PARACETAMOL OVERDOSE - ASSESSMENT AND MANAGEMENT

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Paracetamol overdose may be initially asymptomatic and early and thorough assessment is required.
- Discuss all cases with the NSW Poisons Information Centre (13 11 26), including prior to ceasing acetylcysteine. The Poisons Information Centre number can be dialled anywhere in Australia and can connect you to a clinical toxicologist if clinically indicated.
- Check laboratory result matches the correct units on the nomogram (now in mg/L; previously micromol/L).
- Liquid paracetamol ingestions in children <6 years may have a paracetamol level taken at 2 hours post-ingestion or at time of presentation (if >2 hours post-ingestion). If the paracetamol level is >100 mg/L at 2-4 hours then a repeat level is recommended at 4 hours post-ingestion.
- All modified-release paracetamol ingestion >10 grams or > 200 mg/kg (whichever is less) are to receive at least the full course of acetylcysteine.
- Anaphylactoid reactions to acetylcysteine are rare with the two-bag infusion regimen that is currently used, but usually occur in the first few hours of infusion.
- All deliberate ingestions with self-harm intent (usually in adolescents) require mental health assessment.
- Intravenous paracetamol medication errors are not dealt with in these guidelines, as the treatment thresholds are different from oral ingestion. The Poisons Information Centre or a Clinical Toxicologist should be contacted regarding these cases.
- Authorised Emergency Department nurses are to use Emergency Care Assessment and Treatment (ECAT) protocols.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
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CHANGE SUMMARY

- Due for mandatory review.
- This document is an update and replaces the current SCHN Paracetamol overdose guidelines. Recommend to read the entire document as there are amendments made through out.
- For a liquid paracetamol ingestion where a paracetamol is taken at 2-4 hours, if the level is >100 mg/L a repeat level is recommended at 4 hours post-ingestion. Acetylcysteine is commenced if the 4 h level is above 150 mg/L. The patient can be discharged if the initial paracetamol concentration is <100 mg/L

READ ACKNOWLEDGEMENT

- All clinical staff (medical officers & nurses) working in ED should read and acknowledge they understand the contents of this document.
- Clinical staff working in NETS & ICUs should be aware of this document.
- NSW Poisons Information Centre staff should read and acknowledge they understand the contents of this document.
- Pharmacists should be aware of this document.

TABLE OF CONTENTS

Introduction....4
Sources of Management Advice....4
Forms of Overdose....4
Clinical Presentation....5
Important Medical History....5
Risk assessment....5
Investigations....6
Recommended investigations according to time from paracetamol ingestion....6
Management algorithm for identified overdose....7
Algorithm for management of acute overdose....7
Paediatric (<6 years) liquid paracetamol ingestion....8
Modified-release paracetamol preparations....8
Paracetamol Treatment Nomogram....9
Indications for acetylcysteine in paracetamol overdose:....10
Management algorithm for repeated supra-therapeutic overdose....11
Infusion of Acetylcysteine....12
Acetylcysteine dosage regimen:....12
Ordering Acetylcysteine on eMeds/eMM....13
Side effects of acetylcysteine therapy:....13
Clinical Management....13
Nursing Observations required during acetylcysteine infusion:....14
References....15

Introduction

Paracetamol is available in several different forms, such as syrup or tablets, and as a single medication or in combination with other medications in cold and flu preparations. Refer to e-MIMS for a more complete list of paracetamol containing products.

In young children the most common form of overdose is accidental ingestion. Chronic, repetitive, supra-therapeutic doses can also result in toxicity. In the adolescent group overdose may be related to intentional self-harm and polypharmacy overdose. These patients should have their mental health needs addressed as well as the medical aspects of overdose.

It is important to recognise that a paracetamol overdose is treatable, and the toxic effects may be avoided or reduced by administration of an antidote - acetylcysteine.

To be most effective in protecting against liver damage, acetylcysteine therapy should be commenced within 8 hours of paracetamol ingestion, but acetylcysteine is still effective in late presenting patients at any time.

