventive measures should be employed to reduce TB risk among healthcare workers.
Highlights of Recommendation for 3rd edition TB CPG
Highlights of TB CPG 3rd edition

Epidermiology

Fig. 2: Notification of new TB cases in Malaysia 2005 - 2011
Highlights of TB CPG 3\textsuperscript{rd} edition

**Epidermiology**

- Incidence was 81.4 per 100,000 population in year 2010 – Moderate burden of disease
Highlights of TB CPG 3\textsuperscript{rd} edition

Investigations

• Diagnosis is confirmed by isolating \textit{Mycobacterium tuberculosis} \textit{from clinical samples}

• All patients suspected of having PTB should submit at least two sputum specimens for microscopic examination in a quality-assured laboratory.

• When possible, at least one early morning specimen should be obtained, as sputum collected at this time has the highest yield
Highlights of TB CPG 3rd edition

Investigations – New Tests

**Recommendation 2**
- Light emitting diode-based fluorescence microscopy (LED FM) should be used as the preferred method over the conventional Ziehl-Neelsen light microscopy in diagnosing pulmonary tuberculosis in both high and low volume laboratories. *(Grade C)*
- In implementing LED FM, the need of laboratory staff training, standard operating procedures and appropriate quality assurance should be addressed. *(Grade C)*

**Recommendation 3**
- Nucleic Acid Amplification Tests (molecular methods endorsed by World Health Organization) can be performed for the detection of *Mycobacterium tuberculosis* from clinical specimens. *(Grade C)*

**Recommendation 4**
- Line Probe Assay should be performed to detect rifampicin and isoniazid resistance in smear positive sputum specimens or culture isolates from smear positive and negative specimens. It should be carried out in a tuberculosis (TB) risk level 2 laboratory. *(Grade C)*
- Xpert MTB/RIF can be deployed in state laboratories to scale up the detection of drug resistant tuberculosis for which a TB risk level 1 laboratory will suffice. *(Grade C)*
Highlights of TB CPG 3rd edition

Investigations – usage of LPA

*Repeat if clinically indicated

Highlights of TB CPG 3rd edition

Investigations – smear negative

Recommendation 5
• Commercial serological assay should not be used to diagnose pulmonary and extrapolmonary TB. (Grade C)

Recommendation 6
• Sputum induction should be considered to establish the diagnosis in patients suspected to have pulmonary tuberculosis who are smear negative or unable to produce sputum, whenever appropriate. (Grade C)
• Gastric lavage or bronchoscopy may be considered in patient who is not suitable for sputum induction. (Grade C)

Properly performed sputum induction is the preferred method over bronchoscopy as the sensitivities are 96.3% and 51.9% respectively (p<0.005). The positive yield is higher if the patient has respiratory symptoms (p=0.02) and abnormal radiographs suggestive of active disease (p=0.003).28, level III

Three induced sputum samples have higher sensitivity for detecting TB compared to three gastric washings samples (39% vs 30%; p=0.03).28, level III

In patients who are smear negative for AFB or who have difficulty in producing sputum, bronchoscopy can establish a diagnosis microbiologically or histopathologically in 86.6%30, level III and 83.3%31, level III of cases. Immediate diagnosis can be established in 48.3% of patients.31, level III
Highlights of TB CPG 3rd edition

Investigations – Extrapulmonary TB

**Recommendation 7**

- All attempts should be made to obtain specimen from patients suspected to have extrapulmonary tuberculosis (EPTB) including tissue or fluid from the affected sites for cytology/histopathological examination and Mycobacterium tuberculosis culture. *(Grade C)*

- Mycobacterium tuberculosis culture and sensitivity testing should be performed on specimen taken from patients suspected to have EPTB including biopsy specimen. *(Grade C)*

- Measurement of Adenosine Deaminase level in pleura or cerebrospinal fluid may be considered as an adjunct in diagnosing pleural TB and tuberculous meningitis respectively. *(Grade C)*
Highlights of TB CPG 3rd edition
Investigations - Imaging

**Recommendation 8**
- Chest radiography should be used as the primary imaging modality to aid diagnosis and management of pulmonary and extrapulmonary tuberculosis. *(Grade C)*
- Computerised tomography maybe considered in cases of normal chest radiography but with high clinical suspicion or in the management of complication of pulmonary tuberculosis. *(Grade C)*
Highlightsof TB CPG 3rd edition

