

Toxic Update

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Acetaminophen Poisoning Practice Update

Acetaminophen (e.g. Tylenol®) is the most common pharmaceutical involved in unintentional and intentional poisonings in all age groups in B.C. There are over 250 products on the Canadian market which contain acetaminophen. Both acute and chronic acetaminophen overdose can cause potentially fatal liver toxicity due to accumulation of a toxic metabolite. Acetaminophen serum levels are used to guide the need for antidote therapy in acute overdoses. The antidote N-acetylcysteine (NAC, Mucomyst®) protects against liver injury.

Guidelines for the management of acetaminophen poisoning require regular updating to reflect current information. Two recent practice changes in the management of acetaminophen overdose are described below.

1. Raising the Treatment Threshold for Healthy Children

Healthy children ages 1-6 years who have *acutely* ingested < 200 mg/kg acetaminophen do not require blood level monitoring or treatment. Previously the recommended threshold was 150 mg/kg. Evidence suggests that healthy children between 1-6 years of age are less susceptible to toxicity from *acute* acetaminophen poisoning than adults. There are no confirmed deaths from *acute* acetaminophen poisoning in children < 6 years, and only two well documented cases of severe toxicity, both of which involved massive overdoses. All reported pediatric acetaminophen fatalities have involved *chronic* excessive use of the drug. Compared to older children and adults, healthy young children have a relatively larger hepatic mass, on an organ-weight to total body-weight ratio. This may result in both increased elimination and increased detoxification of the toxic metabolite, protecting them from hepatotoxicity.

Children 1-6 years of age who have increased risk for developing hepatotoxicity require treatment at a lower threshold than healthy children (Table 1). Treatment thresholds for adults, youth and children outside the 1-6 year age range remain unchanged (Table 1).

2. Delayed Release Acetaminophen Products: Risk Assessment

Tylenol 8 Hour Extended Relief Caplets® and Tylenol Arthritis Pain Extended Relief Caplets® are now available in Canada. These 650 mg tablets have an immediate-release outer layer and a delayed release inner core. Most of the acetaminophen dose is released from the tablet matrix within 5 hours, but peak acetaminophen serum concentrations may be delayed 8 hours or longer following ingestion, especially with an overdose. Table 1 includes recommendations for when to draw serum levels after overdose of delayed release acetaminophen products.

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Guidelines for the treatment of acetaminophen poisoning and use of N-acetylcysteine can be found in the BC Drug and Poison Information Centre's (DPIC) Poison Management Manual 4th edition, available in most BC hospital emergency departments or by contacting the poison information specialists and medical toxicologists at DPIC 24 hours/ day.

Table 1. Indications for Serum Acetaminophen Levels

Bloodwork for an acetaminophen level should be drawn ≥ 4 hours after acetaminophen ingestion (or on admission, if time of ingestion is unknown) in the following situations:

Intentional, acute overdose

- All cases of intentional overdose (whether or not acetaminophen is stated in history). Patients with an intentional overdose may be unable or unwilling to provide an accurate history of the quantity ingested or the time of ingestion; serum levels confirm presence of acetaminophen and magnitude of exposure.

Unintentional, acute overdose

- All cases where: *history may be uncertain, or the maximum dose is uncertain* or the ingested acetaminophen dose is greater than the amount listed below by age.

Age	Acetaminophen Level Indicated if Ingested Dose is:
< 12 months	> 150 mg/kg
1-6 years, healthy	> 200 mg/kg
1-6 years, at increased risk*	> 150 mg/kg
7-12 years	> 150 mg/kg
Youth & Adults	> 7.5 g, or > 150 mg/kg if patient is < 50 kg

*Increased risk for hepatic toxicity if: acute febrile illness, poor nutritional status, chronic use of CYP450 enzyme-inducing drugs such as rifampin or phenobarbital, or use of acetaminophen within last 24 hours.

Delayed release products, acute overdose

- Draw the first serum level at ≥ 4 hours post ingestion and plot the value on the nomogram for acetaminophen poisoning.
 - If the first level is *above* the treatment line, begin N-acetylcysteine. A repeat level is not needed.
 - If the first level is *below* the treatment line, repeat the acetaminophen level at 8-10 hours post-ingestion (or 4-6 hours after the first level). If the second level crosses into the treatment range, begin N-acetylcysteine. If the second level is below the treatment line, there is no need for N-acetylcysteine or additional acetaminophen serum levels.

Late Presentation, acute overdose

- Patients who present > 16 hours post-ingestion are at a higher risk for developing hepatotoxicity and require an individualized approach to monitoring levels and antidote treatment. Consult with DPIC for management guidelines.

Chronic overdose

- Acetaminophen serum level *may* be useful for assessing the magnitude of a chronic or repeated acetaminophen overdose; however, the level cannot be accurately plotted on the nomogram for acetaminophen poisoning. Treatment decisions are based on history, clinical status, hepatic function and serum acetaminophen levels.
- Consult with DPIC for management guidelines.

Selected References:

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Delayed Release: Bizovi KE, et al. Ann Emerg Med 1996;28:549-51. Cetaruk EW, et al. Ann Emerg Med 1997;30:104-8. Douglas DR, et al. Acad Emerg Med 1996;3:740-44. Stork CM, et al. Clin Toxicol 1996;34:157-62. Vassallo S. Ann Int Med 1996;125:940.