Sources of Management Advice

- Emergency Department senior clinicians
- Poisons Information Centre (13 11 26), who can connect you to a clinical toxicologist if needed.
- Local toxicology service –for SCH please contact 131126 to be transferred to the Toxicology team (SEATS – South-East Area Toxicology Service)
- Consult NETS (1300 362 500) per local processes for children requiring critical care input, or who are unable to be managed at the local facility for escalation of care.

Forms of Overdose

1. **Acute poisoning:** where a patient self-harms by taking a single large dose of paracetamol, or staggered overdose (several ingestions over greater than 8 hours, but usually less than 24 hours).
2. **Repeated supratherapeutic ingestion:** when patients ingest excessive paracetamol for a therapeutic purpose (e.g. pain, viral illness) or ingest therapeutic doses of paracetamol and have symptoms of acute liver injury (e.g. abdominal pain, nausea and vomiting). Diagnosis is somewhat more difficult and a strong clinical suspicion and careful history and measurement of ALT/AST and paracetamol concentration is key.
3. **Iatrogenic poisoning or therapeutic error:** usually with intravenous (IV) paracetamol where dosing errors are often 10-fold.

Clinical Presentation

Initial assessment, as with all overdoses, should focus on ABC - airway patency and protection, ensuring adequate ventilation and circulatory status - as the patient may have co-ingestion of other medication which cause acute life-threatening signs.

In the acute stages of paracetamol overdose there are often no symptoms, or only mild gastrointestinal effects (vomiting). Patients with delayed presentations, many hours or days after overdose, may have symptoms related to hepatotoxicity (right upper abdominal pain/ tenderness, nausea and vomiting) or liver failure (hypoglycaemia, jaundice, confusion) that develop 3-4 days after the acute ingestion. The antidote (acetylcysteine) can still be effective at this stage.

Important Medical History

- It is important to obtain a complete medical history.
- Check paracetamol doses administered in the previous 24-72 hours
- Is the overdose a single dose, or repetitive (staggered) doses?
- Is the paracetamol a liquid or solid (capsules or tablets) preparation, or an IV injection?
- Is the paracetamol immediate-release or modified release?
- What is the estimated dose based on body weight (mg/kg) that has been ingested?
- What is the exact time of the overdose?
- Are there any other co-ingested medicines?
- Are there child safety issues (non-accidental poisoning or neglect) that need to be addressed?
- Does the patient have any risk factor that increases their risk of liver damage at lower doses, such as malnutrition, neonates, acute liver failure?

Risk assessment

Below is a table[1] which gives the dose of paracetamol that may result in acute paracetamol toxicity. Calculation of dose is based on actual body weight.

Paracetamol oral doses that may be associated with liver injury	
	Adults and children of any age
Acute single ingestion	greater than 200 mg/kg or 10 g **(whichever is less)**
Repeated supratherapeutic ingestion	greater than 200 mg/kg or 10 g **(whichever is less)** over a single 24 hour period
	greater than 300 mg/kg or 12 g **(whichever is less)** over a single 48 hour period
	greater than a daily therapeutic dose per day for more than 48 hours in patients who also have abdominal pain or nausea or vomiting.

Note: Intravenous paracetamol medication errors are not dealt with in these guidelines, as the treatment thresholds are different from oral ingestion. The Poisons Information Centre should be contacted regarding these cases.

Investigations

This table[2] indicates the type and timing of investigations needed:

Recommended investigations according to time from paracetamol ingestion

	Time after paracetamol ingestion		
Test	**1 – 8 hours**	**8 – 24 hours**	**Greater than 24 hours**
Serum paracetamol	**If liquid paracetamol ingestion** in <6 years of age, check at 2 hours or as soon thereafter as possible **If immediate release tablet or capsule paracetamol ingestion** check at 4 hours or as soon thereafter as possible **If modified-release (MR) tablet paracetamol ingestion** check at 4 hours post ingestion or as soon thereafter as possible, and again 4 hours later (e.g. at 4 and 8 hours post-ingestion) **IV paracetamol overdose** (usually iatrogenic error) discuss with the Poisons Information Centre as soon as it is discovered. **AND** prior to acetylcysteine cessation for all modified release ingestions, and those with an initial paracetamol concentration greater than double the nomogram line	On admission **AND** prior to acetylcysteine cessation for all modified release ingestions, and those with an initial paracetamol concentration greater than double the nomogram line	On admission **AND** prior to acetylcysteine cessation for all modified release ingestions, and those with an initial paracetamol concentration greater than double the nomogram line
Transaminases (ALT/AST)	On admission **AND** prior to acetylcysteine cessation	On admission **AND** prior to acetylcysteine cessation	On admission **AND** prior to acetylcysteine cessation
INR/prothrombin time	▬	▬	On admission if abnormal LFT
Creatinine and Urea	▬	▬	On admission if abnormal LFT
Glucose	▬	▬	On admission if abnormal LFT
Venous blood gas	▬	▬	On admission if abnormal LFT

Note: Those with acute liver injury should have 12 hourly LFT's, INR, EUC, VBG, BSL or more frequently if clinically indicated.

ALT = alanine aminotransferase, **AST** = aspartate aminotransferase, ▬ = test not required, **INR** = international normalised ratio

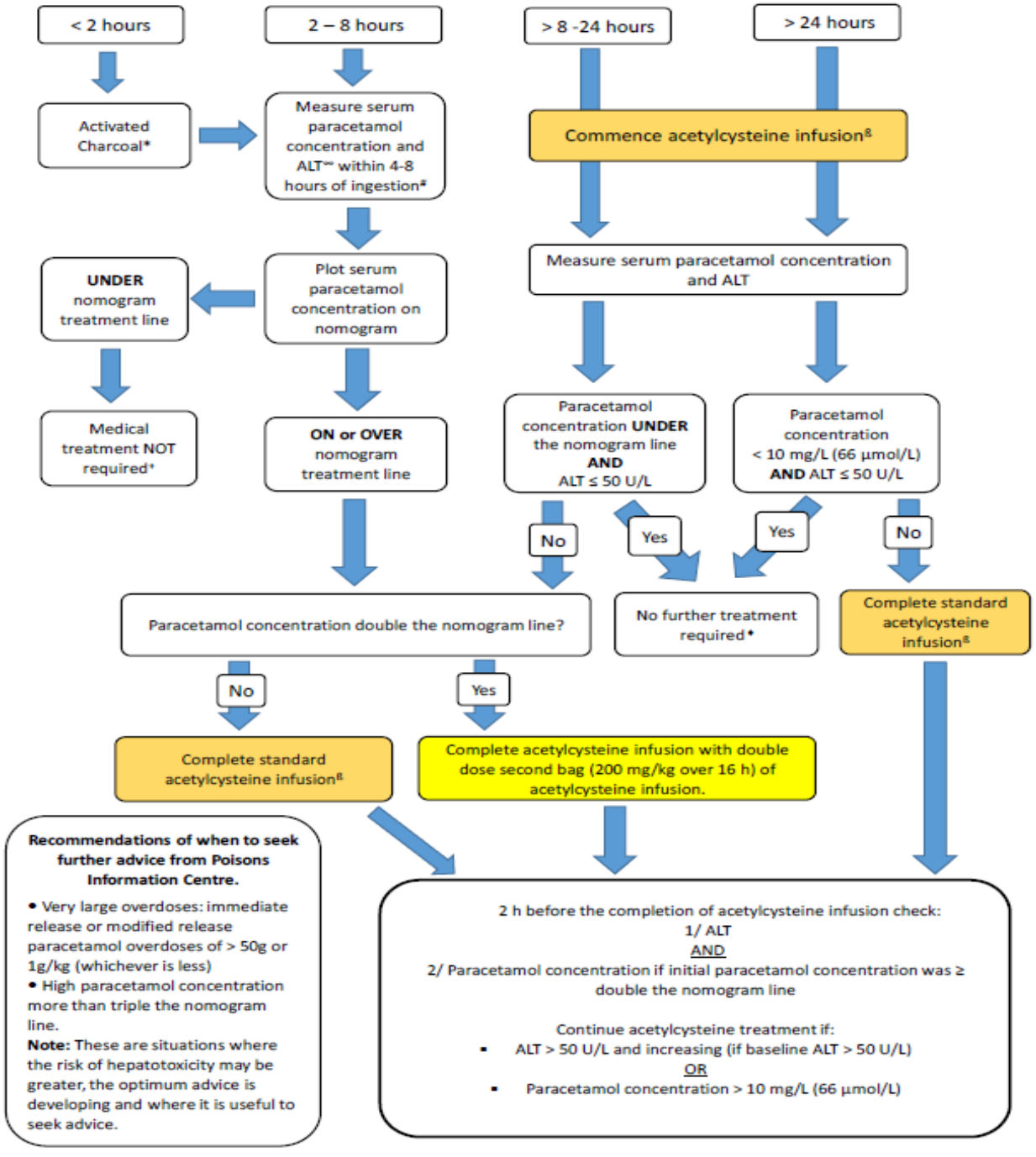
Management algorithm for identified overdose

