# PARACETAMOL OVERDOSE - ASSESSMENT AND MANAGEMENT

## PRACTICE GUIDELINE ©

## DOCUMENT SUMMARY/KEY POINTS

- Paracetamol overdose may be initially asymptomatic and early assessment is recommended.
- Discuss all cases with the Poisons Information Centre (13 11 26) **or** local toxicology service (e.g. for CHW contact WSLHD Toxicology service; for SCH, call SEATS – South-East Area Toxicology Service through the Poisons Information Centre), including prior to ceasing acetylcysteine.
- 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).
- All modified-release paracetamol ingestion >10 grams to receive at least the full course of acetylcysteine.
- Anaphylactoid reactions to acetylcysteine usually occur in the first few hours of infusion but are uncommon with the two-bag infusion regimen.
- 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.





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| **Approved by:** | SCHN Policy, Procedure and Guideline Committee | |
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| **Team Leader:** | Senior Specialist | **Area/Dept**: NSW Poisons Information Centre |

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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.

# 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.

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# 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 reversed 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, though acetylcysteine may still be effective in late presenting patients beyond this time.

## Sources of Management Advice

- Emergency Department senior clinicians
- Specialists in Poisons Information and Toxicologists at the Poisons Information Centre (13 11 26)
- Local toxicology service – call 53111 from CHW or 131126 to be transferred to the Toxicology team

## Forms of Overdose

1. **Acute poisoning:** where a patient has taken a single large dose of paracetamol or staggered overdose (several ingestions over greater than 2 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 is key to obtaining the diagnosis.
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 with acute life-threatening symptoms.

In the acute stages of paracetamol overdose there are often no symptoms, or only mild gastrointestinal effects (vomiting, right upper quadrant abdominal pain/tenderness). Patients

with delayed presentations, many hours or days after overdose, may have symptoms related to hepatotoxicity or liver failure, such as jaundice and hypoglycaemia that develop 3-4 days after the acute ingestion. The antidote (acetylcysteine) may 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, tablets preparation or an IV injection?
- Is the paracetamol immediate-release or modified release?
- What is the estimated dose based on ideal body weight (mg/kg) that has been ingested?
- Are there any other co-ingested medicines?
- Are there child safety issues (non-accidental poisoning or neglect) that need to be addressed?
- Do we know the exact time of the overdose?
- 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 a relative dose of paracetamol ingestion in both single dose overdose and the repetitive overdose format that may result in acute paracetamol toxicity. Calculation of dose is based on actual body weight.

| **Paracetamol dosing that may be associated with hepatic 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 or a Clinical Toxicologist 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<br>**If immediate release tablet paracetamol ingestion** check at 4 hours or as soon thereafter as possible<br>**If modified-release (MR) tablet paracetamol ingestion** check at least 2 levels 4 hours apart (e.g. at 4 and 8 hours post-ingestion) at 4 hours post ingestion or as soon thereafter as possible<br>**IV paracetamol overdose** (usually iatrogenic error) should be discussed with the Poisons Information Centre or a Clinical Toxicologist as soon as it is discovered.<br>**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<br>**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<br>**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<br>**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 |