Treatments

**Recommendation 9**

- New patients with pulmonary tuberculosis should receive daily 2EHRZ and followed by daily 4HR**. (Grade A)
  - Regimen should contain six months of rifampicin. (Grade A)
  - Rifampicin should be rounded to higher recommended dose if tolerated. (Grade C)
  - If ethambutol is contraindicated, streptomycin can be substituted. (Grade A)

**Recommendation 12**

- New patients with pulmonary tuberculosis should receive daily intensive regimen followed by daily maintenance regimen. (Grade A)
  - Thrice weekly maintenance regimen can be considered under direct observation. (Grade A)

**Recommendation 11**

- Patients with sputum positive pulmonary tuberculosis should receive antituberculous drugs for a minimum duration of six months. (Grade A)
Highlights of TB CPG 3rd edition

Treatments-FDC and DOTS

Recommendation 13
• Fixed-Dose Combinations (FDCs) are preferred to separate-drugs combination for the treatment of tuberculosis. (Grade A)
  o In patients who develop toxicity, intolerance or contraindication to specific component drugs, FDCs can be substituted with separate-drug regimens. (Grade A)

Recommendation 14
• When possible, directly observed therapy (DOT), either by healthcare worker or family member, should be adopted to improve compliance in tuberculosis (TB) management. (Grade C)
  o DOT should be patient-centred, incorporating negotiations, and patient’s characteristics and preferences. (Grade A)
• Reminder system for clinic appointments should be encouraged. (Grade A)
• Prompt reminders should be sent to TB patients who default treatment. Failing that, home visit by healthcare workers should be carried out. (Grade B)
• Contact tracing should be done intensively, including home visits to retrieve contacts who do not come for screening. (Grade C)
• Trained non-governmental organisation staff, community members and peers should be used to reinforce compliance to treatment and provide support to patient suffering from tuberculosis. (Grade C)
Highlights of TB CPG 3rd edition

Treatments

**Recommendation 15**
- All extrapulmonary tuberculosis should be treated with antituberculosis treatment for a minimum of six months except for bone (including spine) and joint tuberculosis for 6 - 9 months and tuberculous meningitis for 9 - 12 months. *(Grade C)*
- Streptomycin should be used instead of ethambutol in adult TB meningitis. *(Grade C)*

NICE recommends duration of EPTB treatment as follows:
- meningeal TB – 2 months S/EHRZ+10HR*
- peripheral lymph node TB – should normally be stopped after 6 months
- bone and joint TB – 6 months
- pericardial TB – 6 months

Recommendation on duration of EPTB treatment by WHO are:
- regimen should contain 6 months of rifampicin: 2HRZE/4HR*
- duration of treatment for TB meningitis is 9 - 12 months and bone and joint TB is 9 months

**Recommendation 16**
- Corticosteroids should be used in tuberculous meningitis or pericarditis. *(Grade A)*
Latent TB is defined as infection with *Mycobacterium tuberculosis* complex, where the bacteria may be alive but in the state of dormancy and not currently causing any active disease/symptoms.

**Recommendation 17**
- Latent tuberculosis infection (LTBI) should be diagnosed based on the absence of symptoms, normal/static chest x-ray findings and positive tuberculin skin test (TST) / interferon-gamma release assays (IGRA). *(Grade C)*
- LTBI screening should only be performed on high risk individuals*. *(Grade C)*
- TST should be used as the preferred test in diagnosing LTBI. *(Grade C)*
- IGRA could be used as an alternative test to TST for LTBI especially in certain situations**. *(Grade C)*
- If LTBI testing is inconclusive, the patient should be referred to a specialist with experience in tuberculosis management. *(Grade C)*
- Patients with LTBI may be offered treatment. *(Grade C)*
Highlights of TB CPG 3rd edition

Latent TB – High risk group

- Only individuals who are at high risk of acquiring LTBI or developing TB reactivation should be investigated. Treatment might be considered for those who are positive for LTBI.