Algorithm for management of acute overdose

Decontamination (unlikely to be required in young children).

It is important to note that in children under 6 years old, significant paracetamol overdose with liver injury is uncommon so decontamination with activated charcoal is rarely indicated. Discuss the role of decontamination in paracetamol overdose with the Poisons Information Centre prior to administration of charcoal.

Management for acute immediate release paracetamol exposure with known time of ingestion.



NB: Caution U/L = units/L and µmol/L = micromol/L

NOTE:
*Cooperative adult patients who have potentially ingested ≥ 10g or 200 mg/kg (whichever is less). Paracetamol ingestions ≥ 30g activated charcoal should be offered until 4 hours post ingestion.

~ Baseline ALT measurement.

If paracetamol concentration will not be available until ≥ 8 h post ingestion, commence acetylcysteine while awaiting paracetamol concentration.

ß For acetylcysteine infusion dosage see protocol.

+ Patients should be advised if they develop abdominal pain, nausea or vomiting further assessment is required.

This flowchart is applicable only if the treating clinician is confident of an accurate time of ingestion. Ingestions that are staggered over a period under 8 hours should be treated as a single acute ingestion at the earliest time of ingestion.

Flowchart adapted from Summary Statement: Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand — explanation and elaboration[2]

Paediatric (<6 years) liquid paracetamol ingestion

In children suspected of ingesting >200 mg/kg, measure serum paracetamol level at least 2 hours post-ingestion:

- If the concentration 2 - 4 hours after ingestion is <100 mg/L, acetylcysteine is not required.
- If the 2-hour concentration is ≥ 100 mg/L measure again at 4 hours post-ingestion. If the 4-hour concentration is ≥ 150 mg/L, commence acetylcysteine infusion as per the paracetamol nomogram.
- For children presenting later than 4 hours post ingestion or ≥6 years, treat as per the Acute Ingestion Management Flow-chart (above).

A 2-hour concentration should only be utilised in a well child < 6 years of age with an isolated liquid paracetamol ingestion. In all other cases a 4-hour concentration should be performed.

Modified-release paracetamol preparations

If less than 10 g and <200 mg/kg has been ingested, measure serum paracetamol levels to determine the need for acetylcysteine. Serum paracetamol concentrations should be taken at 4 hours or more post-ingestion (as with standard preparations) and repeated 4 hours later. If either concentration is above the nomogram line, acetylcysteine should be commenced.

