

PARACETAMOL POISONING

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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

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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 (see below)

Consider the worse case scenario, e.g. that all the tablets have been ingested, that no significant spillage/vomiting has occurred and that one child has taken all the medication if multiple children were present. Also consider the worst case scenario with regard to the ingestion time, the possibility of an earlier ingestion time may place a patient above the treatment line, the possibility of a later ingestion time might require another paracetamol level to be measured.

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 for decontamination 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 is only indicated if **all** of the following criteria is 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 \geq 200 mg/kg OR >10 g OR when dose is unknown or uncertain:

This includes most young people who present with ingestions as part of an episode of intentional self harm, unless the presence of paracetamol can be clearly excluded on history.

Tablets or capsules ingested: measure serum paracetamol at 4 hours post ingestion.

Elixir ingested: measure serum paracetamol 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 $\mu\text{mol/L}$ at 2 hours then it is safe to discharge the child with no treatment.
- If the level is above 500 $\mu\text{mol/L}$ at 2 hours, a further level should be measured at 4 hours.

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If the maximum possible dose is <200 mg/kg AND total ingested dose is <10 g :

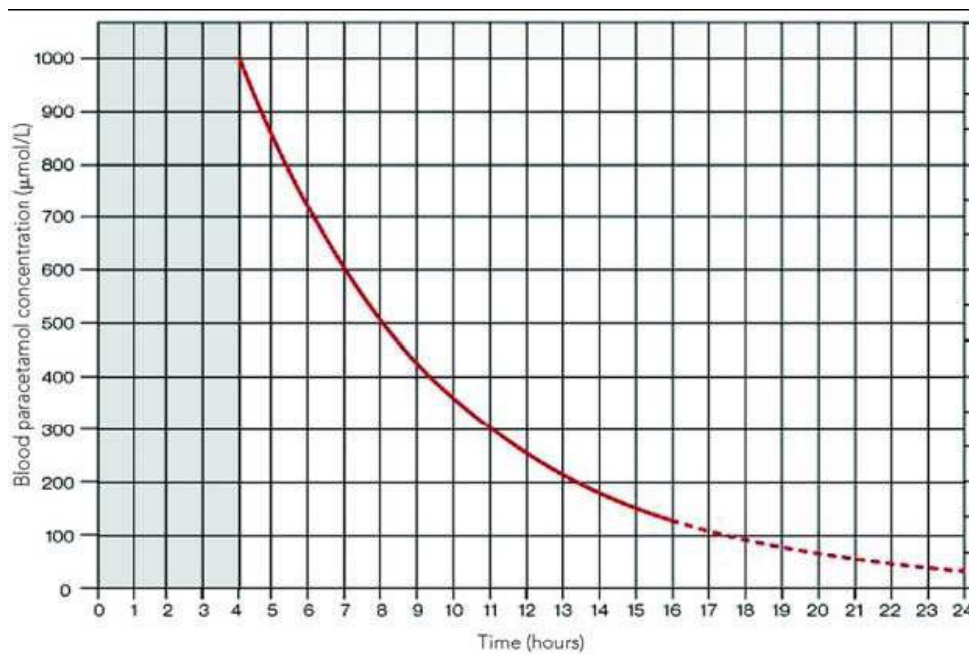
No intervention or drug level necessary

Younger children appear to be less susceptible to hepatotoxicity

The following situations require consultation with senior staff: (see 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



MJA 2008;188 (5); 296-301.

CAUTION:

Ensure the correct units are used when applying plasma paracetamol results to the treatment nomogram. DO NOT confuse mmol/L with μ mol/L, or traditional units (mg/L) with SI units (μ mol/L).

ADHB laboratories report serum paracetamol levels as μ mol/L.

If mg/L used please refer to: 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.

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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 must be taken with infusion volumes (see Table) as life threatening hyponatraemia has resulted from the use of inappropriate volumes of 5% Dextrose.

Allergic reactions (flushing, urticaria, wheeze, angioedema, 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 (see Anaphylaxis guideline). 1 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.

