CASE MANAGEMENT

Tuberculosis is a notifiable disease. Cases must be reported to the regional Medical Officer of Health within 48 hours of identification. The Medical Officer of Health will in turn notify the Provincial Health Officer.

Diagnosis

If the following criteria are met, a diagnosis of active TB will be made:

- Patients with *Mycobacterium tuberculosis* complex demonstrated by culture (i.e. *M. tuberculosis*, *M. africanum*, or *M. bovis*--excluding BCG strain), or

- Patients with significant evidence of activity, even if there is no bacteriological proof (regardless of TST results). Significant activity includes:
  - change on a chest radiograph compatible with active tuberculosis (including idiopathic pleurisy with effusion in close contacts)
  - clinically active nonrespiratory tuberculosis (e.g. lymph node, CNS, bone and joint, genitourinary)
  - post-mortem evidence of active tuberculosis
  - pathology demonstrating caseating granulomatous disease

Nontuberculous Mycobacteria (NTM)

A number of bacteria in the same genus as *M. tuberculosis,* known as nontuberculous mycobacteria or NTM can be acquired through contact with various environmental sources, such as soil, water and animals. NTM disease is often difficult to diagnose. Mycobacteriology is very important.

- Infection with these mycobacteria may cause the individual to become a TST reactor.

- Individuals with NTM may be ill, and may have the same radiologic appearances as with *M. tuberculosis.* Positive smears from NTM cannot be distinguished from positive smears from *M. tuberculosis.*

Responsibilities for Management

Tuberculosis management in Alberta involves a partnership between the patient, their family (or attending) physician, their regional MOH and/or First Nations and Inuit Health Branch of Health Canada, Alberta Health and Wellness (Tuberculosis Control) and/or the Calgary and Capital Health TB Clinics.

It is essential for the control of this disease, that each of the partners takes responsibility for their role in the partnership.

Family (attending) Physician

- Is responsible for the overall clinical care of his or her patient with tuberculosis. This patient care responsibility is shared with a TB specialist from provincial Tuberculosis Control or one of the TB Clinics. Liaison with these specialists is critical.

Provincial Tuberculosis Control and/or the Capital Health or Calgary TB Clinic

- Provides consultative and/or clinical expertise to assist with diagnosis and follow-up of clients suspected of having tuberculosis.

- Makes decisions about treatment for these individuals, and assists with ensuring all cases receive appropriate treatment.

- Ensures a supply of free medication is available for treatment of disease and latent infection, and forwards this medication to the local or regional field staff for appropriate distribution to patients.

- Monitors medication adherence and adequacy of treatment, either directly, or with information provided by the local regional TB program staff.

- Communicates findings and information regarding medications, routine monitoring for side-effects, further investigations needed, etc. with family physician and regional TB program staff in the area in which the patient resides.

- Provincial Tuberculosis Control maintains a registry of all notified cases, and reports these cases nationally to CIDPC.

RHA and/or FNIHB Staff

The Medical Officer of Health, in consultation with TB Control or the Capital Health or Calgary TB Clinic, and with the assistance of local staff, ensures effective and efficient case management in the region. In addition to ensuring adequate resources are available to deliver treatment, the MOH has a crucial role in the co-ordination of staff to deliver the program, and liaison with local physicians, pharmacists, and laboratory/radiology facilities.

Well-trained Public Health or Community Health Nurses (PHNs or CHNs), working with other healthcare staff, are pivotal to the success of tuberculosis treatment and follow-up programs. They co-ordinate care in the community, ensuring that patients obtain the appropriate medication, are monitored for adverse reactions, and see physicians when necessary. Responsibilities include the following:

- Meet with the individual and family to assess their needs and to provide education regarding the disease and treatment.

- Discuss with the individual/family the need for contact investigation and begin the process of collecting names for the contact investigation list.

- Ensure appropriate isolation at home or, if necessary, in hospital if the individual is infectious (i.e. sputum smear-positive, **see Appendix 17**). If the individual remains at home, restrict them from public activities (going to church, shopping, or anywhere on public transportation), and also restrict access of new visitors to the home during the period of infectiousness.
  - Advise clients, if coughing, to cover their nose and mouth with disposable tissue. No special precautions need to be taken with soiled tissues, and they can be disposed of in the regular household garbage.

- Receive medication from TB Control and distribute to patients as directed.

