Guideline: Paediatric Paracetamol Poisoning

Purpose

This guideline applies to all children under 15 years of age with a history of paracetamol poisoning. It aims to guide the assessment and treatment paracetamol poisoning.

It is applicable to Kidz First Emergency Department, clinical wards or in the Intensive Care Unit.

Responsibility

This guideline applies to medical staff with the responsibility of managing the paediatric patient with paracetamol poisoning.

Guideline

Background

Paracetamol is the most common single agent involved in poisonous ingestions in young children. While there is potential for serious liver damage if a large dose is ingested, in practice, it is rare for a child to achieve toxic blood levels by ingesting paracetamol elixir (syrup).

Paracetamol is also commonly involved (often mixed with other drugs) in episodes of intentional self-harm by teenagers. In this situation, relatively large amounts of paracetamol may have been ingested and this may not be disclosed in the history.

It is much more likely that a toxic level will be achieved under these circumstances.

Resuscitation

Immediate threats to airway, breathing and circulation are RARE in isolated paracetamol poisoning. Resuscitation should take priority over decontamination or antidote administration.

Airway

- Airway adjuncts and intubation as required. Consider intubation as per poisoning guideline.

Breathing

- Oxygen and ventilation if required.

Circulation

- Support perfusion as needed.

Disability

- Treatment of hypoglycaemia.
- Maintain normothermia.

Risk Assessment

An accurate history of:

- The maximum possible dose and work out the dose per kg.
- The time of ingestion.
- Possible other drugs ingested.
- Risk factors that may lead to increased hepatotoxicity.

Consider the worse case scenario, that all the tablets has been ingested, that no significant spillage/vomiting has occurred and that one child has taken all the medication if multiple children were present. Also, assume the earliest ingestion time.

Supportive Care

In rare situations of single agent paracetamol ingestion, massive ingestions may be associated with early decreased level of consciousness and lactic acidosis. Good supportive care around:

- Observation.
- Hydration.
- Correction of hypoglycaemia.

Decontamination

There is NO role in paracetamol elixir ingestions. Most of the drug is absorbed within 15 minutes of elixir ingestion and it is very unlikely that a child will receive any intervention within this time frame.

Decontamination with activated charcoal may be considered if all of the following criteria are met:

- Paracetamol capsule or tablet is the ingestant.
- If the dose ingested is >200 mg/kg.
- The child presents within 1 hour of ingestion.
- There is no co-ingestant that may lead to decreasing GCS or seizures.

Paracetamol levels

In single acute ingestion (<8 hours from ingestion):

Maximum possible dose >/= 200mg/kg OR >10g OR when dose is unknown or uncertain:

- This should include young people who present with intentional self-harm in the form of ingestions.
- Ingestion of tablets/capsules: Serum paracetamol measurement at 4 hours post ingestion.
- Ingestion of paracetamol elixir: Serum paracetamol measurement at 2 hours post ingestion (the 2 hour level should only be relied upon in isolated paracetamol ingestions in WELL children).

