PARACETAMOL OVERDOSE - ASSESSMENT AND MANAGEMENT

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- 19/12/2016 :

Please note these guidelines are under review in accordance with updated guidance from:
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.
Available from: https://www.mja.com.au/journal/2015/203/5/summary-statement-new-guidelines-management-paracetamol-poisoning-australia-and

- Check **correct units** are read from the nomogram as variable units are used in Australia (As of 21/12/16 SCH use mg/L and CHW use micromole/L).

- Paracetamol overdose may be initially asymptomatic and early assessment is recommended.
- Discuss all cases with the NSW Poisons Information Centre (13 11 26; internal 53111) **or** local toxicology service (e.g. SEATS – South-East Area Toxicology Service)
- Check correct units are read from the nomogram (micromole/litre).
- Liquid paracetamol ingestions should have a paracetamol level taken at 2 hours post-ingestion.
- Anaphylactoid reactions to N-acetylcysteine [NAC] usually occur in the first few hours of infusion.
- Deliberate ingestions with self-harm intent (usually in adolescents) require mental health assessment.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st June 2014	**Review Period:** 3 years
Team Leader:	Medical Director	**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.

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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 cough and cold flu preparations (e.g. Demazin, Dimetapp – refer to MIMS for a 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 are reversed by administration of an antidote - N-acetylcysteine (acetylcysteine or NAC).
Note: the term NAC will be used for the remainder of this document.

To be most effective in protecting against liver damage, NAC therapy should be commenced within 8 hours of paracetamol ingestion, though NAC may still be effective in late presenting patients beyond this time.

Sources of Management Advice

- Emergency Department senior clinicians
- Toxicologists at the NSW Poisons Information Centre (13 11 26)
- Local toxicology service (e.g. SEATS – South-East Area Toxicology Service, Randwick Campus – contact via Switch)

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. 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

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 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 (NAC) 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.

- Is the overdose a single dose or repetitive doses?
- Is the paracetamol a liquid preparation or an IV injection (e.g. Perfalgan®)?
- Is the paracetamol immediate-release or sustained-release?
- What is the estimated dose per lean 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	200mg/kg (or greater) 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	200mg/kg (or greater) over a single 24-hour period
	greater than 150mg/kg or 6g (whichever is less) per 24-hour period for the preceding 48 hours	150mg/kg (or greater) per 24-hour period for the preceding 48 hours
	greater than 100mg/kg or 4g/day (whichever is less) in patients with predisposing risk factors†	100mg/kg (or greater) per 24-hour period for the preceding 72 hours

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** check at 2 hours or as soon thereafter as possible **If tablet paracetamol ingestion** check at 4 hours or as soon thereafter as possible **NB:** Overdose of **IV paracetamol** (usually iatrogenic error) should be discussed with the Poisons Centre or toxicologist as soon as it is discovered. **NB:** Patients with ingestion of sustained-release (SR) paracetamol should have 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 NAC infusion	On admission
INR/prothrombin time	▬	▬	On admission
Creatinine and Urea	▬	▬	On admission
Glucose	▬	▬	On admission
Arterial blood gas	▬	▬	On admission

ALT = Alanine aminotransferase, **AST** = aspartate aminotransferase, ▬ = test not required
INR = international normalised ratio, **NAC** = N-acetylcysteine or acetylcysteine