- Ensure all medications are taken. In this regard, directly observed therapy **(DOT)** is considered the **standard of treatment** for active TB. The ultimate program goals are to ensure that:
  - all infectious patients are rapidly rendered non-infectious and asymptomatic
  - drug resistance is prevented
  - all patients complete a curative course of treatment

  These goals **may** at times be achieved by means other than DOT.

- Monitor clients for adverse reactions to medication (including arranging for appropriate blood work, vision testing, etc.), and report reactions to the family physician and to TB Control or the TB Clinic.

- Report adherence and tolerance to medication regimen monthly, using the "Treatment Record and Follow-up Form" (see Appendix 14.2).

Hospitalization

▶ Every region needs to have a contingency plan for hospitalization of TB patients who are highly infectious, have severe illness, are drug resistant or intolerant, or are nonadherent with treatment.

▶ Not all regions have isolation rooms with adequate engineering controls to prevent transmission of infection. In this case, it may mean utilizing the services of the University of Alberta Hospital which has a dedicated Tuberculosis Ward (5C3). This ward provides:

- isolation of infectious cases using appropriate engineering controls
- expert consultation, including dealing with drug resistance and drug intolerance
- extensive patient education—the education team consists of expert nurses, physicians, social workers, pastoral care
- detailed discharge planning

▶ If hospitalization is needed for an infectious case, regional staff (public health or local facility) may need to make the arrangements for transportation from the community to the facility, or from the regional facility to the provincial facility.

▶ Public transportation must not be used if the individual is infectious. Transportation must be under conditions that approximate (as much as possible) respiratory isolation. During transportation, the client and those transporting the client must wear a mask that will adequately filter the TB organism.

Use of public transportation is not appropriate if the individual is infectious.

- The cost of transportation is the responsibility of the referring region except when the patient is aboriginal with treaty status.
- First Nations and Inuit Health Branch (FNIHB) of Health Canada is responsible (through the referral unit) for coverage of some non-insured health benefits for treaty status individuals living both on and off reserve. The Branch will assist with issues that arise around transporting people. For example, if an elderly person who does not speak English needs to be transferred to a facility some distance away, FNIHB will arrange for transportation, accommodations and meals for an escort when needed.

The Individual

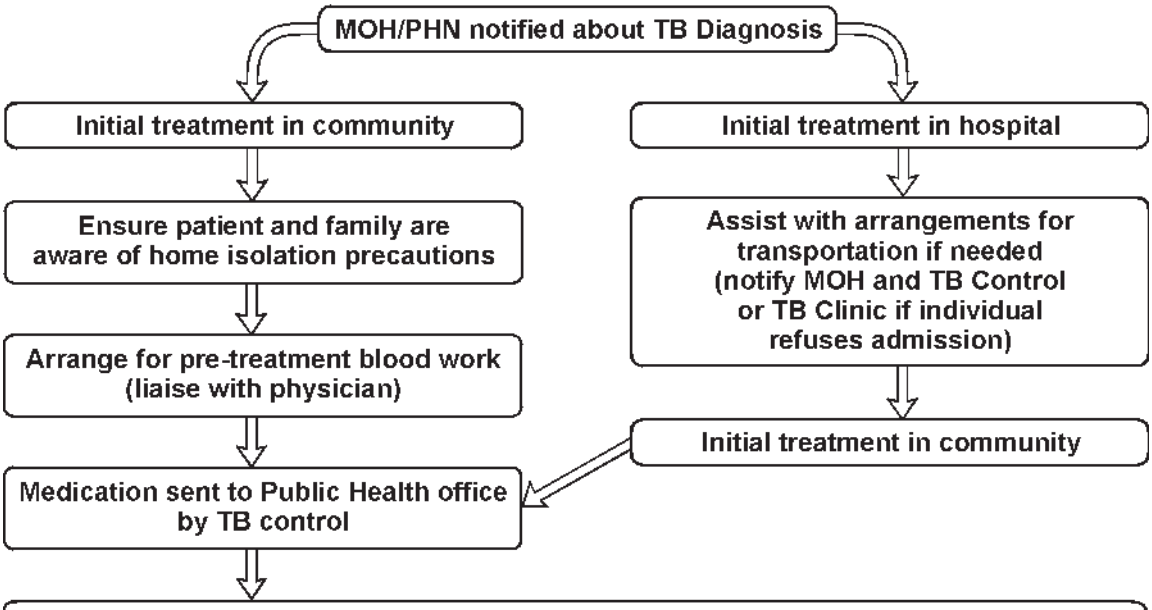
▶ Agrees to the provision of a DOT program and negotiates with regional TB program staff as to when and where this will be carried out (e.g. clinic, home, workplace).