Positive TST for LTBI

<table>
<thead>
<tr>
<th>Positive TST Reaction</th>
<th>Types of Individual</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5 mm</td>
<td>HIV-infected persons</td>
</tr>
<tr>
<td></td>
<td>Organ transplant recipients</td>
</tr>
<tr>
<td></td>
<td>Persons who are immunosuppressed for other reasons</td>
</tr>
<tr>
<td>≥15 mm</td>
<td>Individuals from countries with low incidence of TB</td>
</tr>
<tr>
<td>≥10 mm</td>
<td>Close contacts</td>
</tr>
<tr>
<td></td>
<td>Recent immigrants</td>
</tr>
<tr>
<td></td>
<td>Injecting drug users</td>
</tr>
<tr>
<td></td>
<td>Residents &amp; employees of high risk congregate settings (such as correctional facilities, nursing homes, homeless shelters, hospitals &amp; other healthcare facilities)</td>
</tr>
<tr>
<td></td>
<td>Persons with fibrotic changes on CXR</td>
</tr>
</tbody>
</table>
Highlights of TB CPG 3rd edition

Latent TB – Quantiferon Gold

The Development Group suggests that the situations where IGRAs may be used are as the following:

i. As an alternative to TST for
   • Patients who are not expected to/could not come back for a reading of skin induration after 48 - 72 hours
   • Patients who had recent BCG vaccination or past NTM infection

ii. Where a 2-step test is considered (TST followed by IGRA)
   • Close-contacts whose TST is in the range of 5 - 9 mm
   • Patients who are offered LTBI treatment but are not convinced that they have LTBI
   • Individuals who require annual screening of LTBI such as healthcare providers working in high risk areas)
Highlights of TB CPG 3rd edition

Latent TB – treatment regimen

Active TB must be ruled out before starting LTBI regimen.

Table 3: AntiTB Regimens for LTBI in Adults

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Duration</th>
<th>Interval</th>
<th>Completion criteria</th>
</tr>
</thead>
</table>
| Isoniazid                 | 6 - 9 months | Daily    | • 180 doses in 9 months (6-month regimen)  
                        |              |          | • 270 doses in 12 months (9-month regimen)           |
| Isoniazid + rifampicin    | 4 months     | Daily    | • 120 doses within 6 months                           |
| Rifampicin                | 4 months     | Daily    | • 120 doses within 6 months                           |
| Isoniazid and rifapentine*| 3 months     | Once weekly | • 12 doses                                           |

*Rifapentine is not currently registered in Malaysia. Its use should be restricted to those on DOT (Directly observed therapy).*
Highlight sof TB CPG 3rd edition

TB in children

Recommendation 18
- Children suspected of pulmonary tuberculosis should have sputum examination, chest x-ray and tuberculin skin test performed. (Grade C)
  - Gastric lavage/aspiration should be performed in infants and children who are unable to expectorate sputum. (Grade C)

Recommendation 21
- Non-HIV infected children with latent tuberculosis infection should be treated with 6-month of isoniazid or 3-month of isoniazid plus rifampicin. (Grade C)

Recommendation 22
- Medical therapy should not be offered routinely in BCG lymphadenitis. (Grade C)

Recommendation 19
- All children with tuberculosis should be given standardised treatment regimens and dosages according to the relevant diagnostic categories. (Grade C)
<table>
<thead>
<tr>
<th>TB cases</th>
<th>Regimen^</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensive phase</td>
<td>Continuation phase</td>
</tr>
<tr>
<td>New smear positive PTB</td>
<td>2HRZ</td>
<td>4HR</td>
</tr>
<tr>
<td>New smear negative PTB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less severe EPTB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe concomitant HIV disease</td>
<td>2HRZE</td>
<td>4HR</td>
</tr>
<tr>
<td>Severe form of EPTB</td>
<td>2HRZE</td>
<td>10HR</td>
</tr>
<tr>
<td>TB meningitis/spine/bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previously treated smear positive PTB including relapse and treatment after interruption</td>
<td>3HRZE</td>
<td>5HRE</td>
</tr>
<tr>
<td>Treatment failure TB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDR-TB</td>
<td>Individualised regimen</td>
<td></td>
</tr>
</tbody>
</table>

*Direct observation of drug ingestion is recommended especially during the initial phase of treatment and whenever possible during the continuation phase.
Highlights of TB CPG 3rd edition

TB and pregnancy

Recommendation 24

- All women of child bearing age suspected of tuberculosis (TB) should be asked about current or planned pregnancy. (Grade C)
- First-line antiTB drugs except streptomycin can safely be used in pregnancy. (Grade C)
- First-line antiTB drugs can safely be used in breastfeeding. (Grade C)
- Pyridoxine supplementation should be given to all pregnant and breastfeeding women taking isoniazid. (Grade C)
- Patient on rifampicin should use alternative contraception methods other than oral contraceptives and progesterone-only pills. (Grade C)
# Highlights of TB CPG 3rd edition