Table - NAC infusion guide

Three stage 20 hour infusion for children <20kg		
1. 150mg/kg NAC:	diluted in 3ml/kg	5% dextrose,infused over 15min
2. 50mg/kg NAC:	diluted in 7ml/kg	5% dextrose,infused over next 4 hours
3. 100mg/kg NAC:	diluted in 14ml/kg	5% dextrose,infused over the next 16h
Three stage 20 hour infusion for children 20kg to 50 kg		
1. 150mg/kg NAC:	diluted in 100ml	5% dextrose,infused over 15min
2. 50mg/kg NAC:	diluted in 250ml	5% dextrose ,infused over next 4 hours
3. 100mg/kg NAC:	diluted in 500ml	5% dextrose,infused over the next 16
Three stage 20 hour infusions for children >50kg		
1. 150mg/kg NAC:	diluted in 200ml	5% dextrose,infused over 15-60 min
2. 50mg/kg NAC:	diluted in 500ml	5% dextrose ,infused over next 4 hours
3. 100mg/kg NAC:	diluted in 1000ml	5% dextrose,infused over the next 16h

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Timing of investigations

Recommended investigations according to time from paracetamol ingestion to N-acetylcysteine treatment

Test	1-8 hours	8-24 hours	24+ hours
Serum paracetamol	At 4 hours or as soon thereafter as possible	On admission	On admission
ALT/AST	—	On admission and at the END of N-acetylcysteine infusion	On admission
INR	—	—	On admission
Creatinine and urea	—	—	On admission
Glucose	—	—	On admission
Arterial blood gas	—	—	On admission

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

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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

In the case of intentional overdose in an older child or adolescent psychiatric review prior to discharge is mandatory

If Non-Accidental Injury is a possibility involve the appropriate services.

Prevention

The prevention of unintentional poisoning, including paracetamol, should be promoted throughout the community.

Child resistant closures and packaging have been shown to reduce the incidence of childhood poisoning.

Other measures that are likely to be successful include:

- Prescribing and dispensing smaller volumes of elixir.

- Educating families about safe storage of medications, out of reach of children with a child resistant latch.

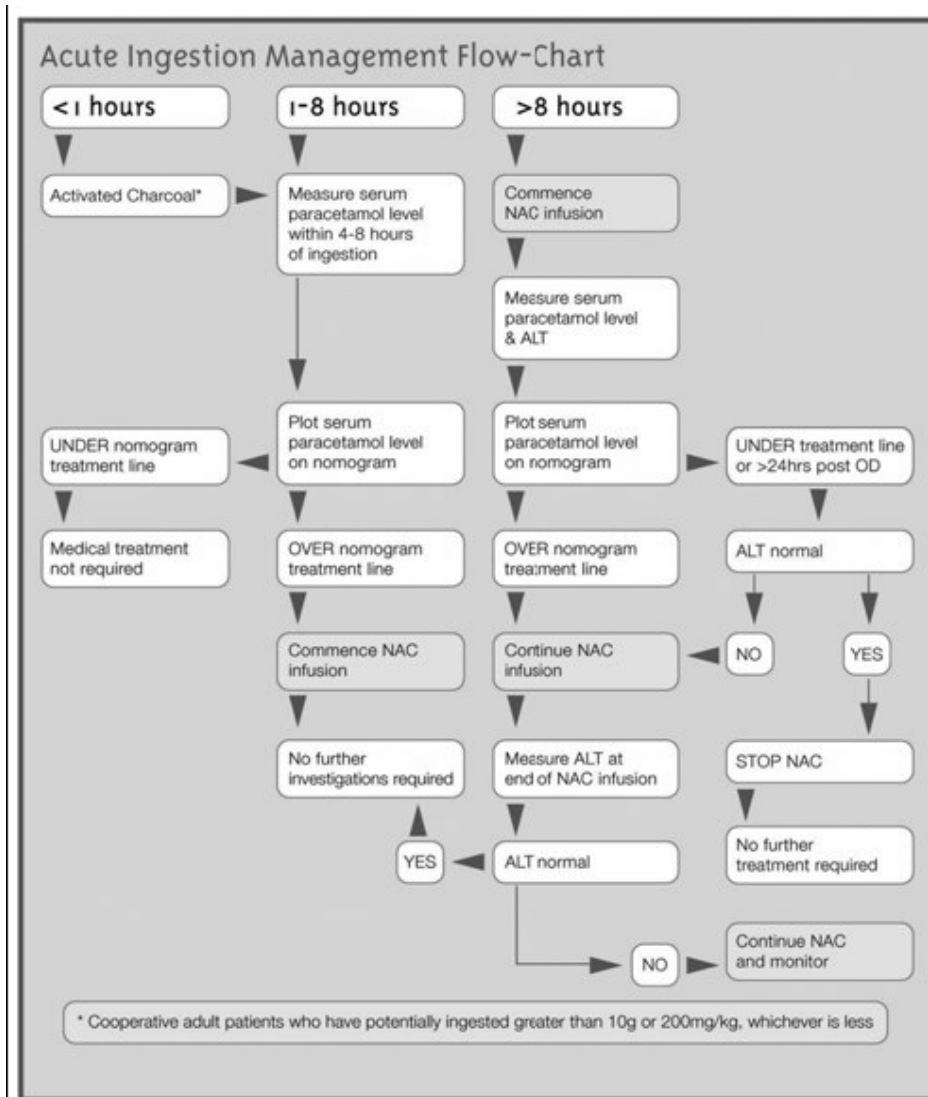
- A home visiting program to target this advice,