▶ Keeps appointments for medication administration and any follow-up needed.

▶ Reports any problems to regional TB program staff.

▶ Discloses information when indicated, to enable timely and complete follow-up of contacts.

Algorithm for PHN Responibilities in Case Management



Medication dispensed as agreed upon with patient (DOT)
- *Notify* TB Control if 2 consecutive doses (daily *or* twice weekly) are missed

Report every month (more often if necessary):
- Symptoms of TB–cough, fever, night sweats, weight loss
- Drug compliance–number of doses required, and number actually taken
- Tolerance to medication:
  - Symptoms that may be due to a drug reaction
  - Results of tests done to monitor drug toxicity (for example, AST results, visual acuity and colour discrimination)

Chest radiograph (respiratory cases)–at the end of the initial phase of treatment, and following treatment completion unless otherwise ordered.

Sputum (respiratory cases)–weekly (or more often) until smear negative (on three consecutive specimens), then at the end of the initial phase of treatment and the end of the continuation phase.

Treatment of Tuberculosis Disease

Cure can be achieved in different ways, all of which include **the ingestion of drugs to which the organism is susceptible**.

Treatment of TB is aimed at achieving a lifetime cure of the disease, preventing drug resistance, and preventing further transmission of the infection in the community.

- Collaboration between TB Control and/or the TB Clinic, family physician, Public Health services and the client will determine the best mode of treatment.

- Anti-tuberculosis drugs are always given in combination for a period of **several months**—*M. tuberculosis* is usually slow to produce disease and equally slow to respond completely to drug treatment.

- Several factors must be taken into account in determining which drugs are to be used and the length of treatment. These include:
  - the type of disease being treated
  - the drugs that are available for treatment (cases due to drug-resistant isolates will need longer courses of treatment than those due to drug-susceptible isolates)
  - patient adherence to treatment
  - potential drug interactions

Treatment Regimens

In general, treatment is divided into 2 phases as described below. As new information emerges, and new studies are completed, these phases and the regimens involved may be modified by the Provincial TB Consultant, in conjuction with the Tuberculosis Control Committee of Alberta.

Initial or Intensive Phase (also called "front-end loading")

In accordance with the Fifth Edition of the *Canadian Tuberculosis Standards*, 3 or 4 drugs are given daily (using DOT) for 2 months (60 doses).

- The choice of drugs depends on drug susceptibility testing. If susceptibilities are not known at the onset of treatment, 4 drugs are usually prescribed, and adjustments are made once susceptibility test results are available.

Adherence to medication during this intensive phase is important, in that it:

- results in rapid symptomatic relief, rapid reduction in infectiousness, and reduced mortality
- reduces the possibility of the individual developing drug-resistant TB
- significantly increases the possibility that the client will complete treatment in 6 months

Maintenance or Continuation Phase

Two drugs (usually isoniazid and rifampin if the organism is susceptible) are given either daily or twice weekly using DOT for an additional 4 to 7 months. This eliminates any persisting bacteria not destroyed in the initial phase, and reduces the likelihood of relapse.

Medications Used in the Treatment of Tuberculosis

The following medications are referred to as the "first-line drugs" for the treatment of TB. They are the most effective drugs with which to combat the disease. It is important that they not be used indiscriminately. If resistance to these drugs develops, the treatment of tuberculosis is often more expensive, more complicated, and its duration is much longer.

All drugs for the treatment of TB are provided free-of-charge through Tuberculosis Control. *Physicians should never write prescriptions to local pharmacies for these drugs.*

Second-line drugs for the treatment of TB will not be discussed in any detail, as their use is still uncommon, and should always be carefully undertaken by one of the tuberculosis experts in the province. See Appendix 4 for information regarding "second-line" drugs for TB treatment. If a client is sent home on anything but the first-line drugs, information regarding administration and monitoring for adverse reactions will be discussed.

Isoniazid (INH)

Isoniazid is an active anti-tuberculous agent, which was first used in 1952. Its mode of action is still not completely understood, and it is effective only against the genus *Mycobacterium*. It is rapidly and almost completely absorbed, and peak blood levels are reached within 30 to 60 minutes after ingestion. Absorption is inhibited by the presence of food in the stomach.

