Completion of Treatment

The end of treatment occurs when the patient has ingested every dose of anti-TB drugs in accordance with the recommended standards in this TB manual and, in consultation with the Internal Medicine Specialist, TB Specialists and with the OCPHO. The completion of TB treatment for respiratory TB involves:

- Thorough review of patient's case and treatment, including compliance
- Physical assessment
- CXR at treatment completion
- Three consecutive sputa for AFB at treatment completion
- Complete **NWT Active Tuberculosis Drug Treatment and Progress Record**
- For cases of non-respiratory TB follow-up after treatment is individualized and will be determined by the Internal Medicine Specialist

If all signs and symptoms of TB have resolved, no follow-up is required if the patient is low-risk for re-infection and not living in a TB-endemic community. If treatment is considered *inadequate*, follow-up will be determined in consultation with the Internal Medicine Specialist and the OCPHO.

Surveillance

Generally, all patients who have completed their treatment and are considered cured from their TB do not require follow-up or surveillance.

Patients who require follow-up after treatment include the following:

- Patients with inadequate regimens
- Patients who were non-adherent to their regimen
- Patients with multidrug or extensively drug resistant TB
- Patients with HIV co-infection

For these patients it is recommended to provide regular follow-up every 6 months or yearly for up to 3 years. If patients are reporting symptoms such as persistent cough, or fever, it may suggest TB disease relapse. Therefore these patients must be provided with a follow-up examination.

All patients should be told to return at any time in the future for evaluation of symptoms that suggest disease relapse, such as persistent cough or fever, hemoptysis or unexplained weight loss.

Drug-Resistant Tuberculosis

Globally, the rate of drug-resistant TB is increasing. In Canada, two systems are used to track drug-resistant TB:

- The Canadian TB Reporting System and;
- The Canadian TB Laboratory Surveillance System.

The major risk factors for drug-resistant TB in Canada are previous treatment and foreign birth. Drug-resistant TB should be suspected in patients who have:

- Previously been treated for active TB,
- Originated from, resided in or travelled to a country where drug-resistant TB is highly prevalent or;
- Been exposed to a person with infectious drug-resistant TB.

A person is considered to have drug-resistant TB if the bacteria strain that caused their disease is resistant to one or more of four FLD used for TB treatment (i.e. INH, RMP, PZA, and EMB). In Canada, INH resistance is the most common pattern of first-line drug resistance.

Drug-resistant TB cases, confirmed or suspected, are difficult to clinically manage and must be referred to a TB Specialist.

Table 8.14: Type of Drug Resistance

Type of Resistance	Description
Mono-resistant TB	Tuberculosis due to bacteria resistant to **one of the four** first line drugs (i.e. INH)
Polyresistant TB	Tuberculosis due to bacteria resistant to **two or more** first line drugs (i.e. INH and RMP)
Multidrug-resistant TB (MDR-TB)	Tuberculosis due to bacteria resistant to INH ***and*** RMP **with or without resistance** to other first or second line drugs (described below)
Extensively drug-resistant TB (XDR-TB)	Tuberculosis due to bacteria resistant to at least INH ***and*** RMP ***PLUS*** Resistance to any fluoroquinolone (second line anti-TB drug; a class of antibiotic) ***AND*** Resistance to at least one of the three injectable second line drugs (including capreomycin, kanamycin, amikacin)

Previous treatment for TB is an important consideration in determining risk of drug resistance. If a patient has a history of previous TB treatment, it is important to note the following:

- Patient has taken anti-TB medication(s) for one month or more at any time in the past but has not completed full treatment
- Patient lived in a TB-endemic country where drug resistance is prevalent
- Patient's drug regimen did not include INH and RMP throughout its entire course and was less than 12 months in duration
- DOT was not used, or patient reported missed doses
- Patient was exposed to a person with infectious drug-resistant TB

Prevention of drug-resistant TB can be achieved by doing the following:

- Prescribe at least two anti-TB drugs to which the bacteria strain is susceptible
- It is imperative to give TB drug regime by DOT
- Never introduce a single drug to a failing regimen
- Case management of all TB patients is necessary

Traditionally, drug resistance in TB has been classified into three types:

1. Primary Drug Resistance:

When previously untreated patients are diagnosed to have drug-resistant organisms, presumably because they have been infected from an outside source of resistant bacteria. Primary drug resistance is uncommon in Canadian-born people unless they have travelled abroad to a country with a high prevalence of anti-TB drug resistance.

2. Acquired Drug Resistance:

When patients who initially have drug-susceptible TB bacteria later become drug-resistant as a result of inadequate, inappropriate or irregular treatment or, more importantly, because of non adherence in drug taking. Acquired drug resistance is uncommon in Canadian-born people, perhaps because directly observed therapy (DOT) is frequently used to promote treatment adherence.