## TB and pregnancy

<table>
<thead>
<tr>
<th>Active PTB diagnosed before delivery</th>
<th>Active PTB diagnosed after delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2 months before</td>
<td>&lt;2 months before</td>
</tr>
<tr>
<td><strong>Smear negative just before delivery</strong></td>
<td><strong>Smear positive just before delivery</strong></td>
</tr>
<tr>
<td>No prophylaxis for infant</td>
<td>Give prophylaxis: Isoniazid for six months OR isoniazid for three months followed by TST</td>
</tr>
<tr>
<td>BCG at birth</td>
<td>Defer BCG at birth, give after stopping isoniazid</td>
</tr>
</tbody>
</table>


**Recommendation 23**

- BCG should not be given to babies on prophylactic tuberculosis (TB) treatment. *(Grade C)*
- Prophylactic TB treatment should be given to babies born to mothers with active pulmonary TB except those diagnosed more than two months before delivery who have documented smear negative before delivery. *(Grade C)*
Highlights of TB CPG 3rd edition

Active TB and HIV

Recommendation 27
- Active tuberculosis should be ruled out in all HIV-positive patients. (Grade C)

Recommendation 28
- In all HIV-positive patients suspected of pulmonary tuberculosis, sputum tuberculosis (TB) culture should be done regardless of smear acid fast bacilli status. (Grade C)
- TB culture and biopsy specimen should be obtained to diagnose extrapulmonary TB in HIV-positive patients. (Grade C)
- Interferon-Gamma Release Assays should not be used alone in diagnosing active TB in HIV-positive patients. (Grade C)

Recommendation 29
- Antituberculosis (antiTB) regimen offered to HIV-positive adults should be the same as for HIV-negative adults. (Grade C)
  - Daily treatment should be offered in the maintenance phase. (Grade C)
- Minimum duration of antiTB treatment to be considered in HIV-infected adults is:
  - six months for pulmonary tuberculosis. (Grade C)
  - six to twelve months for extrapulmonary tuberculosis. (Grade C)
Highlights of TB CPG 3rd edition

Latent TB and HIV

Algorithm 3: TB Screening and IPT in HIV-Positive Patients

1. HIV-positive patients

2. Screen for TB with any of the following: current cough, fever, weight loss, night sweats

3. If No, Assess IPT contraindications
   - No: Give IPT
   - Yes: Defer IPT

4. If Yes, Investigate for TB
   - Yes: Treat for TB
     - Other diagnosis – appropriate treatment and consider IPT
     - Not TB – follow-up and consider IPT
   - No: Screen for TB regularly

Note: In healthcare facilities where Mantoux test is available, the test can be done to select HIV patients suitable for IPT.
Highlights of TB CPG 3rd edition

Anti TB and HIV HAARTs

**TB-HIV CO-INFECTION**

- Isoniazid prophylaxis therapy for 6 months should be offered to all HIV patients after *active TB is ruled out*.
- Highly Active Antiretroviral Therapy (HAART) during TB treatment reduces mortality & results in earlier sputum smear/culture conversion.

<table>
<thead>
<tr>
<th>CD4 count (cells/μl)</th>
<th>Timing of HAART initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>2 weeks after starting intensive phase of antiTB treatment</td>
</tr>
<tr>
<td>&gt;50</td>
<td>After completion of intensive phase of antiTB treatment</td>
</tr>
</tbody>
</table>

- Efavirenz is the preferred Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) in combination with 2 Nucleoside Reverse Transcriptase Inhibitors for HIV-TB co-infection.
- Immune Reconstitution Inflammatory Syndrome (IRIS) usually occurs within 3 months of antiTB treatment, typically within 2 - 12 weeks after starting HAART:
  - Especially in patients with CD4 <50 cells/μl, anaemia or EPTB
  - Major manifestations are fever or lymphadenitis
- Co-trimoxazole prophylaxis should be given for TB-HIV co-infection & throughout antiTB treatment.
Highlights of TB CPG 3\textsuperscript{rd} edition