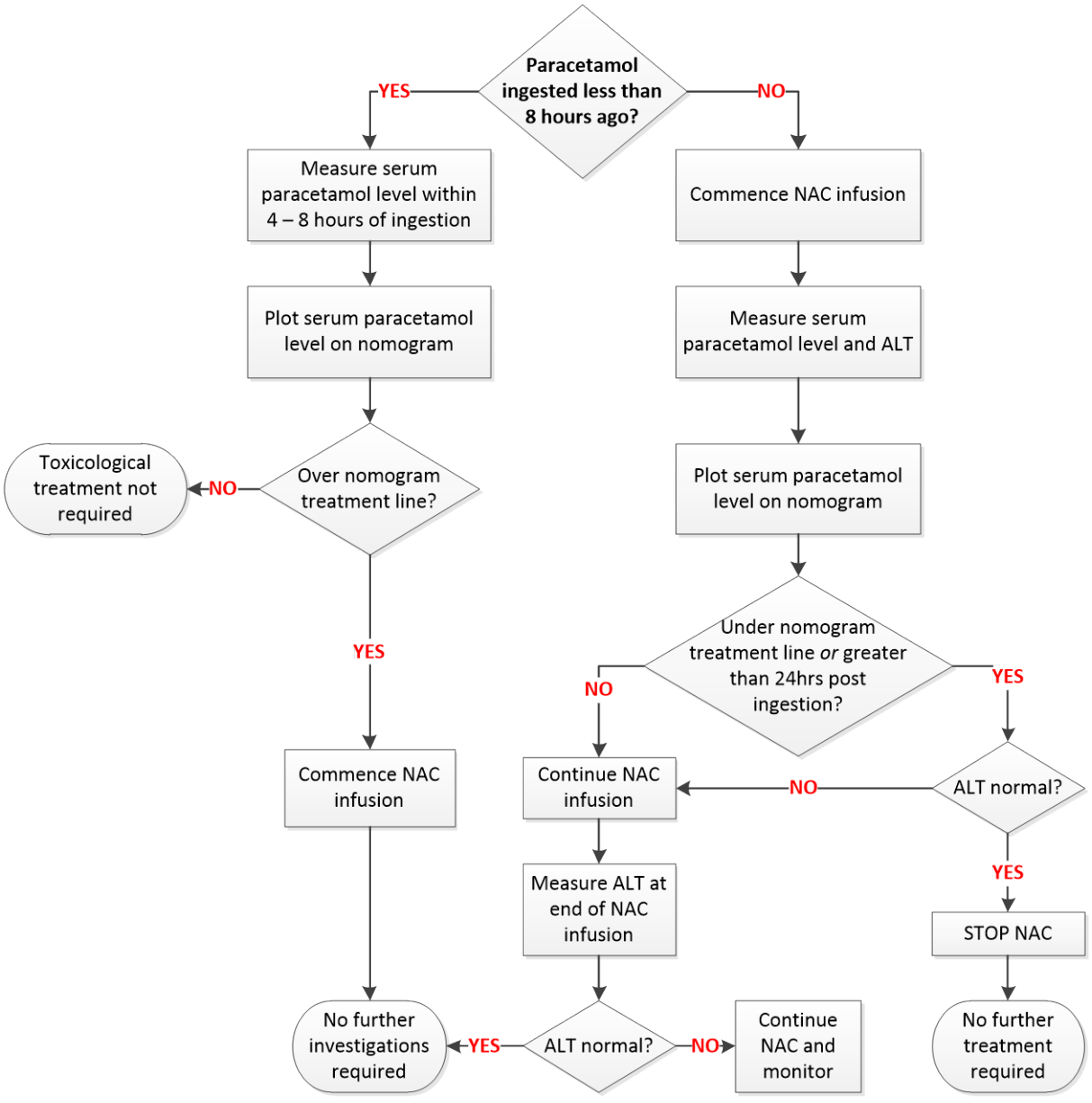
Management algorithm for identified overdose

Algorithm for management of acute overdose

- **Decontamination** (unlikely to be required in 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 ipecac, activated charcoal or gastric lavage is rarely indicated. Discuss the role of decontamination in paracetamol overdose with a toxicologist or Poisons Centre prior to administration of charcoal.