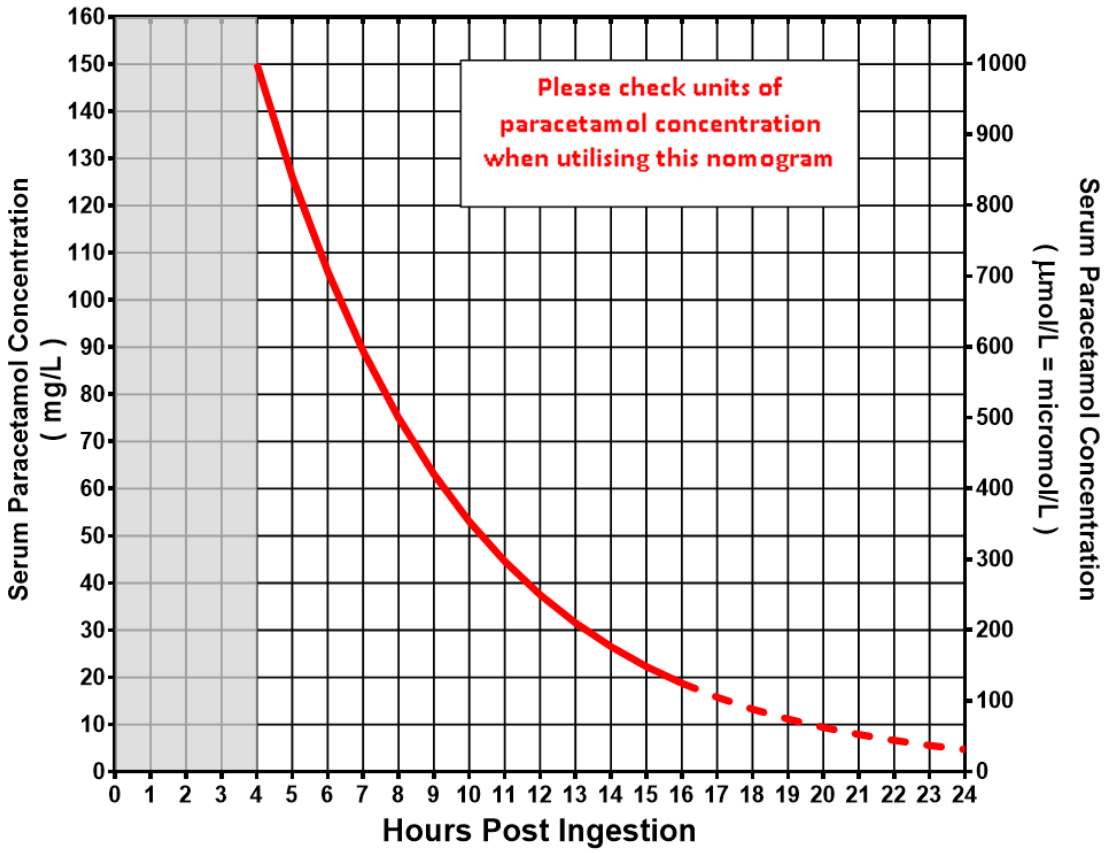
If more than 10 g or 200 mg/kg (whichever is less) has been ingested commence acetylcysteine.

- Give activated charcoal up to 4 hours post-ingestion.
- Commence acetylcysteine in all patients. All patients to receive at least a full 20 hour course of acetylcysteine.
- Measure serum paracetamol concentration at 4 or more hours post-ingestion, then again 4 hours later to guide acetylcysteine dose and need for further decontamination.
- Measure ALT on presentation.

If more than 30 g or 500 mg/kg has been ingested, or the paracetamol concentration is greater than double the nomogram line, discuss with the Poisons Information Centre and increase the dose of acetylcysteine.

- The second bag in the standard intravenous acetylcysteine regimen should be doubled to 200 mg/kg intravenous acetylcysteine over 16 hours.

Paracetamol Treatment Nomogram



This nomogram should be used in cases of acute single immediate-release ingestion of paracetamol where:

- Time of ingestion is known and
- Serum paracetamol level has been obtained between 4 - 24 hours post-ingestion

If the measured level is **below** the line, no treatment is required. Measured level on or above the line needs to be treated with acetylcysteine.

The nomogram should not be used to assess need for treatment of potentially toxic modified-release ingestions. However, paracetamol concentrations are useful to guide further management such as acetylcysteine dosage (e.g. the need for increased or prolonged treatment) and need for further decontamination in these scenarios.