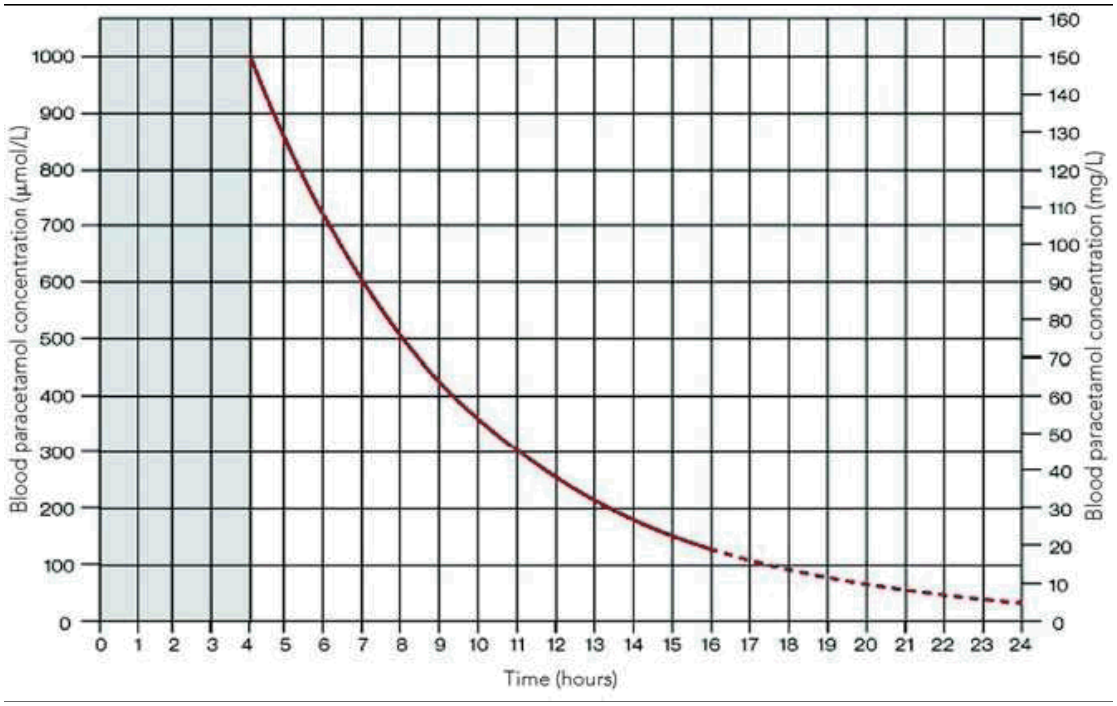
- If the level is below 500 µmol/L (0.5 mmol/L) at 2 hours then it is safe to discharge the child with no treatment.
- If the level is above 500 µmol/L (0.5 mmol/L) at 2 hours, a further level should be measured at 4 hours.

<u>If the maximum possible dose is <200 mg/kg OR total ingested dose is 10 g (whichever is lower):</u>
No intervention or drug level necessary.
Younger children appear to be less susceptible to hepatotoxicity.

The following situations require consultation with senior staff: (Appendix 2):

- Chronic/repeated ingestions.
- Late presentation >8 hours post ingestion.
- Unknown time of ingestion.
- Symptoms/signs of toxicity: Anorexia, nausea, vomiting, RUQ tenderness.
- Chronic illness-known liver disease, malnutrition.

Nomogram



CAUTION:

Ensure the correct units are used when applying plasma paracetamol results to the treatment nomogram. DO NOT confuse mmol/L with µmol/L, nor traditional units (mg/L) with SI units (µmol/L).

CMDHB laboratory reports their levels in mmol/L.

Use the left vertical scale on the nomogram.

Antidote-N-acetylcysteine (NAC)

- Treatment with NAC is indicated for those children with levels above the threshold shown on the nomogram.
- NAC is 100% effective at preventing hepatotoxicity if started within 8 hours of ingestion.
- Toxicity may still be reduced if it is started up to 24 hours after ingestion.
- Delays in treatment with NAC can be associated with worse outcomes. Therefore treatment should be started immediately in children who present >8 hours after a significant ingestion or who are symptomatic of toxicity. Their further management should be discussed with senior staff.
- Care should be taken with infusion volumes (see infusion tables). Life threatening hyponatraemia has resulted in inappropriate use of large volumes of 5% dextrose. Despite product information, 0.45% NaCL + 2.5% dextrose or 0.9% NaCl can be used instead of 5% dextrose as a diluent if hypoglycaemia is not present or anticipated.

Allergic reactions (flushing, urticaria, wheeze, angiodema, and hypotension)/fever have been commonly reported but are rarely severe. They are dose dependant and usually occur during the rapid administration of Phase 1.

Minor symptoms (flushing, urticaria) can be managed with hydrocortisone/ promethazine and slowing (not stopping) the phase 1 infusion such that it is completed over 1 hour.

More serious symptoms (angioedema, wheeze, hypotension) require the infusion to be ceased and symptoms managed appropriately. One hour after symptoms have abated, the infusion can be restarted, with caution, at the slower rate i.e. over 1 hour.

N-acetylcysteine therapy should NOT be stopped early even if a subsequent blood paracetamol level shows a result now below the line predicting toxicity.

NAC infusion guideline (use online NAC Calculator for all patients)

For <20 kg:

Three stage 20 hour infusion for children **<20 kg:**

1. 150 mg/kg NAC*:* diluted in 3 ml/kg 0.45% NaCl+2.5% dextrose or 5% dextrose, infused over 15 minutes (can be given over 60 minutes).

