IDENTIFICATION AND MANAGEMENT OF CANCER PATIENTS WITH LATENT OR ACTIVE TUBERCULOSIS

1. PURPOSE & SCOPE

To identify patients being managed at Peter MacCallum Cancer Centre with latent or active tuberculosis (TB). TB risk may only be identified by careful history taking and must be done prior to consideration of chemotherapy, radiation therapy and surgery.

This guideline addresses:
- Risk factors for TB Infection
- Latent TB
- Active TB
- Isolation instructions for patients with confirmed or suspected TB

2. TARGET AUDIENCE

All Peter MacCallum Cancer Centre staff

3. PROCEDURE

It is important that patients at **HIGH RISK** of reactivation OR with possible **ACTIVE DISEASE** are promptly referred to the Infectious Diseases Service.

- Patients at **HIGH RISK** of reactivation (see 6.0)
- Possible latent TB:
  - Positive QuantiFERON® TB Gold
  - Indeterminate QuantiFERON® TB Gold AND imaging (including FDG-PET) has abnormalities unrelated/unlikely due to malignancy

4. RESPONSIBILITIES

All PMCC clinical staff

5. TUBERCULOSIS INFECTION/REACTIVATION

**Tuberculosis** or **TB** is an infection caused by *Mycobacterium tuberculosis*. In Australia there are just over 1000 cases of TB diagnosed each year, with approximately 400 of these in Victoria. The rate of TB varies widely within Australia, ranging from around 1 per 100,000 in those born in Australia to over 400 per 100,000 in those born in TB endemic countries.

Transmission of TB occurs mainly by inhalation of infectious droplets, produced during coughing by people with active pulmonary TB. Most people infected with TB are asymptomatic (**latent TB**) and are not infectious. Patients with malignancy are at increased risk of TB reactivation and TB is often more severe and difficult to diagnose in these patients. TB can also masquerade as malignancy.

**TB reactivation will usually occur within the first 12 weeks of chemotherapy.**

**Active TB** commonly presents with a chronic cough (+/− haemoptysis), fevers and night sweats, weight loss and general malaise. Radiology findings might include cavitatory lesions, upper lobe infiltrates, pleural effusions. They will be FDG PET avid. Although less common than pulmonary TB, extra pulmonary TB may also occur and involve sites such as lymph glands, brain, genitourinary system, bone and joints and the gastrointestinal system. A discordant response to chemotherapy in a high-risk patient might indicate TB reactivation.
When should you suspect active TB?

- Any pulmonary radiological changes suggestive of active TB
- High risk patient PLUS lymphadenopathy in sites deemed unlikely due to the malignancy
- History suggestive of active TB (see 9.1)
- Positive TB PCR or AFB culture from any clinical specimen*
- Granulomatous inflammation in any clinical specimen*
- Lymphocytic ascites or pleural effusion*

All cases of suspected active TB require an urgent ID referral. This should be made prior to any procedures to ensure the appropriate specimen and microbiological requests are obtained. Also, patients with open TB (i.e pulmonary) are an infection control risk.

Investigation will usually require a sputum specimen (x 3) OR, if non-productive a bronchoalveolar lavage. Lymphadenopathy should be referred to surgery for excisional biopsy (preferred over an FNA due to the quantity of specimen required for microbiology tests)

All clinical specimens, including sputum, bronchoalveolar lavage fluid, pleural fluid, peritoneal fluid or tissue, should be sent for:

- Histology or cytology
- AFB stain
- M. tuberculosis culture
- M. tuberculosis PCR
- Other – as guided by ID unit

Samples put only into formalin will not be able to be cultured and important information will be lost

6. PATIENTS AT HIGH RISK OF TB REACTIVATION OR INFECTION

1. Those born/living in a TB endemic country including:
   - Asia, Middle East, Africa, Papua New Guinea and Pacific islands, Central and Eastern Europe, South America
   - NB the highest risk for TB reactivation is within the first 2 years of arrival

2. Those with a high degree of TB exposure including:
   - Close contacts of smear-positive pulmonary TB cases (family members, household contacts and other contacts with more than 8 hours of exposure) and healthcare workers with exposure to TB patients in high prevalence countries.
   - NB. This requires active history taking by treating team