There is a natural occurrence of resistance to INH in about 1 in a million organisms. The assumption is made that more than 1 million organisms must be present before TB disease is seen. Therefore, INH is always used in combination with another drug when used for treating active disease. The second drug will destroy any naturally occurring drug resistant mutants in the population of bacteria.

If infection has occurred, but no disease is detected, it is safe to assume that fewer than 1 million organisms are present, and the use of INH alone to prevent future reactivation is acceptable practice.

▶ **INH Overdose**

- INH combines with pyridoxine (Vitamin B6) in the blood, and in high doses can rapidly deplete the body stores of Vitamin B6. This effect is seen with doses of 80-150 mg/kg.
- Depletion of Vitamin B6 can be very serious. Early symptoms include nausea, vomiting, dizziness, slurred speech, blurred vision, dilated pupils, tachycardia, and sometimes retention of urine. Stupor, coma and seizures may then follow. These seizures, if not controlled, may lead to death from brain damage, aspiration or hypoxia.
- The risk of overdose must always be considered in patients provided a 1 month supply of the drugs (the equivalent of 150 mg/kg if taken all at once) for self-administration.

▶ **Treatment of Overdose**

- As soon as an overdose of INH has been recognized (even in the absence of symptoms), **the same dose of pyridoxine as the dose of INH ingested should be given intravenously**. For example, a child who has ingested 3.0 gm. of INH would be given 3.0 gm. of pyridoxine. If the dose of INH is not known, 5.0 gm. of pyridoxine should be given intravenously.

- This dose of pyridoxine should be repeated in 2 hours if the response to treatment has been incomplete. A total dose of pyridoxine 25gm. may be required in the first 12 hours.
- Diazepam (Valium) should be given to control seizures (2 mg by rectum for babies over the age of 6 months, or 5-10 mg intravenously for older children and adults). Phenytoin (Dilantin) should not be given as it increases levels of INH.

A supply of intravenous pyridoxine should be available in all local hospitals.

Rifampin (RMP)

Rifampin has been in general use since 1970. It acts by inhibiting DNA-dependent RNA polymerase activity in dividing cells, and is effective against mycobacterium as well as some gram positive and gram negative organisms. It is readily absorbed and reaches peak blood concentrations 2 to 4 hours after ingestion. Absorption is inhibited by the presence of food in the stomach.

Take a careful medication history and consult with a pharmacist to discuss potential drug interactions with rifampin.

When given intermittently, usual daily doses are used because intermittent high dose administration is likely to cause hypersensitivity reactions, including thrombocytopenia and anaphylaxis.

Rifampin is a liver enzyme inducer and increases the metabolism (thus decreasing the blood levels) of other drugs metabolized by the liver, such as anticoagulants, oral hypoglycemia agents, corticosteroids, oral contraceptives, phenytoin, etc. Patients on birth control pills will have to use alternate forms of birth control while on rifampin.

Pyrazinamide (PZA)

Pyrazinamide has been used since 1952. Its mechanism of action is unknown, but it is active only at acid pH.

Pyrazinamide inhibits the renal excretion of urates, and will often lead to high levels of uric acid in the blood. This is usually of no consequence. Rarely it may lead to acute episodes of gout in persons predisposed to gout, in which case the drug may need to be discontinued.

Ethambutol (EMB)

Ethambutol is bacteriostatic at low dosage (15 mg/kg) and bactericidal at high dosage (25 mg/kg). It works by inhibiting cell metabolism, causing cell death. It is active only against organisms of the genus *Mycobacterium*. It is about 75-80% absorbed after an oral dose, and reaches peak blood concentrations about 2 to 4 hours after ingestion. Absorption does not seem to be affected by food in the stomach.

Ethambutol is excreted from the body mainly in the urine. There is a fine line between the blood level needed to be effective and the toxicity level. In individuals with impaired renal function, there is

marked accumulation of medication in the system. For this reason, renal function (serum creatinine) should be measured before beginning treatment.

Ethambutol may cause optic neuritis (about 6% of patients), with decreased visual acuity and loss of red-green colour discrimination. These effects are uncommon at the lower dosage (15 mg/kg), and for this reason, dosages are usually reduced after the initial phase of treatment. They are usually reversible when detected early and the drug is discontinued promptly.

- Visual acuity and red-green colour discrimination should be tested monthly while on treatment, and the client should be advised to report promptly any changes in vision.
- Because these changes may be unilateral or bilateral, each eye must be tested separately and both eyes tested together.