2. 50 mg/kg NAC*:* diluted in 7 ml/kg 0.45% NaCl+2.5% dextrose or 5% dextrose, infused over next 4 hours.

3. 100 mg/kg NAC: diluted in 14 ml/kg0.45% NaCl+2.5% dextrose or 5% dextrose infused over the next 16 hours.

For 20-50 kg:

Three stage 20 hour infusion for children **20-50 kg:**

1. 150 mg/kg NAC*:* diluted in 100ml 0.45% NaCl+2.5% dextrose or 5% dextrose*,* infused over 15 minutes (can be given over 60 minutes).

2. 50 mg/kg NAC*:* diluted in 250 ml 0.45% NaCl+2.5% dextrose or 5% dextrose, infused over next 4 hours.

3. 100 mg/kg NAC: diluted in 500 ml 0.45% NaCl+2.5% dextrose or 5% dextrose*,* infused over the next 16 hours.

For >50 kg:

Three stage 20 hour infusions:

1. 150 mg/kg NAC diluted in 200 ml 5% dextrose or 0.45% NaCL +2.5% dextrose infused over 60 minutes.

2. 50 mg/kg NAC diluted in 500 ml 5% dextrose or 0.45% NaCL +2.5% dextrose infused over next 4 hours.

3. 100 mg/kg NAC diluted in 1000 ml 5% dextrose or 0.45% NaCL +2.5% dextrose infused over the next 16 hours.

Clinical features of NAC adverse reaction:

Wheeze, rash, mild hypotension.

Usually during the initial 2 stages.

More likely to be severe in patients with asthma.

Management.

Supportive.

Stop or slow the infusion, then restart after treatment.

Treat with antihistamines and prednisone.

Risk factors for Paracetamol Toxicity

- Use of P450 2E1 inducing drugs eg phenobarbitone, carbamazepine.
- Induction of the P450 2E1 iso-enzyme leads to increased conversion of paracetamol to its toxic metabolite NAPQI.
- Malnourishment, fasting, acute or chronic illness.
- Recent significant fasting or illness, such as eating disorders (eg. Anorexia nervosa), or chronic illness such as HIV/AIDS may reduce intracellular glutathione levels increasing toxicity of NAPQI.
- Chronic alcoholism.

Alcohol consumption at these levels may both induce iso-enzyme P450 2E1 and reduce intracellular glutathione stores.