Follow up

**Flow Chart for the Recommended 6-months Treatment of PTB**

<table>
<thead>
<tr>
<th>Visit</th>
<th>Duration</th>
<th>Regimen</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>0 M</td>
<td>EHRZ/SHRZ</td>
<td>FBC, RBS, RP, LFT, HIV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sputum AFB direct smear</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sputum MTB C&amp;S</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CXR</td>
</tr>
<tr>
<td>2.</td>
<td>2 - 4 weeks</td>
<td>EHRZ/SHRZ</td>
<td>LFT</td>
</tr>
<tr>
<td>3.</td>
<td>2 M</td>
<td>HR HPR\textsuperscript{3}</td>
<td>LFT if necessary, CXR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sputum AFB direct smear*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sputum MTB C&amp;S if smear remains positive</td>
</tr>
<tr>
<td>4.</td>
<td>4 M</td>
<td>HR HPR\textsuperscript{3}</td>
<td>Sputum AFB direct smear and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CXR only if there is no clinical improvement</td>
</tr>
<tr>
<td>5.</td>
<td>6 M Completion of 6 months treatment</td>
<td>Sputum AFB direct smear</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CXR</td>
</tr>
</tbody>
</table>

Patients with initial sputum smear negative should have repeat sputum smear at two months of antiTB treatment. If still negative, no further sputum sample is required.

*If smear AFB remains positive at two months, refer to specialists with experience in TB management and repeat sputum AFB and sputum MTB C\&S at three months.

HPR\textsuperscript{3}=thrice weekly of isoniazid and rifampcin
Highlights of TB CPG 3rd edition

Follow up

Recommendation 36
- Patients with initial sputum smear positive should have repeat sputum smear at two and six months of antituberculous (antiTB) treatment. (Grade C)
- Patients with initial sputum smear negative should have repeat sputum smear at two months of antiTB treatment. If still negative, no further sputum sample is required. (Grade C)
- Patients who remains sputum positive at two months should be referred to specialist with experience in tuberculosis (TB) management. (Grade C)
- Sputum *Mycobacterium tuberculosis* culture and sensitivity testing should be obtained at the start of antiTB treatment. (Grade C)
- Chest x-ray should be performed at two and six months of antiTB treatment. (Grade C)
- Follow-up within one month of starting antiTB treatment is advisable. (Grade C)
- Follow-up may not be conducted routinely after completion of antiTB treatment. Patients should be well-informed on symptoms of TB recurrence. (Grade C)
- Patients should be monitored for complications of antiTB drugs. (Grade C)
Highlights of TB CPG 3rd edition

Adverse Drug Events

Risk factors of ADRs of antiTB drug include:
- Age >40 years (OR=3.9, 95% CI 1.75 to 9.4173, level III; HR=2.9 95% CI 1.3 to 6.3174, level II-2)
- Overweight/obesity (OR=2.1, 95% CI 1.27 to 3.9)173, level III
- Smoking (OR=2.00, 95% CI 1.03 to 3.87)173, level III
- Alcoholism (RR=3.0, 95% CI 1.1 to 7.9)176, level III
- Anaemia (OR=2.1, 95% CI 1.1 to 3.9)173, level III
- Baseline ALT more than twice upper limit of normal (OR=5.9, 95% CI 1.2 to 10.1)178, level II-2
- Baseline aspartate aminotransferase more than twice upper limit of normal (OR=4.3, 95% CI 1.7 to 8.6)178, level II-2
- EPTB (p=0.017)177, level III
- MDR-TB medication (OR=11.1, 95% CI 6.3 to 19.6)173, level III
- HIV infection (HR=3.8, 95% CI 1.05 to 13.4174, level II-2; p=0.018177, level III)
- CD4 count <350 cells/mm3 (RR=2.6, 95% CI 1.4 to 5.0)175, level III
- Hepatitis B virus infection (p=0.0018)178, level II-2
- Hepatitis C virus infection (OR=2.9, 95% CI 1.1 to 8.0)178, level II-2
- Concomitant use of other hepatotoxic drug (OR=1.3, 95% CI 1.1 to 2.4)178, level II-2

Recommendation 38
- Hepatobiliary system should be monitored closely in patients with risk factors prescribed with antituberculosis drugs. (Grade C)
**Highlights of TB CPG 3rd edition**

**Adverse Drug Events – liver**

**Algorithm 2: Management of DIH**

- **EHRZ/SHRZ**
  - DIH
    - Stop treatment
      - Interim Regime
        - EHS/ERS
          - EHR/S
          - SEF
          - SEFHR
          - SEFHR
          - HEF/REF: S or HEFZ/REFZ

**Recommendation 37**

- Antituberculosis (antiTB) drugs should be stopped when the serum transaminase level reaches three times the upper limit of normal for symptomatic patients. (Grade C)
- AntiTB therapy can be recommenced by slow sequential introduction. (Grade C)
- Use of non-hepatotoxic regimens can be considered for patients with drug-induced hepatitis but will need a longer duration of therapy. (Grade C)
- Expert consultation is advisable in treating tuberculosis patients with drug-induced hepatitis. (Grade C)
Highlights of TB CPG 3rd edition