Streptomycin (SM)

Streptomycin was discovered in 1944. It works by interfering with the bacterial cell proteins. It is not absorbed from the gut, and is therefore only given in parenteral form. Peak blood concentrations are reached about 1 to 2 hours after administration.

Streptomycin is excreted from the body mainly through the urine. In individuals with impaired renal function, it will accumulate and may reach dangerously high blood levels. For this reason, individuals with any renal impairment need to be monitored very closely.

There is risk of eighth nerve toxicity with the administration of streptomycin (especially in the presence of renal impairment). This may lead to permanent loss of inner ear function. Symptoms include nausea, vomiting, vertigo, nystagmus and ataxia, tinnitus, and varying degrees of hearing impairment. Monthly audiograms are necessary. Streptomycin is also teratogenic to the fetus's eighth cranial nerve, and should not be used in pregnancy.

First-line drugs for the treatment of tuberculosis

Drug and Daily Dose	Twice Weekly Dose	More Common Side-Effects	Less Common Side-Effects	Monitoring	Comments
Isoniazid (INH) ***Supplied : Tablets - 100 and 300 mg Liquid - 50 mg/5 ml (Parenteral formulation also available)*** Dose: Adult: 5-10 mg/kg (to max. 300 mg/day) Child: 5-10 mg/kg/day (to max. 300 mg)	Adult 900 mg Child 15-30 mg/kg (to max. 900 mg/day)	• hepatotoxicity (nausea, vomiting, abdominal discomfort, anorexia, fatigue) accompanied by increased transaminase (AST, ALT) levels	• peripheral neuropathy (controlled by co-administration of pyridoxine) • arthralgia • convulsions • psychotic symptoms (rare) • rash	See "Isoniazid (INH) Preventive Therapy Fact Sheet" page 6-16.	Exclude interactions with other medications. • If Dilantin is co-administered with isoniazid, the Dilantin level will be increased and dosage needs to be adjusted accordingly. Consider **overdose potential.**
Rifampin (RMP) ***Supplied: Capsules - 150 and 300 mg Syrup formulated from capsules—10 mg/ml (Parenteral formulation also available)*** Dose: Adult:10-20 mg/kg (to max. 600 mg/day) Child: 10-20 mg/kg/day (to max. 600 mg)	Adult 600 mg Child 10-20 mg/kg (to max. 600 mg/day)	• hepatotoxicity (as with INH) • orange discoloration of urine and body secretions, (tears, urine, saliva, perspiration)	• hypersensitivity • purpura • gastroenteritis • renal shutdown (rare) • memory loss • arthralgia • leukopenia (rare) • thrombocytopenia (rare)	See "Rifampin Preventive Therapy Fact Sheet" page 6-17.	Exclude interactions with other medications (e.g. decreased effectiveness of birth control pills). Orange discoloration of tears will **stain soft contact lenses**; sweat can stain white shirts.

First-line drugs for the treatment of tuberculosis

Drug and Daily Dose	Twice Weekly Dose	More Common Side-Effects	Less Common Side-Effects	Monitoring	Comments
Pyrazinamide (PZA) ***Supplied: Tablets - 500 mg*** Dose: Adult: 15-30 mg/kg (to max. 2000 mg/day) Child: 15-30 mg/kg/day (to max. 2000 mg) Dosage adjustment needed if patient is on dialysis	Adult: 50-70 mg/kg (to max. 3000 mg/day) Child: 50-70 mg/kg (to max. 2000 mg/day)	• hyperuricemia • arthralgia	• hepatoxicity • photosensitivity • gout	• See "PZA Preventive Theraphy Fact Sheet" see page 6-19 • transaminase levels as with INH and Rifampin • uric acid if gout is suspected	Exclude interaction with other medications. Not recommended in pregnancy.
Ethambutol (EMB) ***Supplied: Tablets - 100 mg and 400 mg*** Dose: Adult: 15-25 mg/kg (to max. 2500 mg/day) Child: 15-25 mg/kg/day Avoid in patients with renal failure	Adult and child 50 mg/kg	• retrobulbar neuritis • nausea	• slight uric acid elevation	• baseline visual acuity and colour discrimination • repeat visual acuity and colour discrimination monthly	Exclude interactions with other medications. Report any visual changes immediately.
Streptomycin (SM) ***Supplied: Vials– 1000 and 4000 mg (Parenteral formulation only)*** Dose: Adult: 15-20 mg/kg IM (to max. 1000 mg/day) Child: 20-40 mg/kg IM (to max. 1000 mg/day) Dosage adjustment needed if patient is on dialysis	Same as daily dose Same as daily dose	• 8th nerve toxicity, esp. vestibular • hypersensitivity reactions • nausea	• nephrotoxicity • numbness and tingling around mouth	• symptoms Baseline and then monthly: • Urea • Creatinine • audiogram	Report balance problems or vertigo promptly. If renal impairment, monitor closely. Reduce dose in older patients. Do not give during pregnancy.