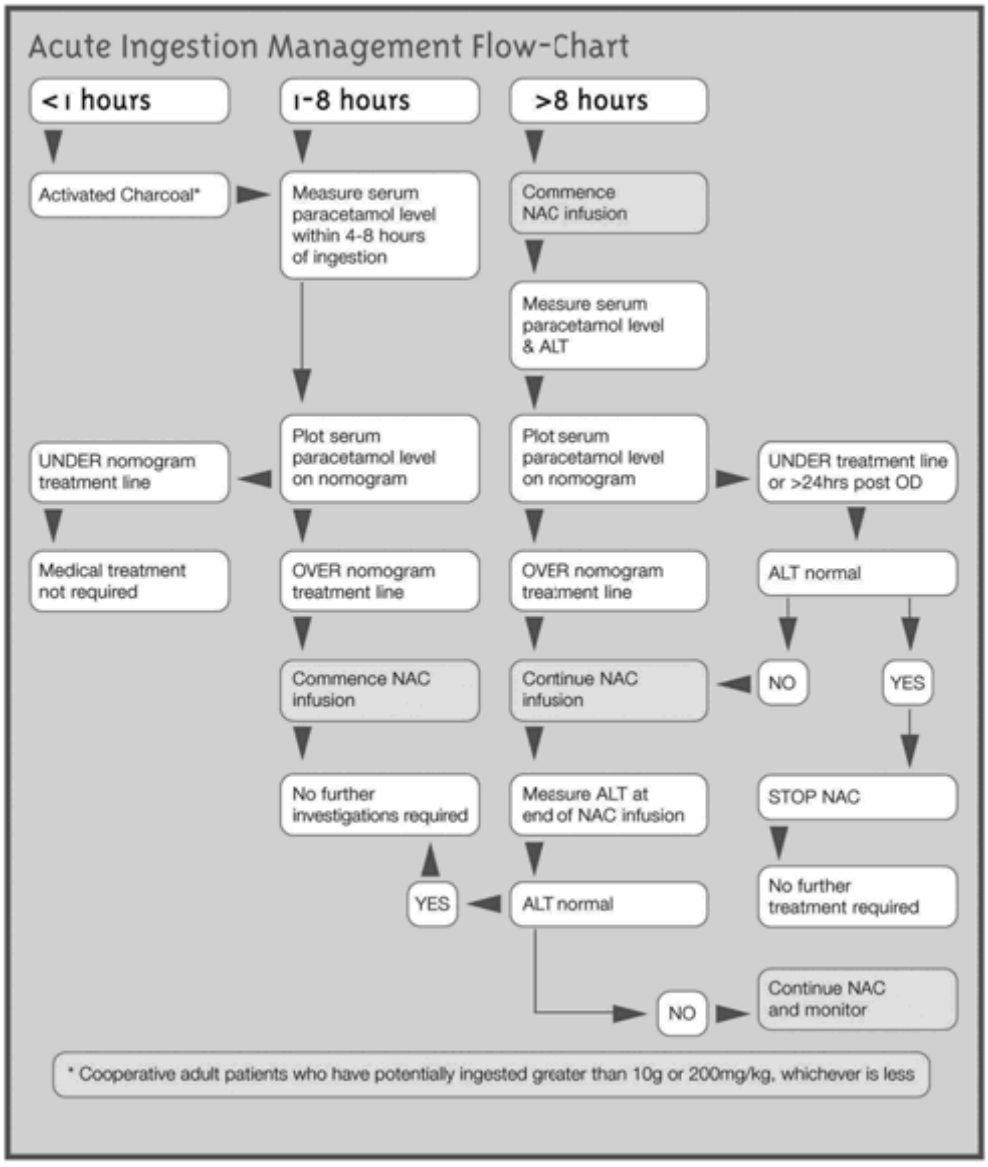
Gilbert's syndrome, Crigler-Najjar syndrome.

Individuals suffering these genetic defects may be at greater risk of paracetamol toxicity.