Adverse Drug Events - Skin

When severe cutaneous ADRs occur, antiTB drugs need to be discontinued until the rashes subside. Thereafter, individual drug is reintroduced sequentially to identify the offending drug. A suitable regimen can be provided when an offending drug is identified and if possible the regimen should include isoniazid and rifampicin (the two most potent drugs). If the offending drugs are both isoniazid and rifampicin, desensitisation may be required. Desensitisation is done by careful administration of increasing doses of the drug under close supervision. It should not be attempted for HIV patients. Desensitisation is only done if one is unable to devise a suitable regimen without the offending drugs. If a suitable drug combination is available, it is not necessary to perform desensitisation. Given that the management of significant cutaneous ADRs can be complex, consultation with specialists with experience in this field is recommended.
Highlights of TB CPG 3rd edition

Screening and Prevention

Algorithm 4: Contact Tracing

Site of disease

- Pulmonary/ laryngeal/pleural
  - Sputum AFB smear positive
    - Contact tracing should be done
  - Sputum AFB smear negative
    - Cavitary disease
      - Contact tracing should be considered
    - Non-cavitary disease
      - Contact tracing should be considered if sufficient resources

- Extrapulmonary
  - Contact tracing is indicated to find primary source
Highlights of TB CPG 3rd edition

Screening and Prevention

Algorithm 5: Investigations For Contact Tracing in Adults

PTB Close Contact*

Symptomatic

Evaluate for active TB
- CXR
- Sputum AFB
- Mantoux test (optional)

Diagnosis confirmed - treat
Diagnosis inconclusive - refer specialist

Asymptomatic

Mantoux test

≥10 mm
- Chest x-ray
- Normal - manage as latent TB infection
- Abnormal - evaluate for active TB

<10 mm
- Discharge with advice**

*Immunocompetent close contacts
**To seek medical advice if patient has symptoms suggestive of TB such as fever, cough etc. for more than two weeks.
Highlights of TB CPG 3rd edition
Screening and Prevention

Algorithm 6: Management of Children with Positive History of Contact with Tuberculosis

- **Child (Contact)**
  - **Mantoux Test**
    - ≥10 mm
      - CXR
        - Normal
          - Asymptomatic
            - ≥5 years old: Follow-up
            - <5 years old: Treat as LTBI
        - Abnormal
          - Symptoms suggestive of TB
            - Treat as TB
    - <10 mm
      - CXR
        - Symptomatic
          - Check BCG
        - Asymptomatic
          - Investigate further
            - No scar: BCG
            - Scar present: Follow-up
Highlights of TB CPG 3rd edition

Referral

Recommendation 10
- Physician with experience in tuberculosis (TB) management should be consulted for all patients requiring retreatment of TB. (Grade C)

Recommendation 39
- Multidrug-resistant tuberculosis must be suspected in previously treated patient with tuberculosis and sputum samples for culture and sensitivity must be sent at diagnosis. (Grade C)

Recommendation 26
- Frequency of pyrazinamide and ethambutol should be adjusted in patients with tuberculosis (TB) and renal failure. (Grade C)
- Streptomycin should be avoided if possible in patients with TB and renal failure. (Grade C)
- Physician with experience in TB management should be consulted for all TB patients with renal impairment. (Grade C)

Recommendation 25
- Regular monitoring of liver enzymes should be performed in patients on antituberculosis treatment with pre-existing liver disease or at risk of drug-induced hepatitis. (Grade C)
- Expert consultation is advisable in treating tuberculosis patients with advanced or unstable liver disease. (Grade C)
Highlights of TB CPG 3rd edition

Referral

**Recommendation 43**

- The following conditions should be referred to specialists with experience in tuberculosis (TB) management:
  - Unsure of TB diagnosis
  - Retreatment of TB
  - Adverse events following antiTB drugs
  - Multidrug-resistant and extremely drug-resistant TB
  - Extrapulmonary TB except for tuberculous lymphadenitis
  - Renal and/or liver impairment with TB
  - HIV-TB co-infection
  - Smear negative TB
  - Smear positive after two months of treatment
  - All children diagnosed with TB
  - Maternal TB
  - Complex TB cases requiring surgical intervention  (**Grade C**)
Highlights of TB CPG 3rd edition

Upcoming ....

Training session for TB CPG -
Coming up