# 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 SCH, call SEATS – South-East Area Toxicology Service)
- Check **correct units** are read from the nomogram (previously micromol/L and now mg/L).
- Liquid paracetamol ingestions in children < 6 years should have a paracetamol level taken from 2 hours post-ingestion.
- Anaphylactoid reactions to acetylcysteine usually occur in the first few hours of infusion.
- Deliberate ingestions with self-harm intent (usually in adolescents) require mental health assessment.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.



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|---|---|---|
| **Approved by:** | SCHN Policy, Procedure and Guideline Committee | |
| **Date Effective:** | 1st August 2017 | **Review Period**: 3 years |
| **Team Leader:** | Clinical Toxicologist | **Area/Dept**: NSW Poisons Information Centre |

# CHANGE SUMMARY

- This document is a new SCHN guideline and replaces individual CHW and SCH Paracetamol overdose guidelines.

# 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 (e.g. Demazin, Dimetapp – refer to 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 (e.g. for SCH, call SEATS – South-East Area Toxicology Service, Randwick Campus – contact via Switch or 0423 366 022)

## Forms of Overdose:

1. **Acute poisoning:** Where a patient has taken a single large dose of paracetamol.
2. **Repeated supratherapeutic ingestion:** when there has been a repetitive dose given too frequently or over daily recommended maximum doses. 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 be towards 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


This Guideline may be varied, withdrawn or replaced at any time.

with delayed presentations, many hours or days after overdose, may have symptoms related to hepatotoxicity or liver failure which appears 3-4 days after the acute ingestion, such as jaundice and hypoglycaemia. The antidote (acetylcysteine) may still be effective at this stage.

## Important Medical History

A careful history is important and a number of factors in the history need to be obtained.

- Check previous doses administered in the previous 24-72 hours
- Is the overdose a single dose or repetitive doses?
- Is the paracetamol a liquid preparation or an IV injection?
- Is the paracetamol immediate-release or sustained-release?
- What is the estimated dose per ideal body weight (mg/kg) that has been ingested?
- Are there any other co-ingested drugs?
- 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[2] 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.

| Paracetamol dosing that may be associated with hepatic injury | | |
|---|---|---|
| | **Adults and children >6 years of age** | **Children aged 0-6 years** |
| **Acute single ingestion** | greater than 200mg/kg or 10g (whichever is less) over a period of less than 8 hours | greater than 200mg/kg over a period of less than 8 hours |
| **Repeated supratherapeutic ingestion** | greater than 200mg/kg or 10g (whichever is less) over a single 24-hours period | greater than 200mg/kg over a single 24-hour period |
| | greater than 150mg/kg or 6g (whichever is less) per 24-hour period for the preceding 48 hours | greater than 150mg/kg per 24-hour period for the preceding 48 hours |
| | greater than 100mg/kg or 4g/day (whichever is less) per 24-hour period for more than 48 hours in patients with abdominal pain, nausea, vomiting or at high risk of toxicity. | greater than 100mg/kg per 24-hour period for more than 48 hours |

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

## Investigation

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 tablet paracetamol ingestion** check at 4 hours or as soon thereafter as possible<br>**NB:** Overdose of **IV paracetamol** (usually iatrogenic error) should be discussed with the Poisons Centre or toxicologist as soon as it is discovered.<br>**NB:** Patients with ingestion of sustained-release (SR) paracetamol should have at least 2 paracetamol levels taken 4 hours apart (e.g. at 4 and 8 hours post-ingestion). | On admission | On admission |
| Transaminases (ALT/AST) | ▬ | On admission AND at end of acetylcysteine infusion | On admission |
| INR/prothrombin time | ▬ | ▬ | On admission |
| Creatinine and Urea | ▬ | ▬ | On admission |
| Glucose | ▬ | ▬ | On admission |
| Venous blood gas | ▬ | ▬ | On admission |