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

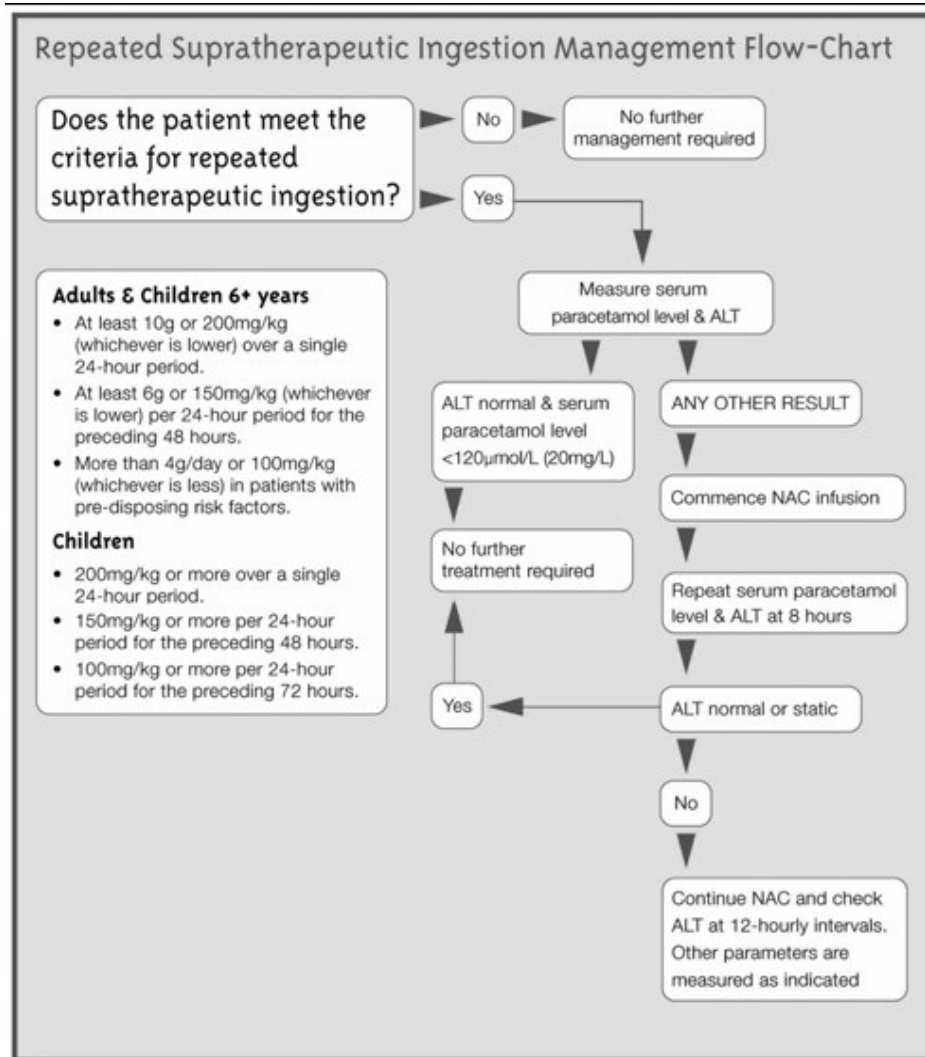
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Appendix 1: Acute Ingestion Management



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Appendix 2: Repeated supratherapeutic ingestion management



Repeated supratherapeutic ingestion:

Age 0-6 years,

- $\geq 200\text{mg/kg}$ over a single 24 hour period
- $\geq 150\text{ mg/kg}$ per 24 hour period over the preceeding 48 hours
- $\geq 100\text{ mg/kg}$ per 24 hour period over the preceeding 72 hours

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Age > 6 years.

- >200mg/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 preceeding 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 µmol/L, these children are safe for discharge with no further treatment required.

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