3. Initial Drug Resistance:

When drug resistance occurs in patients who deny previous treatment but whose history of prior drug use cannot be verified. In reality it consists of true primary resistance and an unknown amount of undisclosed acquired resistance. These patients are classified as having *initial* rather than primary drug resistance.

Management of Drug-Resistant TB

For the management of all drug-resistant TB cases the following is required:

- Adequate drug-susceptibility testing
- The appropriate use of first and second line anti-TB drugs according to drug susceptibility results
- Access to experienced health care specialist who will direct the management of drug-resistant TB. **This is a mandatory requirement.**

Any patient with drug-resistance to INH and RMP must undergo drug susceptibility testing for second line anti-TB drugs.

Second-Line Anti-Tuberculosis Treatment

Treatment for drug-resistant TB is usually with a **daily** regimen (particularly the initial phase of treatment), under **DOT**. Otherwise there is a greater risk of inadequate treatment or treatment failure. Drug serum levels are also required if drug malabsorption is suspected. If an anti-TB drug regimen is changed because there is suspect of treatment failure, there must be a minimum of two new drugs added. The drug susceptibility of the added drugs must be confirmed or it must be known that the patient has never received the new added drugs. Refer to **Canadian TB Standards, 7th Edition**, for further information on treatment and drugs used for multidrug-resistant TB.

Recommendations for Treatment of INH Mono-resistant TB

- All patients suspected of drug-resistant TB must be started on four first-line anti-TB drugs while awaiting drug susceptibility results
- In the NWT DOT is used for all TB cases. It is especially important in patients with sputum smear-positive respiratory disease or co-infection with HIV
- Regimens for the treatment for INH mono-resistant TB are:

Table 8.15: Regimens for the Treatment of INH Mono-resistant TB

Regimen	Initial Phase	Continuation Phase
1	2 months daily (INH), RMP, PZA, EMB*†	4–7 months daily or thrice weekly RMP, PZA, EMB
2	2 months daily (INH), RMP, PZA, EMB*†	10 months daily or thrice weekly RMP, EMB
3	2 months daily (INH), FQN, RMP, PZA, EMB*‡	4–7 months daily or thrice weekly FQN/RMP/EMB

* If treatment was started with a standard 4-drug regime, INH can be stopped when resistance is documented.

† If a patient has extensive disease a Fluoroquinolone (levofloxacin and not moxifloxacin) can be added to the regimen especially during the initial phase.

‡ PZA is recommended here but in most trials this drug was not included in the regime.

Recommendations for Treatment of RMP Mono-resistant TB

RMP mono-resistant TB is uncommon except in HIV-infected patients. It is estimated RMP monoresistance occurs approximately 10% of the time. Therefore, 90% of time RMP resistance is accompanied by another drug-resistance, such as INH. **RMP resistance should strongly signal suspicion for MDR-TB cases.**

Table 8.16: Regimens for the Treatment of RMP Mono-resistant TB

Regimens	Initial Phase	Continuation Phase
1	2 months daily INH, PZA, EMB, FQN*	10–16 months daily or thrice weekly INH, EMB, FQN
2	2 months daily INH, PZA, SM (or other aminoglycoside/polypeptide daily or thrice weekly)	7 months daily or thrice weekly INH, PZA, SM
3	2 months daily INH, PZA, EMB daily†	16 months daily or thrice weekly INH, EMB

INH = isoniazid, PZA = pyrazinamide, EMB = ethambutol, FQN = levofloxacin or moxifloxacin, SM = streptomycin

*For treatment in patients with extensive cavitary disease or to shorten the duration of treatment (e.g. 12 months), addition of an injectable agent for at least the first 2 months is recommended.

† An injectable agent may strengthen the regimen in patients with extensive disease

Recommendations for Treatment of PZA or EMB Mono-resistant TB

Monoresistance to PZA or EMB is rare. Isolated PZA resistance occurs with exposure and infection with *M. bovis*. Therefore it can serve as a critical tool for laboratories to differentiate between *M. tuberculosis* from *M. bovis* or *M. bovis BCG*.

- Patients with mono-resistant TB to PZA should have their total duration of treatment as 9 months or more
- Patients with mono-resistant TB to EMB, the standard regimens do **not** change

Multidrug-Resistant (MDR-TB) and Extensively Drug-Resistant (XDR-TB) Tuberculosis

A patient with MDR-TB or XDR-TB will need treatment with second-line treatment. Second-line anti-TB drugs are considered less effective, require extended periods of treatment (20–24 months or more) and can cause more side effects than first-line drugs. When on treatment, these patients can be infectious for a longer period of time before improvements are seen.

When the drug susceptibility results are available, then the treatment regimen can be determined.

Surgery is considered in cases of MDR-TB/XDR-TB when the bacteria drug-resistance pattern shows a high probability of treatment failure. Removal of diseased lung by resection is an option for these patients to improve their chances of cure.