Adverse Reactions/Treatment Induced Side Effects

***Hepatitis* has been associated with INH use.** It is defined as liver enzyme (AST/ALT) levels to be 5 times the upper limit of normal without symptoms or 3 times the upper limit of normal with symptoms. If either of those parameters are met at any time during treatment, INH must be stopped and treating practitioner and OCPHO notified. Hepatitis occurs more frequently and is usually worse in elderly clients or those who consume alcohol daily. It can be reversible if the medication is stopped. Patients should be advised to watch for the following symptoms indicative of toxicity from the medication:

Table 8.5: Symptoms of Toxicity

INH or RMP induced side-effects
• Unexplained weight loss
• Fatigue
• Headache
• Dizziness
• Sleepiness or insomnia
• Nausea
• Anorexia
• Jaundice
• Gastrointestinal upset and/or abdominal pain
• Joint pain
• Bruising
• Rash

Patients taking INH or RMP who experience possible adverse reactions should be advised to consult their health care provider immediately. If they cannot contact their health care provider, they should stop INH or RMP until they can be seen and assessed.

Liver enzyme monitoring should occur on a monthly basis (or more frequently if deemed necessary by Internal Medicine or TB Specialist) for the following patients:

- Pre-existing liver disease
- Concomittant use of hepatotoxic drugs
- History of, or current ethanol abuse
- Prior INH hepatitis
- ≥35 years
- Pregnant or within 3 months of postpartum
- Anyone exhibiting symptoms

Risk of Drug Toxicity

The risk of INH toxicity must be weighed against the risk of developing active TB. The most significant side effect is INH hepatitis, which usually occurs within the first three to six months of administration. (http://www.rxmed.com/b.main/b2.pharmaceutical/b2.1.monographs/CPS-%20Monographs/CPS-%20(General%20Monographs-%20I)/ISONIAZID.html)

Early signs of liver toxicity are nausea, anorexia and an elevation of alanine transferase (ALT). The patient should be advised to contact his or her healthcare provider immediately should he/she have symptoms of liver failure such as jaundice, dark urine, light-coloured stools, bleeding tendency, pruritus, confusion, and coma.

Liver toxicity is rare under the age of 20, but complicates INH treatment in:

- 0.3% in the 20–34 age group
- 1 to 2% in the 35–49 age group
- 3% in the over 50 age group

Less serious, but more common side effects include erythematous itchy rash, lethargy, and arthralgia. Peripheral neuropathy is a more serious reaction.

Patients **35 years and older** receiving INH should be monitored with weekly symptom inquiry and ALT levels done monthly.

Patients in the age range of **15–34 years** of age should:

- Have an initial baseline ALT level measured
- Be rechecked one month after starting INH prophylaxis, and or/if side effects to anti TB meds is suspected
- Symptom inquiry weekly

Patients **15 years or younger** should have an ALT level measured at baseline and then only if signs and symptoms are indicative of liver toxicity.

INH is toxic in large doses and should be dispensed with great caution. If there is any risk of overdosing, purposeful or otherwise, discretion should be used when dispensing any amount of INH.

INH Drug Overdose

The antidote to an INH overdose is injectable pyridoxine (vitamin B6). It is a **must stock** item in all pharmacies.

Table 8.6: INH Drug Overdose

INH Drug Overdose
Below is the recommended antidote for INH overdose. Consult with your on-call physician/ pediatrician **IMMEDIATELY** and initiate treatment. Consider calling the **PADIS – Poison and Drug Information Services, Alberta and Northwest Territories contact: 1-800-332-1414.** Management of INH overdose includes supportive care focusing on patient's cardiovascular status, protecting the airway, abolishing seizure activity and correcting metabolic acidosis. As soon as an overdose of INH has been recognized (even in the absence of symptoms), Pyridoxine IV should be administered to prevent neurotoxic effects. The same dose of Pyridoxine (Vitamin B6) as the dose of INH ingested should be given intravenously. • For example, a child who has ingested 3.0g of INH should be given 3.0g of pyridoxine. If the dose is not known, Pyridoxine should be given intravenously in a dose of 5g in adults or 70mg/kg (maximum dose 5g) in children, at a rate of 1g every 2–3 minutes (CP, 2013). • This dose of pyridoxine should be repeated in two hours if the response to treatment has been incomplete. A total dose of 25g may be required in the first 12 hours. • A single dose of activated charcoal should be considered at a dose of 1g/kg. • Diazepam IV with addition of Phenobarbital or Propofol may be used in addition to Pyridoxine to treat convulsions. • Diazepam (Valium) should be given to control seizures (2mg by rectum for babies over the age of six months, or 5–10mg intravenously for older children and adults). Phenytoin (Dilantin) **should not** be given as it increases levels of INH. Please note INH also increases serum levels (Dart, 2004). • Once the patient is stabilized, refer to an internal medical specialist or pediatrician for further medical treatment.