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

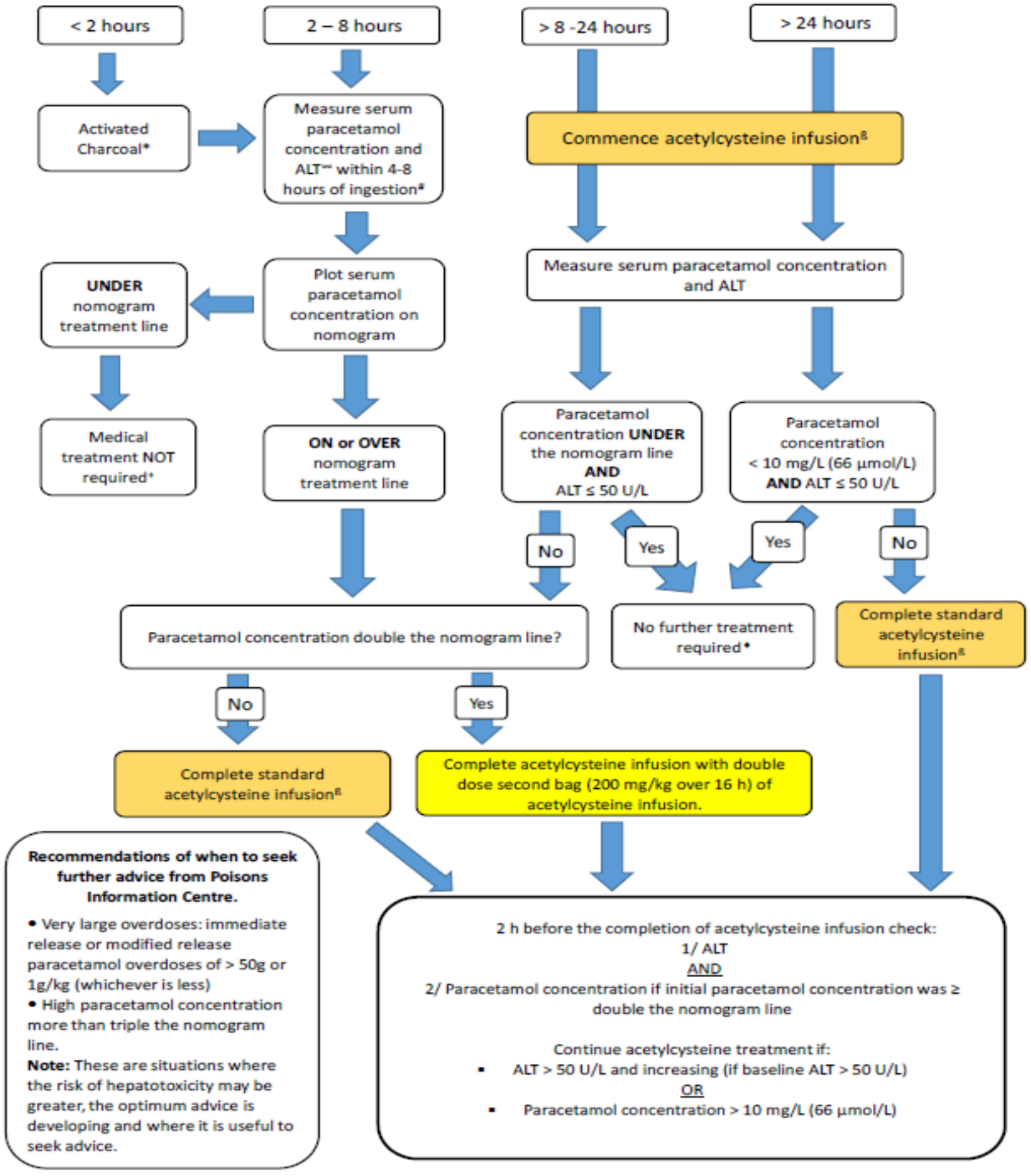
## Management algorithm for identified overdose

### *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 and hepatic injury is uncommon and use of decontamination techniques such as activated charcoal or gastric lavage is rarely indicated. Discuss the role of decontamination in paracetamol overdose with the Poisons Information Centre or Clinical Toxicologist prior to administration of charcoal.

- **Management for acute 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 <150 mg/L, acetylcysteine is not required.
- If the 2 hour concentration is ≥150 mg/L measure again at 4 hours post-ingestion. If the 4 hour concentration is still ≥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 more than 10 g or 200 mg/kg (whichever is less) has been ingested commence acetylcysteine.

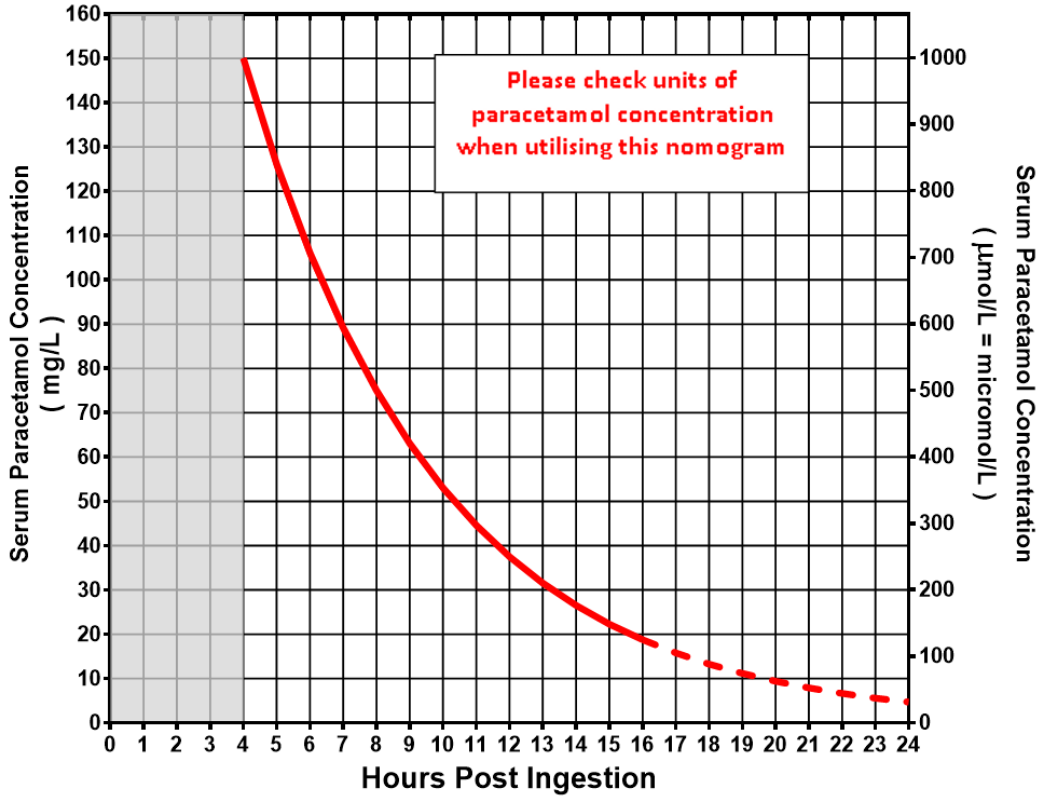
- Give activated charcoal up to 4 hours post-ingestion.
- Commence acetylcysteine in all patients. All patients to receive at least a full 20 hour course of acetylcysteine.
- Measure serum paracetamol concentration at 4 or more hours post-ingestion, then again 4 hours later to guide acetylcysteine dose 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 the dose of acetylcysteine should be increased.