Directly Observed Treatment (DOT)

Directly Observed Treatment is the most effective strategy available for assuring adherence to treatment. It means:

- making sure that **all** doses of medications are taken and swallowed in the presence of a trained observer
- documenting that all medications have been taken, and recording any side-effects observed

DOT is the recommended method, and is considered the **standard of medication delivery** in Alberta for all cases of TB. Recommendations for DOT are not based on the assumption that any particular patient may be non-compliant with treatment. But treatment regimens are always long, require the patient to take more than 1 drug, must continue long after the patient feels well, and may even make them feel a little unwell. Even the most motivated individual often has difficulty completing a full treatment regimen under these circumstances.

DOT is a strategy which is supported by the World Health Organization. It is becoming widely used worldwide, as more countries develop the capacity to detect TB and provide medications to all who need it.

DOT **must always** be used when the individual:

- has sputum smear-positive pulmonary TB – this individual is considered very infectious, and therefore a public health risk
- has TB and HIV co-infection
- is on intermittent drug treatment
- is known to be non-adherent with treatment regimens – these individuals are at higher risk of developing drug-resistant tuberculosis
- has mental health problems which would lead the practitioner to question either the ability of the individual to be adherent, or the safety of self-administered treatment
- has multi-drug resistant TB

The Benefits of DOT

When explaining to clients the need for DOT, the following points may be used.

- DOT encourages successful completion of treatment by providing assistance with taking the medication.
- With DOT, most clients only need to take their medicine 2 or 3 times each week in the continuation phase, and sometimes for a portion of the initial phase.
  - The regime will often be shorter than for daily, self-administered treatment (example—6 months instead of 9 months).
- The person providing DOT makes sure the client is going for regular check-ups, watches for side-effects and provides TB information.
- DOT gives the client the opportunity to ask questions and reduce fears about TB and its treatment.
- DOT will improve the likelihood of permanent cure.
- DOT will reduce the likelihood of acquired drug resistance.
- DOT will also allow for the rapid identification of those who abscond.

Program Considerations

Treatment regimens are always long and often place some restrictions on individuals' lifestyles and sometimes, even work life. Because of the importance of adherence to treatment, it is imperative that those delivering treatment be flexible, and negotiate with patients to achieve the best outcome. Issues such as where and when medications will be delivered are important. Sometimes it is best for the patient to present to the health centre, sometimes home visits work best, and sometimes the local park or coffee shop is the best solution. Decisions must be made taking both the patient's and the pill dispenser's needs into account.

The Public or Community Health Nurse (PHN or CHN) always provides for the delivery of medication to the patient, and watches him/her swallow them.

- Once the patient is established on DOT, another responsible person in the community (e.g. CHR, teacher, neighbour, etc.) often can be trained to supervise the taking of medication.
- Pill dispenser manuals are available from Alberta Health and Wellness to assist in the training of community pill dispensers.
- Care must be taken in the selection of these individuals. The nurse must ensure that the community pill dispenser is:
  - responsible, and will deliver **and** observe the swallowing of each dose
  - capable of monitoring, documenting and reporting side-effects to the PHN/CHN
  - acceptable to the patient
  - not in a position to be influenced by the patient (e.g. family member, employee)

The nurse retains the ultimate responsibility for ensuring that the treatment regimen is followed, adverse reactions are monitored, and necessary lab work is done. Because of this, frequent meetings with the pill dispenser, and at least monthly meetings with the patient are recommended.

Each case should be reviewed with the pill dispenser frequently (every week to 2 weeks) by the PHN/CHN.