Ensure that the units of measurement are the same as the scale used on the nomogram

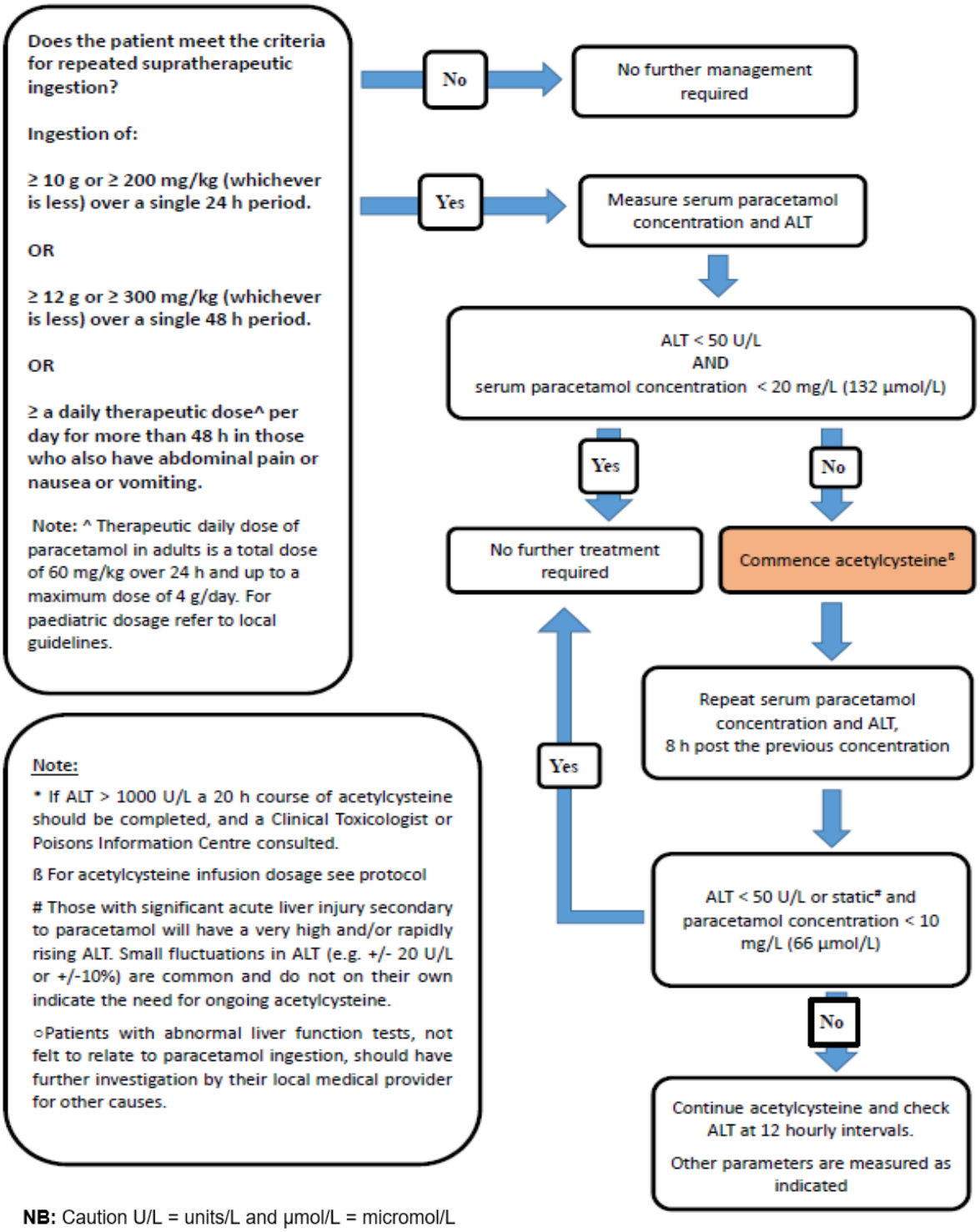
Indications for acetylcysteine in paracetamol overdose:

- Single ingestion and serum paracetamol level (taken 4 - 24 hours post-ingestion) is above treatment line on the nomogram.
- Ingestion of modified release paracetamol ≥200 mg/kg or ≥10 g (whichever is less), or if ingested less than this dose where either of the two serum paracetamol levels (taken 4 hours apart) is above the nomogram line.
- Repeated supratherapeutic ingestions – see algorithm below.
- Acute liver injury (ALT >50 units/L) in those patients presenting ≥ 8 hours post ingestion.
- When serum paracetamol levels will not be available for ≥ 8 hours post-ingestion.
- Indications for increased dose of NAC, please consult the Poisons Information Centre.
- Acute ingestion of modified or immediate release paracetamol with a paracetamol level greater than double the nomogram line.
- Modified release massive ingestions of more than 500 mg/kg or 30g

Discuss other presenting scenarios with the Poisons Information Centre.