- The second bag in the current standard intravenous acetylcysteine regimen should be doubled to 200 mg/kg intravenous acetylcysteine over 16 hours. These patients should also be discussed with a Clinical Toxicologist or Poisons Information Centre.

**If <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.**

## Paracetamol Treatment Nomogram




If the measured level is **below** the line, no treatment is required. Measured level above the line needs to be treated with acetylcysteine. This nomogram should only 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

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

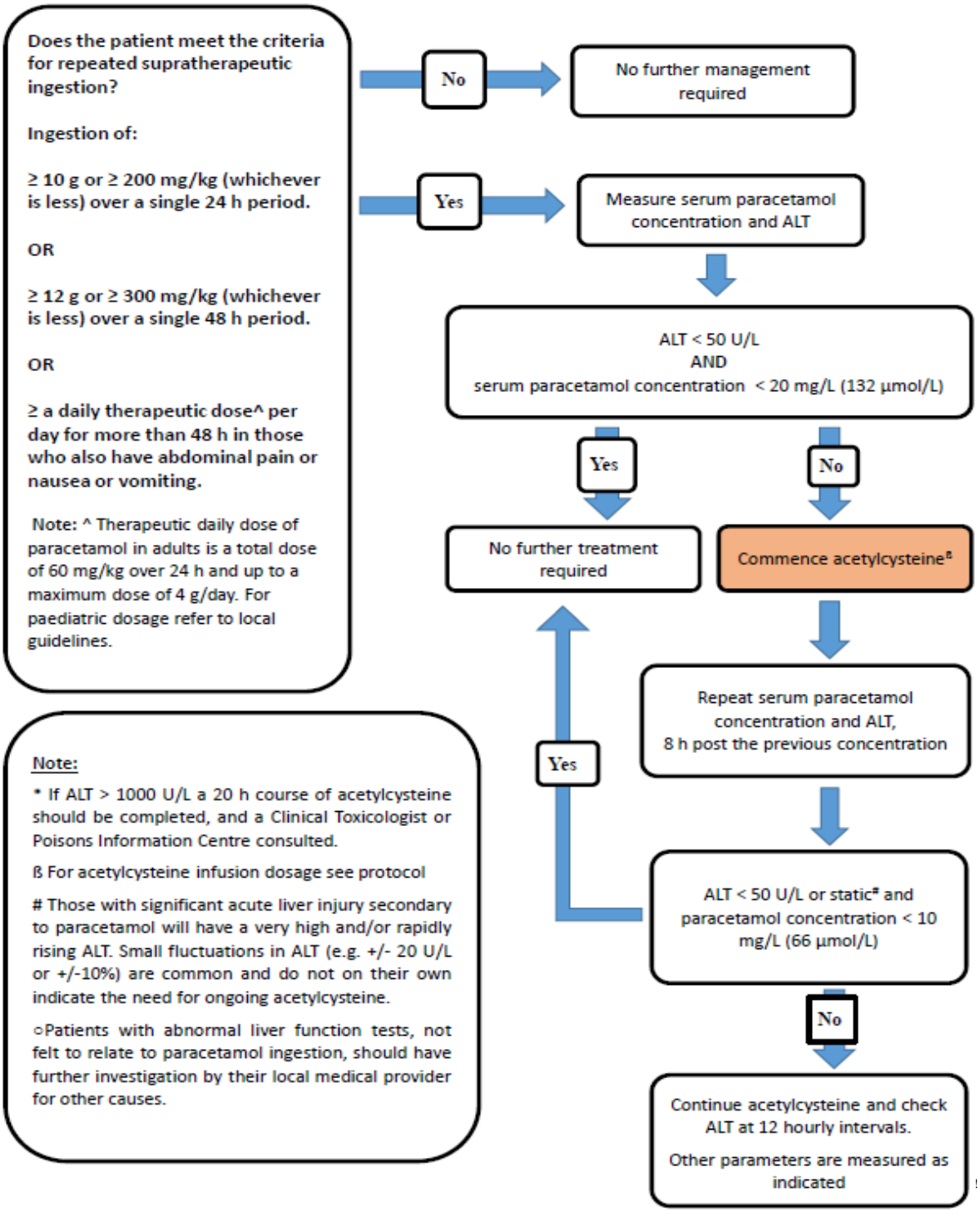
## Indications for acetylcysteine in paracetamol overdose:

- Single ingestion and serum paracetamol level (taken 4 - 24 hours post-ingestion) is above treatment line on the nomogram.
- Ingestion of liquid paracetamol with a 4 hour serum paracetamol level above 150 mg/L.
- 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.
- Modified release massive ingestions of more than 500 mg/kg or 30g or acute ingestion of modified or immediate release paracetamol with a paracetamol level greater than double the nomogram line need an increased acetylcysteine dose and urgent consultation.
- 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.

Discuss other presenting scenarios with the Poisons Information Centre or a Clinical Toxicologist

# 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

## 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 (Acetylcysteine-DBL/Link®)
- Acetylcysteine should be ordered in SCHN using the eMeds/eMM (see below)

***Acetylcysteine dosage regimen:***

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

Discuss further treatment or changes to the acetylcysteine regimen with the Toxicology team; importantly DO NOT cease acetylcysteine without speaking to the Toxicology team, except in cases of anaphylactoid reactions (as discussed below).

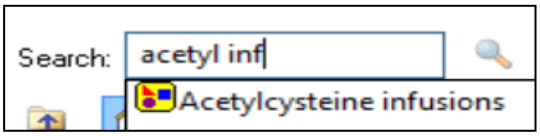
**NB:**

- If acetylcysteine is required beyond the initial 20-hour course, it should be charted as acetylcysteine 150 mg/kg diluted in 14 mL/kg glucose 5% (max 1000 mL) over 24 hours.
- 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.

*Acetylcysteine may be diluted in sodium chloride 0.9% if using Acetylcysteine-DBL® or Acetylcysteine-Link®

***Ordering Acetylcysteine on eMeds/eMM***

- Acetylcysteine should be ordered using the eMeds/eMM




- 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** – 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 (e.g. anti-emetics, antihistamines, steroids, adrenaline). The 1st infusion may be recommenced at half the rate or, if on the 2nd infusion, at the same rate. Discuss severe reactions with a toxicologist.

***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 haemodynamically unstable from other **co-ingestions**, high dependency may be needed and Intensive Care Unit should be consulted for ongoing monitoring. The toxicologist on call should also be consulted in the ongoing care of these cases. Instability may also suggest an undisclosed co-ingestion or a significant reaction to the acetylcysteine infusion.
- Patients with deliberate self-poisoning should have a mental health assessment. 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 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 the patient requires 15 minutely observations for heart rate, respirations, blood pressure for the first hour of infusion.
- The first 2 hours of 1st infusion should take place in a monitored area. In Emergency Department this is in the Resuscitation Area or Observation beds.
- If any reaction noted the infusion needs to be stopped for one hour. Seek medical advice.

- 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.
2. Chiew AL et al. Summary Statement: Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand — explanation and elaboration MJA 2019; doi: 10.5694/mja2.50428 https://www.aci.health.nsw.gov.au/__data/assets/pdf_file/0005/558527/Guidelines-for-management-of-paracetamol-poisoning-2019.pdf
3. Wong A & Graudins A. N-acetylcysteine regimens for paracetamol overdose: Time for change? Emerg Med Australas, 2016; 28: 749-51
4. McNulty R et al. Fewer adverse effects with a modified two-bag acetylcysteine protocol in paracetamol overdose. Clinical Toxicology, 2018; 56(7): 618-621.