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

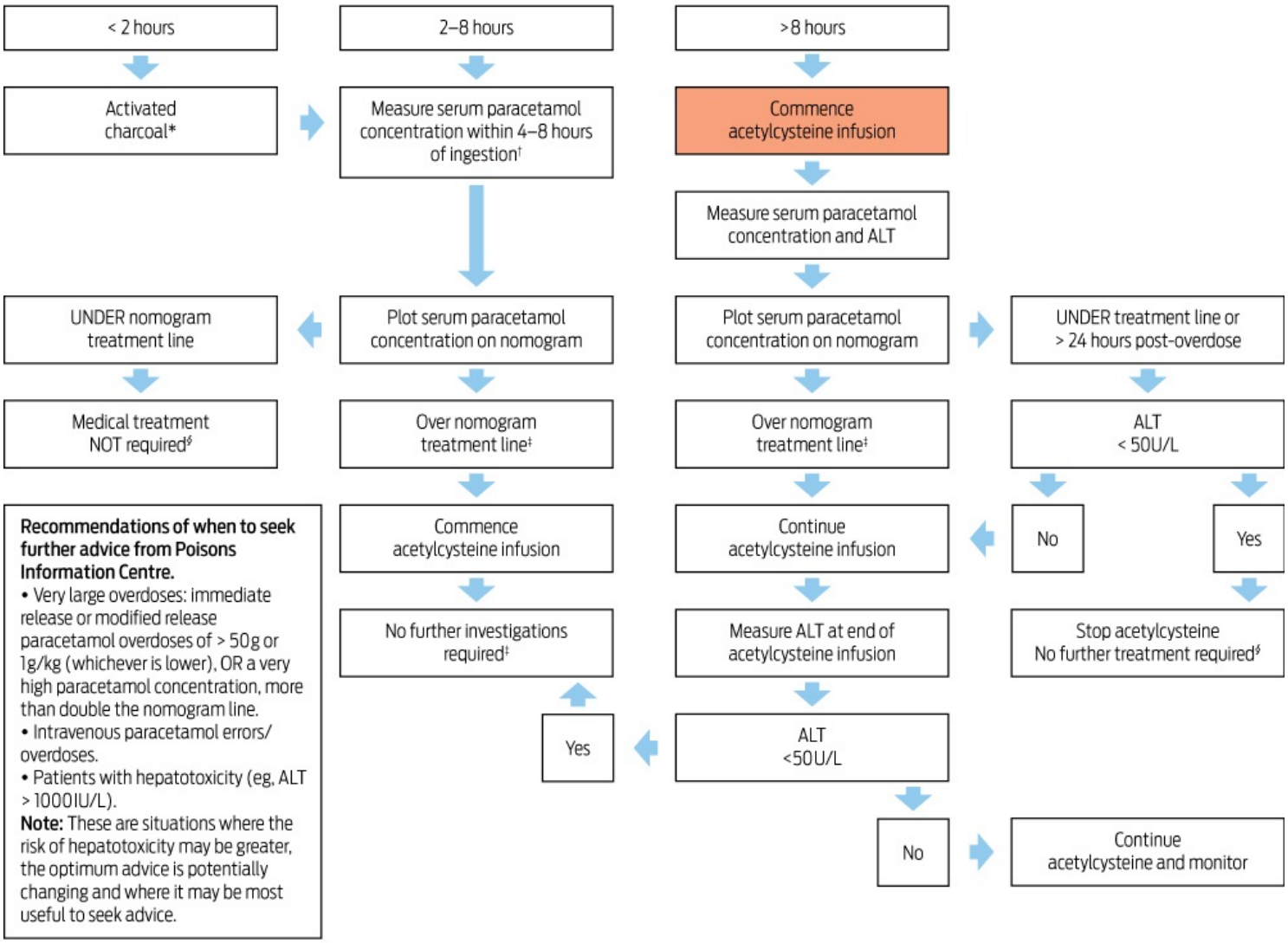
## Management algorithm for identified overdose

***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 a toxicologist or Poisons Information Centre prior to administration of charcoal.

- **Management for acute paracetamol exposure with known time of ingestion:**




**Charcoal should be considered within 2 hours for large deliberate ingestions > 10g (or 200mg/kg, whichever is less). For ingestions of more than 30g or for sustained-release products activated charcoal should be offered until 4 hours post-ingestion.*

*† If paracetamol concentration will not be available until > 8 hours post-ingestion, commence acetylcysteine while awaiting paracetamol concentration.*

*‡ Those patients with initial paracetamol concentrations more than double the nomogram line may benefit from an increase in acetylcysteine dose. These patients should have serum paracetamol and ALT concentrations checked at the end of the acetylcysteine infusion.*

*§ Patients should be advised that 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 reference 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 (1000 micromol/L), acetylcysteine is not required.
- If the 2 hour concentration is > 150 mg/L (1000 micromol/L), measure again at 4 hours post-ingestion. If the 4 hour concentration is still > 150 mg/L (1000 micromol/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).