Monitoring for Adverse Effects of Treatment

Before Beginning Treatment

The following baseline measurements are necessary to properly prescribe treatment and allow for subsequent documentation of toxicity:

- Hepatic enzymes (AST, ALT and Bilirubin)
- CBC, WBC and platelet count
- Serum creatinine
- Serum glucose
- Urinalysis
- Visual acuity and red-green colour discrimination if ethambutol is prescribed
- Audiometry if streptomycin is prescribed
- HIV serology

Routine Monitoring Once Treatment Has Begun

All clients on medication need routine monitoring to assess adverse effects from the medication. Each time medication is dispensed, assessment for symptoms relating to adverse reactions from the particular medications should be performed. In general, the blood work monitoring of patients on INH, rifampin or pyrazinamide are similar to those outlined on the preventive therapy fact sheet available for each of the drugs (see Appendices 5, 6, 7 and 8).

Other recommendations regarding monitoring for specific adverse effects and any blood work that needs to be done will be specified in the "action column" of the *Update Form* that will accompany the medication on delivery to the health centre. In older patients, or patients with underlying liver disease, more frequent monitoring of blood work (e.g., every 2 weeks) at the discretion of the tuberculosis consultant, may be necessary.

Symptoms suggesting treatment failure or drug toxicity, and any abnormal blood work need to be reported to the family physician and to TB Control or the Capital Health or Calgary TB Clinic.

Monitoring Response to Tuberculosis Treatment

Clinical Response

Most patients will have an excellent response to treatment, and will become asymptomatic within a few weeks. For example, fever usually resolves within 2 weeks of effective treatment. Regular inquiry for symptoms of tuberculosis must be carried out on any individual being treated for tuberculosis.

- If the individual remains symptomatic or symptoms recur (see page 2-6), report this to the family physician and TB Control or the Capital Health or Calgary TB Clinic.

Bacteriological and Radiological Response

The following are *general* guidelines for determining response to treatment of tuberculosis. Depending on the individual circumstances, patient specific recommendations for monitoring will be provided by Tuberculosis Control or the Capital Health or Calgary TB Clinic.

Respiratory Case Follow-up

Sputum

- At the outset, if the case is smear-positive from airway secretions, collect sputum specimens until at least 3 consecutive specimens, on 3 different days are smear-negative.
- Once smears have converted to negative, collect at the end of the initial phase of treatment, and at the completion of the continuation phase.
- Collect specimens 6 and 12 months after treatment is completed, to ensure cure has been achieved.

Chest Radiograph

- The interval between radiographs depends on the site of disease and the clinical circumstances.
- Respiratory cases will require radiographs at least twice: at the end of the initial phase of treatment (approximately 2 months) and at the end of treatment.
    - Follow-up radiographs will be done 6 and 12 months after treatment completion.

Non-respiratory Case Follow-up

Following completion of treatment, individuals with non-respiratory tuberculosis will need a chest radiograph, sputum examination, and a physical assessment by the family physician to determine response to treatment.

Twelve months following the end of treatment, the patient should be re-evaluated by the family physician to ensure there has been no relapse of disease. This re-evaluation must consist of, at minimum, a physical examination of the site of disease. If the physician has any concern about the possibility of relapse, or any question of the reliability of history of adequate treatment, a chest radiograph and sputum examination for AFB may be requested.

Drug-resistant Tuberculosis

It is uncommon to find resistance to first-line anti-tuberculosis drugs in isolates from Canadian-born TB patients. On the other hand, isolates from foreign-born TB patients are not uncommonly resistant to 1 or more first-line drugs, most often isoniazid and/or streptomycin. Because the foreign-born constitute an increasingly large proportion of TB patients in Canada, the proportion of all *M. tuberculosis* isolates in Canada that are drug resistant is increasing. Drug resistant TB is generally more difficult to treat.

Drug resistance in tuberculosis can be classified into 3 types:

- **Primary drug resistance** – when previously untreated individuals are found to have drug-resistant organisms. Primary resistance results when an individual is infected by someone who has drug resistant TB disease.
- **Acquired drug resistance** – when individuals who initially have drug susceptible tubercle bacilli later become drug-resistant. This is usually due to inadequate, inappropriate, or irregular treatment or, more importantly, due to non-adherence in taking the prescribed medication.
- **Initial drug resistance** – when drug resistance is reported in individuals who deny previous chemotherapy but whose prior drug use history cannot be confirmed.

Isolates may be resistant to a single first-line drug, or to a combination of drugs.

- Isolates resistant to a **single drug** are most often resistant to isoniazid, and there are effective alternatives for the treatment of these cases.