Other risk factors for TB infection or reactivation may include:

- Indigenous Australians
- Age over 65 years
- Residents and employees of correctional facilities, nursing homes, and homeless shelters
- Chronic alcohol or drug use

7. SCREENING FOR LATENT TB WITH QUANTIFERON® GOLD

Most people infected with TB are asymptomatic (latent TB) and are not infectious. Patients with malignancy are at increased risk of TB reactivation and TB is often more severe and difficult to diagnose in these patients. TB can also masquerade as malignancy.
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- Patients who are to receive chemotherapy or radiation therapy AND have a HIGH RISK for TB infection or reactivation
- Patients with a diagnosis of lung cancer
- Patients with a diagnosis of lymphoma
- Patients with HIV

QuantiFERON® TB Gold must be performed before commencement of chemotherapy or radiation therapy. Contact pathology for the QuantiFERON® TB Gold IT kit.

<table>
<thead>
<tr>
<th>QuantiFERON result</th>
<th>Interpretation</th>
<th>Follow up required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>ACTIVE or LATENT TB infection</td>
<td>Chest Xray (or other imaging if being done for cancer workup)</td>
</tr>
<tr>
<td></td>
<td>Time of TB acquisition uncertain</td>
<td>If cough present - 3x Sputum samples for AFBs, TB culture and TB PCR</td>
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<tr>
<td></td>
<td>False positive results can occur in the presence of three Non-tuberculosis mycobacterium: M. marinum, M. szulgai, M. kansaii</td>
<td>ID referral</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>TB infection status uncertain</td>
<td>As above</td>
</tr>
<tr>
<td>Negative</td>
<td>A negative QG does NOT exclude infection.</td>
<td>Maintain suspicion for TB if born in endemic country or household contact with TB</td>
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<tr>
<td></td>
<td>TB infection still possible as sensitivity may be as low as 73% in immunocompromised patients.</td>
<td>Collect specimens for AFBs, TB culture + TB PCR as indicated</td>
</tr>
</tbody>
</table>

8. USE OF TB PROPHYLAXIS IN LATENT TB INFECTION

Patients with latent TB may be commenced on isoniazid 300 mg daily PRIOR to commencement of chemotherapy. This is prescribed with pyridoxine 25 mg daily (Vit B6). The duration of prophylaxis is 9 months.

The patient should be educated about possible side-effects and toxicity of isoniazid. Most common are hepatitis and rash. LFTs should be monitored initially weekly then monthly. Isoniazid should be ceased if AST or ALT is 3-5 times above normal.

9. INFECTION PREVENTION

a. Confirmed pulmonary or laryngeal TB.

- Place any patient with confirmed pulmonary or laryngeal TB (i.e AFB detected on sputum or BAL and/or positive TB culture) in a negative pressure room with appropriate signage on door
- Manage with full respiratory precautions (gown and N95 mask)
- Educate the patient and their visitors about the modes of TB transmission (TB patient visitor information sheet hyperlink)
- When transporting the patient outside the isolation room, ensure the patient wears a N95 mask.
- Initiation and/or continuation of anti-TB therapy will be directed by the ID unit

b. Suspected TB awaiting confirmation
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- Place any patient with suspected pulmonary or laryngeal TB in a negative pressure room with appropriate signage on door
- Manage with full respiratory precautions as for confirmed TB
- If negative pressure room unavailable – discuss with ID and infection prevention
- When transporting the patient outside the isolation room, ensure the patient wears a N95 mask.

c. Discontinuation of TB isolation

- TB isolation can be discontinued in the following situations and only in consultation with the ID unit
- The diagnosis of smear positive TB has been excluded following appropriate number and type of respiratory specimens.
- The patient with active TB is not longer considered infections – i.e they have completed 2 weeks anti-TB treatment and confirmed smear negative.

10. RELATED MATERIAL

- Collection of Induced Sputum
- Notification of Infectious Disease
- Single room isolation
- TB Patient Visitor Information Sheet
- TB Staff Information sheet

11. REFERENCES


CDC Guidelines for preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, MMWR, 2005.