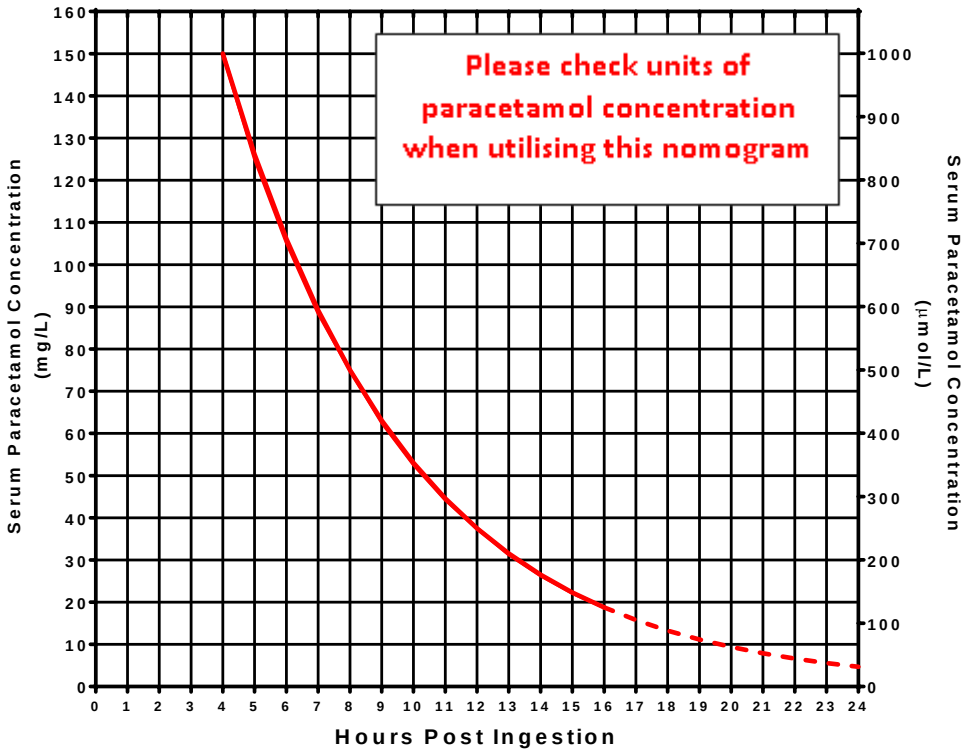
### *Sustained-Release Paracetamol Preparations*

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

- Measure serum paracetamol concentration at 4 or more hours post-ingestion, then again 4 hours later if the first concentration is below the nomogram line.
- If serial paracetamol concentrations taken 4 hours apart are below the nomogram line and decreasing, acetylcysteine may be discontinued, otherwise continue the full 20 hour course of acetylcysteine to its completion.

**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





This Guideline may be varied, withdrawn or replaced at any time.

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 ingestion of paracetamol where:

- Time of ingestion is known and
- Serum paracetamol level has been obtained between 4 and 16 hours post-ingestion

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

The indications for acetylcysteine in paracetamol overdose:

- Single ingestion and serum paracetamol level (taken 4-16 hours post-ingestion) is above treatment line on the nomogram.
- Ingestion of liquid paracetamol with a 4 hour serum paracetamol level above 150mg/L (1000 micromol/L).
- Ingestion of sustained release paracetamol ≥ 200mg/kg or ≥ 10 gram (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.
- Established hepatotoxicity (deranged transaminases or coagulations studies).
- When serum paracetamol levels will not be available for > 8 hours post-ingestion
- Massive ingestion (more than 30g or 400mg/kg or paracetamol level is greater than double the nomogram line) needs special attention and urgent consultation
- Discuss other presenting scenarios with a Toxicologist.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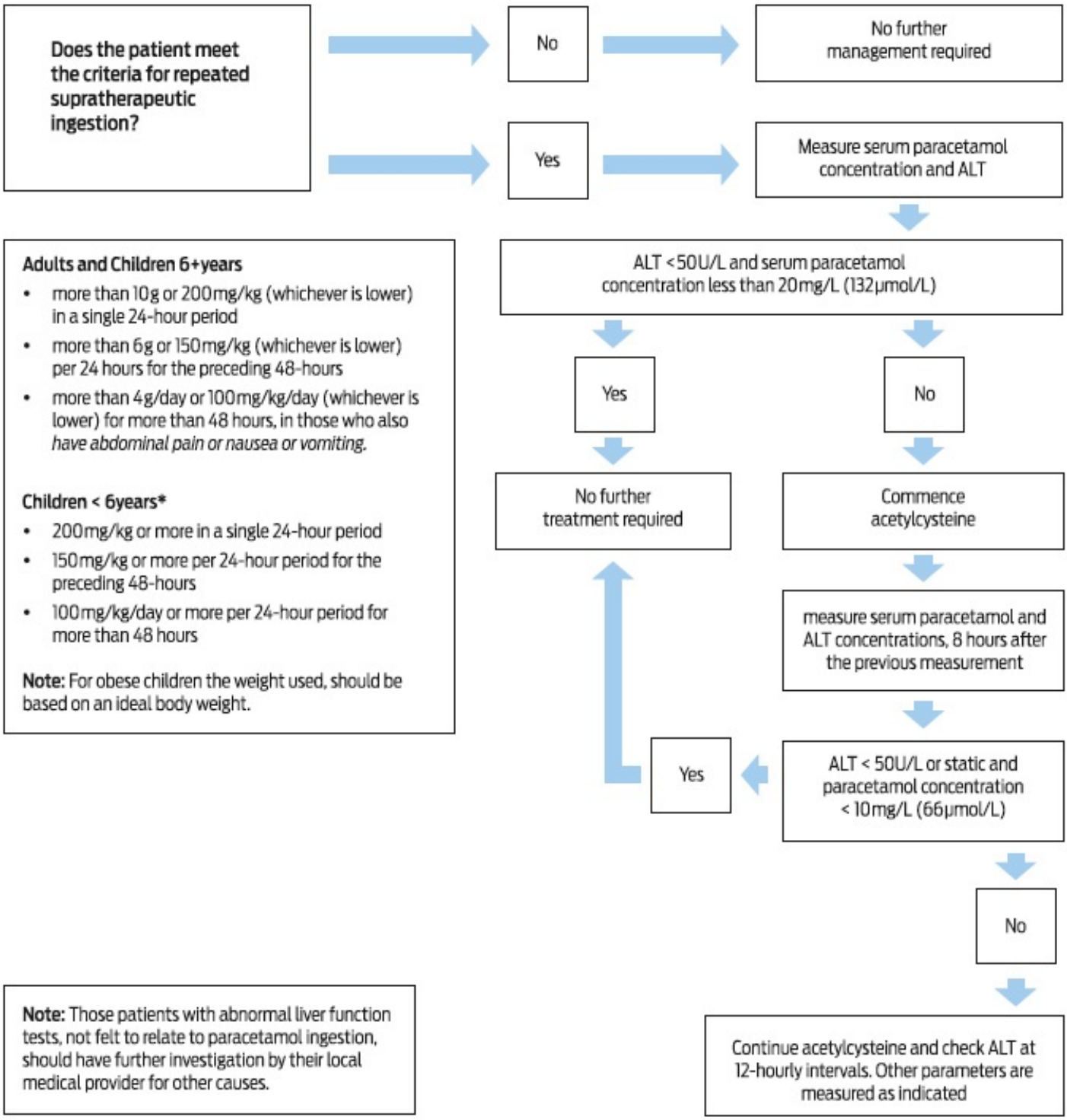
# Management algorithm for repeated supra-therapeutic overdose

Note: Do NOT use Paracetamol Treatment Nomogram



## Infusion of Acetylcysteine

Note: in the previous guideline acetylcysteine was referred to as NAC (N-acetylcysteine). However, NAC is not an approved abbreviation, and acetylcysteine must be written in full.

- Acetylcysteine is administered as a series of two intravenous infusions according to the regimen below. This two bag infusion protocol replaces the previous 3 bag protocol. It has been shown to be simpler, have a reduced rate of adverse reactions and not inferior to the 3 bag protocol.[3,4]
- Acetylcysteine is available at SCHN as 2g in 10mL (Acetylcysteine-DBL/Link®) and 6g/30mL (Acetadote®)

***Acetylcysteine dosage regimen:***

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

  **NB:**

  - If acetylcysteine is required beyond the initial 20 hour course, it should be charted as acetylcysteine 150mg/kg diluted in 14mL/kg 5% glucose(max 1000mL) over 24 hours.
  - Acetylcysteine dosing should be calculated using actual body weight, except in obese children where ideal body weight should be used. Ensure fluid volumes are appropriate for each patient based on age, fluid restrictions and other factors.

***Side effects of acetylcysteine therapy:***

- **Gastrointestinal upset** – nausea, vomiting, abdominal pain, diarrhoea
- **Anaphylactoid reactions** – 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 1hr 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 infusion. During this period the patient needs close observation for side effects and anaphylactoid symptoms described above. After 2 hours of 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 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. Paracetamol. In: Therapeutic Guidelines: Toxicology & Wilderness, V15. Melbourne: TG Ltd. 2015.
2. Chiew AL et al. Summary Statement: New guidelines for the management of paracetamol poisoning in Australia and New Zealand. MJA 2015; 203 (5): 215-8. https://www.mja.com.au/sites/default/files/issues/203_05/Guidelines_paracetamol_Aus_NZ_2015.pdf
3. Wong A & Graudins A. N-acetylcysteine regimens for paracetamol overdose: Time for change? Emerg Med Australas, 2016; 28: 749-51
4. Wong A & Graudins A. Simplification of the standard three-bag IV acetylcysteine regimen for paracetamol poisoning results in a lower incidence of adverse drug reactions. Clin Toxicol, 2016; 54: 115-9.

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