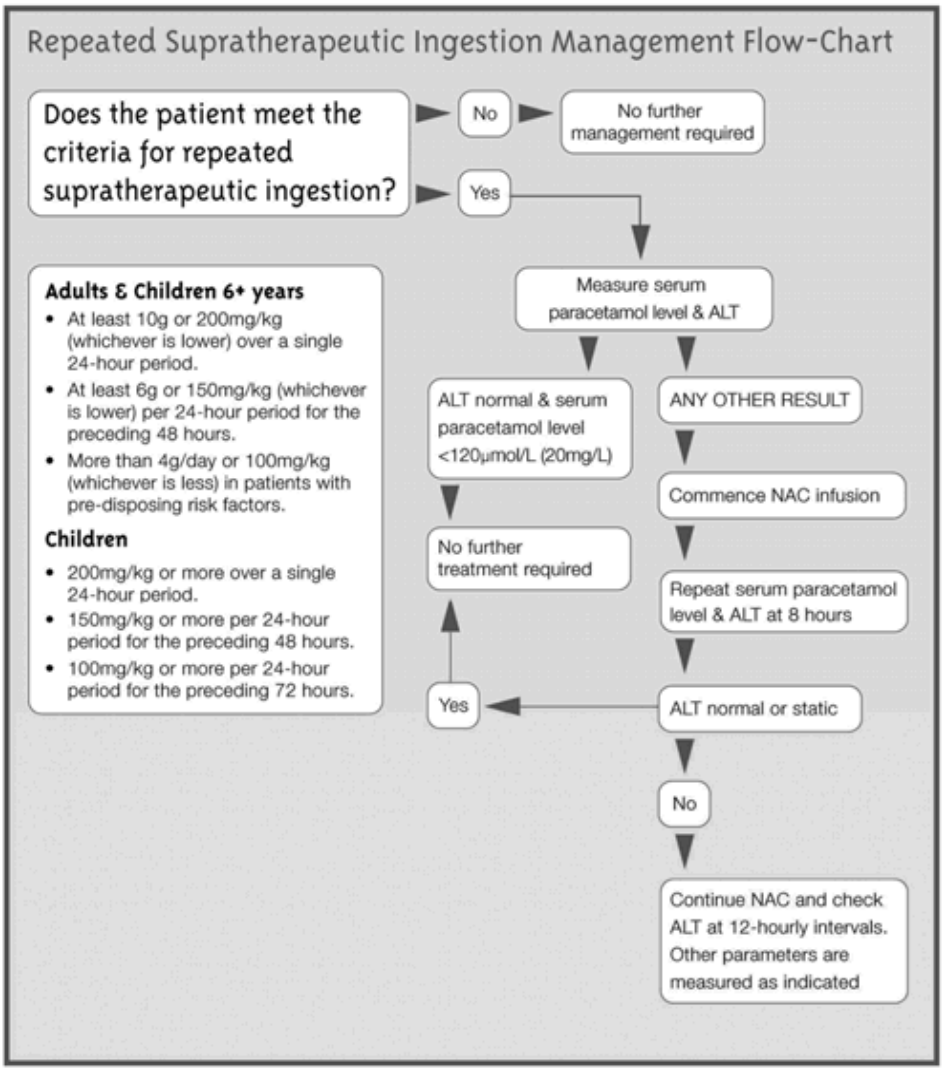
Disposition

- The vast majority of single paediatric accidental ingestions will require no treatment and will be discharged from the emergency department.
- Prior to discharge parental education re: safe storage of medication, child supervision etc should be undertaken.
- Children <15 who require NAC should be admitted under the paediatric service as children should spend <12 hours ideally in the Paediatric Short stay area.
- Adolescents 15-17 can remain in ED SSP or ED SSU adults under Emergency Medicine.
- In the case of intentional overdose in an older child or adolescent, psychiatric review prior to discharge is mandatory.
- If NAI is a possibility involve the appropriate services.

Appendix 1-Acute Ingestion Management



Appendix 2: Repeated supratherapeutic ingestion management



In repeated supratherapeutic ingestion:
In 0-6 years:

- >/=200 mg/kg over a single 24 hour period.
- >/=150 mg/kg per 24 hour period over the preceding 48 hours.
- >/=100 mg/kg per 24 hour period over the preceding 72 hours.

In age>6 years:

- >200 mg/kg or >10 g (whichever is lower) over a single 24 hour period.
- >150 mg/kg or >6 g (whichever is lower) over a single 24 hour period over the preceding 48 hours.
- >100 mg/kg or >4 g (whichever is lower) over a single 24 hour period in patients with predisposing risk factors.

These children require a paracetamol level and an ALT level. If ALT normal and paracetamol level <120 □mol/L, these children are safe for discharge with no further treatment required.

Appendix 3: Timing of investigations

Investigations according to time from paracetamol ingestion to NAC treatment

	Time after Paracetamol ingestion		
Test	1-8 hours	8-24 hours	24+ hours
Serum Paracetamol	At 4 hours or as soon after as possible	On admission	On admission
ALT/AST	---	On admission AND at end of NAC infusion	On admission
INR	---	---	On admission
Creatinine and urea	---	---	On admission
Glucose	---	---	On admission
Arterial blood gas	---	---	On admission

References:

1. Daly FS, Fountain JS, Murray L et al. Guidelines for the management of paracetamol poisoning in Australia and New Zealand-explanation and elaboration. MJA 2008;188 (5); 296-301
2. Chan C, Shepherd M. Profile of Paediatric Paracetamol Poisoning.
3. Prescott LF, Illingworth RN, Critchley JA et al. Intravenous N-acetylcysteine:the treatment of choice for paracetamol poisoning. Br Med J. 1979;2:1097-1100
4. Bailey B, McGuigan M. Management of anaphylactoid reactions to intravenous N-acetylcysteine. Ann Emerg Med 1998;31(6), 710-715

Definitions

Terms and abbreviations used in this document are described below:

Term/Abbreviation	Description

Associated Documents

Other documents relevant to this guideline are listed below:

NZ Legislation	None
CMDHB Clinical Board Policies	None
NZ Standards	None
Organisational Procedures or Policies	None
Other related documents	Starship Hospital Guidelines Paracetamol Poisoning. Guidelines for the management of paracetamol poisoning in Australia and New Zealand.