Management algorithm for repeated supra-therapeutic overdose

Note: Do NOT use Paracetamol Treatment Nomogram



NB: Caution U/L = units/L and µmol/L = micromol/L

Flowchart adapted from Summary Statement: Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand — explanation and elaboration[2]

Infusion of Acetylcysteine

- Acetylcysteine is administered as a two-bag intravenous infusion according to the regimen below. It has been shown to be simpler, have a reduced rate of adverse reactions and similar efficacy to the previous three-bag protocol.[3,4]
- Acetylcysteine is available at SCHN as 2 g in 10 mL (=200mg/mL: Reconstitution not required) (Acetylcysteine-DBL/Link®)
- Acetylcysteine should be ordered using the eMeds/eMR (see below)

Acetylcysteine dosage regimen:

- 1st infusion – Acetylcysteine 200 mg/kg diluted in 7 mL/kg glucose 5% OR sodium chloride 0.9% (max 500 mL) over 4 hours, *followed by*
- 2nd infusion – Acetylcysteine 100 mg/kg diluted in 14 mL/kg glucose 5% OR sodium chloride 0.9% (max 1000 mL) over 16 hours.

Discuss further treatment or changes to the acetylcysteine regimen (such as doubling of the second infusion- see Algorithm for Management of acute overdose and Modified-release paracetamol preparations) with the Poisons Information Centre. Importantly, DO NOT cease acetylcysteine without speaking to the Poisons Information Centre, except in cases of anaphylactoid reactions (as discussed below).

NB:

- Remove the corresponding fluid (diluent) volume from the infusion bag then add the calculated acetylcysteine. The volume of acetylcysteine needs to be included in the total volume of the infusion fluid.

  e.g.: Total volume of 1st infusion Acetylcysteine (200mg/kg=15mL) + diluent in a 15kg child = 105mL at 7mL/kg.

- Acetylcysteine should be calculated using **ACTUAL body weight (max 110 kg),** ensure fluid volumes are appropriate for each patient based on age, fluid restrictions and other factors. Ideal weight should be used to quantify the extent of paracetamol overdose in obese children.

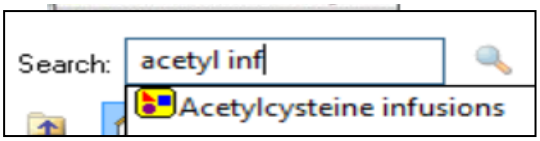
Examples of acetylcysteine dose and volume based on actual weight.

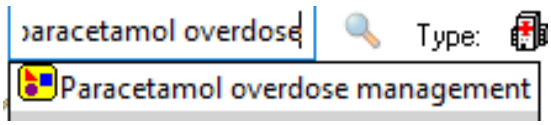
Patient's body weight	INITIAL INFUSION (200mg/kg of acetylcysteine to be added to 7mL/kg of 5% glucose or 0.9% sodium chloride)			SECOND INFUSION (100mg/kg of acetylcysteine to be added to 14mL/kg of 5% glucose or 0.9% sodium chloride)		
	Dose of Acetylcysteine	Volume of Acetylcysteine	Total volume of diluent (fluid) and acetylcysteine	Dose of Acetylcysteine	Volume of Acetylcysteine	Total volume of diluent (fluid) and acetylcysteine
15 kg	3 g	15 mL	105 mL	1.5 g	7.5 mL	210 mL
20 kg	4 g	20 mL	140 mL	2 g	10 mL	280 mL
25 kg	5 g	25 mL	175 mL	1.5 g	12.5 mL	350 mL

- If acetylcysteine is required beyond the initial 20-hour course, it should be charted as acetylcysteine 100 mg/kg diluted in 14 mL/kg glucose 5% OR sodium chloride 0.9% (max 1000 mL) over 16 hours[1].