- **Multi-drug resistant tuberculosis** (MDRTB) refers to resistance to at least isoniazid and rifampin. The treatment of MDRTB usually requires the use of second-line drugs (see Appendix 4).
  - Second-line drugs for the treatment of TB are known to be less effective, more expensive and may have many more adverse reactions than the first-line drugs.
  - Treatment regimens for MDRTB must be individualized, but in general, 4 to 6 drugs are given over an extended period of time, and every dose **must** be directly observed to have been taken (daily or even several times a day).
  - When patients are sent home on any of these second-line drugs, information about the medication, adverse reactions and monitoring should be provided to the staff in the field.

Important strategies to reduce the development of resistance include:

- central co-ordination of the TB Program, including monitoring and provision of TB drugs, to ensure adequate treatment supply
- directly observed therapy to ensure adherence to the prescribed regimen
- treatment of TB disease with at least 2 (and preferably 3) drugs to which the organism has been demonstrated to be susceptible
- never introducing a single drug to a failing regimen

Prevention of drug resistance must be given high priority when treating tuberculosis.

Resistance to antituberculous medication should be considered when treating:

- foreign-born persons from TB endemic countries or Canadian-born individuals who have recently resided in a country with a high prevalence of TB
- anyone who has previously been treated for tuberculosis or received preventive therapy for latent TB infection
- contacts of an individual who is known to have (or thought to have) drug-resistant tuberculosis
- individuals who have cavitary pulmonary TB. These patients are thought to be more prone to drug resistance because they harbour greater numbers of bacilli
- anyone whose treatment is failing including:
  - patients who, while on treatment, remain smear-positive after the fifth month of treatment
  - patients who are initially smear-negative and become smear-positive after the second month of treatment

  } smear criteria

  - patients whose cultures remain positive after the fifth month of treatment

  } culture criteria

- rarely when one or more drugs are malabsorbed, or when all are absorbed but one or more drugs fails to penetrate the tuberculous lesion

Tuberculosis in Infants and Children

Tuberculosis in infants and children is more likely to manifest itself in life-threatening nonrespiratory forms such as central nervous system TB and disseminated TB. Therefore, it is critical to make an early diagnosis and commence treatment promptly.

- TB disease in infants and young children is rarely infectious, but almost always indicates a recent infection. Contact-investigation is aimed primarily at finding the source of the child's infection, and is called a "source case investigation."

- When dealing with children who have a cough and who are old enough to follow instructions, sputum collection should be attempted. However, because adequate sputum specimens are very difficult to collect from young children, gastric aspiration is often necessary (see Appendix 3.3).

Isolation of Cases of Tuberculosis

All patients who are admitted to active treatment facilities with suspected or confirmed infectious TB must immediately be isolated until proven to be non-infectious.

- If no isolation room meeting the criteria for respiratory isolation is available, arrangements should be made to transfer the patient to a facility that has rooms that meet such criteria. (For isolation room criteria, see "*Guidelines for Preventing the Transmission of Tuberculosis in Health Care Facilities and Other Institutional Settings*," pages 15-17.)

- If there is a delay in transfer, the patient must be kept in a separate room with the door closed, and anyone entering must wear a mask that is capable of filtering 95% of particles of 1 micron or larger.

- Any time the patient needs to leave the room, he or she must wear a mask.

Management of Recalcitrant Persons

Recalcitrant persons are defined as those individuals who are unwilling or unable to take appropriate precautions to prevent transmission of the diseases listed in Schedule 3 of the "*Communicable Diseases Regulation.*" This includes those with a diagnosis of active tuberculosis. They pose a risk to the health of the public.

A stepped intervention must be used in dealing with recalcitrant persons. For the purposes of ensuring adequate treatment of active tuberculosis and protecting the public, the following steps apply:

Step 1 If the client misses 2 consecutive doses of medication while on twice weekly high dose treatment (or the equivalent if on daily medication), notify the MOH or designate (TB co-ordinator) and Tuberculosis Control or the TB Clinic.

Step 2 The MOH or designate will attempt to determine if the patient is unwilling or unable to take the medication.

Step 3 Through negotiation with the patient, the MOH or designate will attempt to re-establish the medication regimen.

Step 4 If these steps fail, the MOH, in consultation with the Provincial TB Consultant will issue an order for detention under the *Public Health Act.*

These people require this extreme public health measure, not because of their medical condition per se, but because they pose a risk to public safety.

"Detention" could be anything from a supervised group home to a secure ward in a health care institution, and will be decided on an individual basis.