Ordering Acetylcysteine on eMeds/eMM

- Acetylcysteine should be ordered using the eMeds/eMR. Image may differ in other LHDs.





Powerplan for the 2-bag acetylcysteine infusion is available and can be ordered as acetylcysteine infusions or paracetamol overdose management.

- If not already in the eMR, enter the ACTUAL weight (not dosing weight) for the child – maximum 110 kg
- Enter the diluent fluid volumes for 1st and 2nd infusions – the system will calculate the infusion rate

Side effects of acetylcysteine therapy:

- **Gastrointestinal upset** – nausea, vomiting, abdominal pain, diarrhoea
- **Anaphylactoid reactions (non IgE anaphylaxis)** – uncommon with two-bag regimen, symptoms include rash, itch, wheeze, shortness of breath (SOB), hypotension – most commonly occur during the 1st infusion. In the event of an anaphylactoid reaction, acetylcysteine therapy should be ceased for 1 hour and the patient treated as per standard management (or local guidelines) of anaphylaxis (e.g. adrenaline, oxygen, bronchodilators, fluids, anti-emetics, antihistamines, steroids). The 1st infusion may be recommenced at half the rate or, if on the 2nd infusion, at the same rate. Discuss severe reactions with the Poisons Information Centre.

Clinical Management

- A patient with a **paracetamol-only overdose** who is medically stable and only treated with acetylcysteine infusion should have cardiorespiratory monitoring in Emergency Department with close observation by nursing staff and rapid access to medical staff for 2 hours after commencement of the 1st infusion. During this period the patient needs close observation for side effects and anaphylactoid symptoms described above. After 2 hours of the 1st infusion the patient can be managed in a ward environment with routine 4 hourly observations and without continuous cardiorespiratory monitoring.
- For patients who are hemodynamically unstable from other **co-ingestions**, high dependency may be needed, and Intensive Care Unit should be consulted for ongoing monitoring. The Poisons Information Centre should be consulted on the ongoing care of these cases. Instability may also suggest an undisclosed co-ingestion or rarely a significant reaction to the acetylcysteine infusion (including reaction to acetylcysteine therapeutic error). Facilities external to the SCHN should call the NETS hotline 1300 362 500 for any child requiring PICU/HDU.

- Patients with deliberate self-poisoning should have a mental health assessment prior to discharge. Adolescent female patients with deliberate poisoning should have a screening pregnancy test.
- **Disposition** – will depend partly on the stability of the patient and whether there is co-ingestion of other medication. The patient should be admitted under the general medical team. In cases of liver damage, the Paediatric Gastroenterology team should be consulted.

Nursing Observations required during acetylcysteine infusion:

- Observe for any side effects or allergic reaction to the acetylcysteine infusion: nausea, vomiting, rash, itch, wheeze, shortness of breath, hypotension. These occur within 120 minutes of starting the infusion.
- On commencement of infusion, ensure a full set of baseline observations have been done then15 minutely observations for heart rate, respirations (including SpO_2), blood pressure for the first hour of infusion.
- The first 2 hours of 1st infusion should take place in a monitored area with cardio-respiratory monitoring. In Emergency Department this is in the Resuscitation Area or Observation beds.
- If any significant reaction (i.e. shortness of breath, wheeze, hypotension) are noted the infusion needs to be stopped for one hour. Seek Poisons Information Centre advice. Note nausea and vomiting are very common and acetylcysteine should not be ceased if just these occur.
- When recommenced, the 1st infusion is started at half the rate (or same rate for 2nd infusion).
- After the first 2 hours of the infusion the child can be transferred to the ward if medically stable. Patients on acetylcysteine infusions may be managed in a general medical ward and do not necessarily require Intensive Care. Monitoring with 4 hourly observations for heart rate, respiration and blood pressure is required for 24 hours while the infusion is in process.

References

1. Toxicology and Toxinology: Paracetamol poisoning monograph. eTG complete [digital] Melbourne Therapeutic Guidelines: Ltd. 2020.
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