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

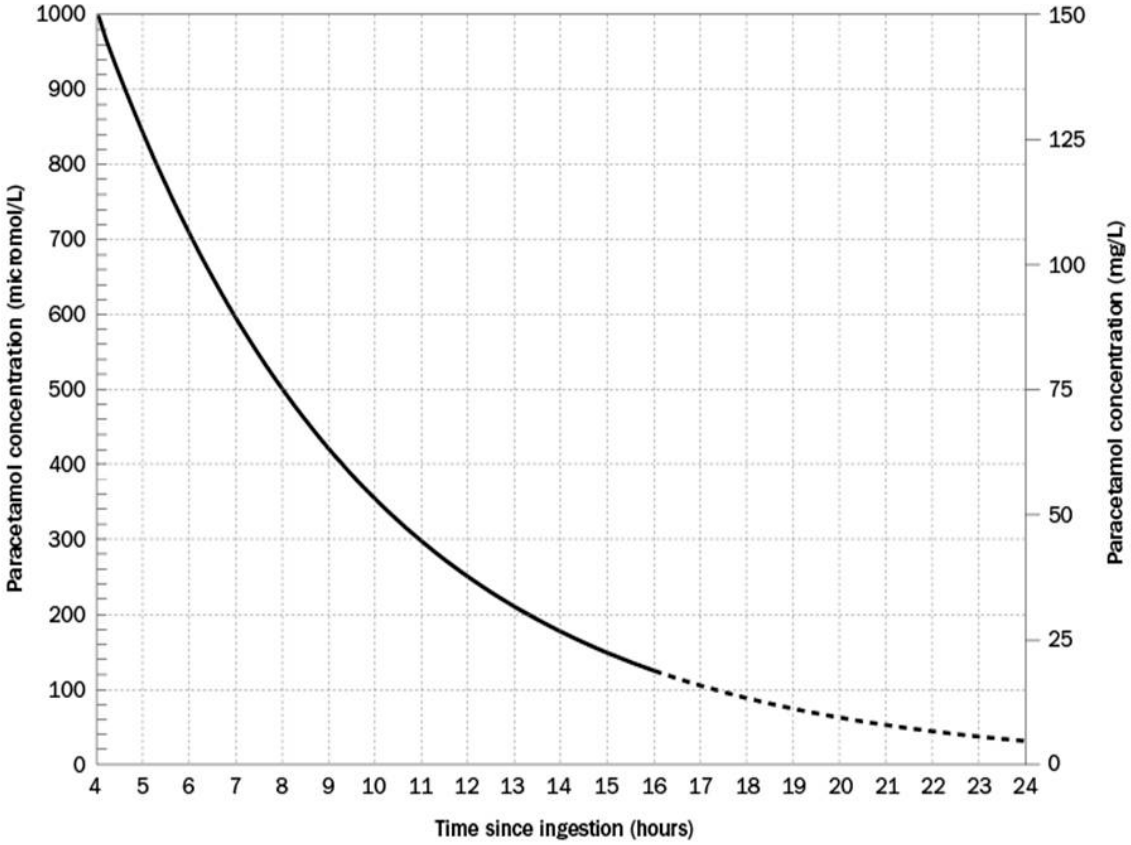


ALT = alanine amino transferase, NAC = N-acetylcysteine or acetylcysteine

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.

The Paracetamol Treatment Nomogram[1]



Measured level below the line no treatment is required. Measured level above the line needs to be treated with NAC. This nomogram should only be used in cases where:

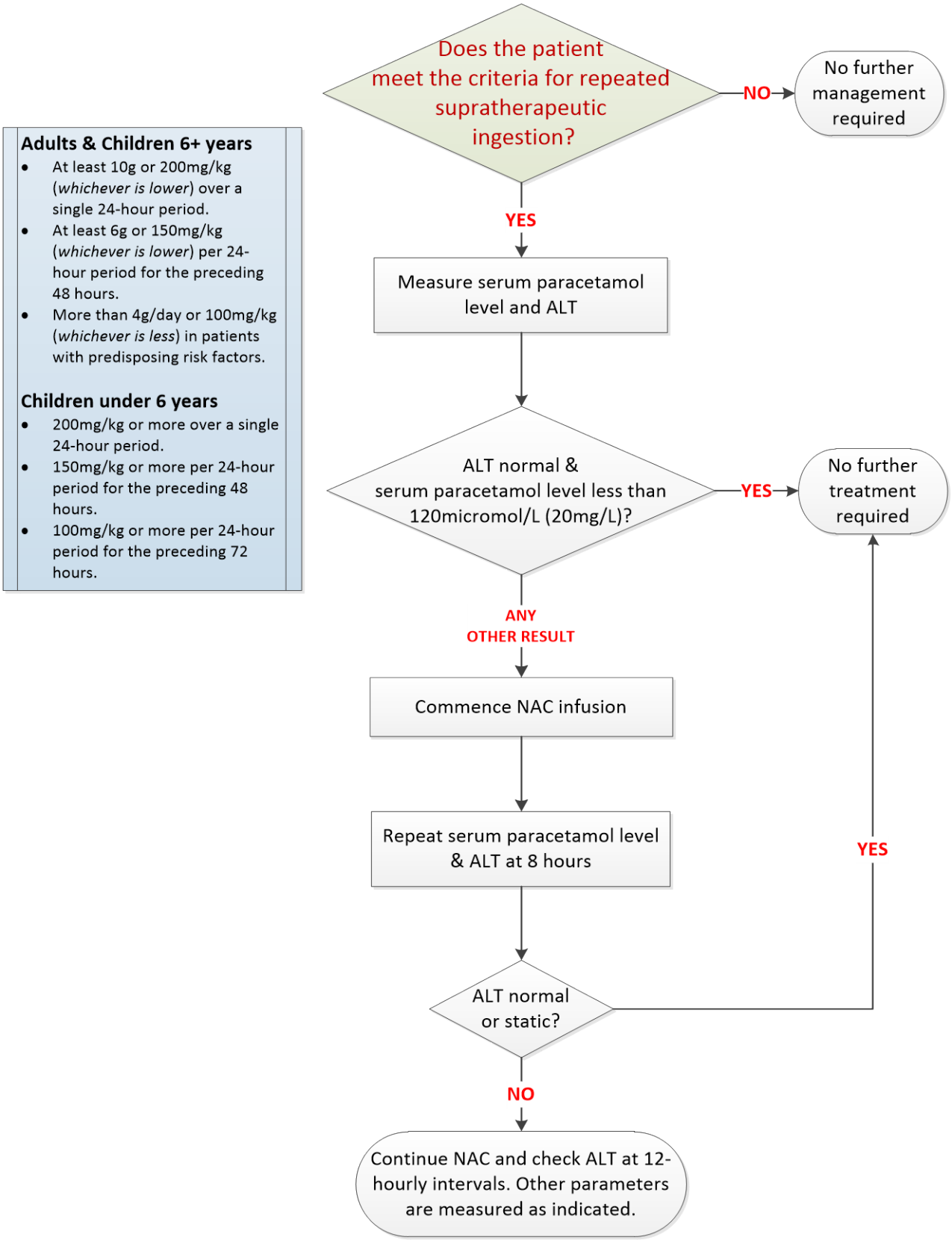
- Acute single ingestion of paracetamol
- Time of ingestions is known
- Paracetamol level may be obtained between 4 and 16 hours post-ingestion

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

The indications for NAC in paracetamol overdose:

- Single ingestion and paracetamol level (taken 4-16 hours post-ingestion) is above treatment line on the nomogram.
- Ingestion of liquid paracetamol with a 2-hour level above 1500 micromol/L.
- Ingestion of sustained release paracetamol where either of the 2 levels (taken 4 hours apart) is above the nomogram line.
- Repeated supratherapeutic ingestions – see algorithm below.
- Established hepatotoxicity (deranged transaminases or coagulations studies).
- Discuss other presenting scenarios with Toxicologist.

Management algorithm for repeated supra-therapeutic overdose[2]



ALT = alanine aminotransferase. NAC = N-acetylcysteine or acetylcysteine

Infusion of NAC

NAC is administered as a series of three infusions according to the regimen below. NAC is available at SCHN as 2g in 10mL (Acetadote®, Acetylcysteine-DBL/Link®). For more information on dilution and compatibility:

- **At CHW:** Refer to the CHW Paediatric Injectable Medicines Handbook: http://chw.schn.health.nsw.gov.au/o/apps/pharmacy/injectables/search.php?name=acetylcysteine.
- **AT SCH**: Refer to the SCH Paediatric Injectable Guideline: http://sch.sesahs.nsw.gov.au/departments/pharmacy/resources/sch_paediatric_injectable_guidelines.pdf

NAC dosage regimen:

- 1st infusion – 150 mg/kg in 3mL/kg glucose 5% (max 200mL) over 60 minutes, *followed by*
- 2nd infusion – 50 mg/kg in 7mL/kg glucose 5% (max 500mL) over 4 hours, *followed by*
- 3rd infusion – 100 mg/kg in 14mL/kg glucose 5% (max 1000mL) over 16 hours.

  NB:
  - If NAC is required beyond the initial 21 hour course, it should be charted as 150mg/kg in 5% glucose (14mL/kg; max 1000mL) over 24 hours.
  - NAC dosing should be calculated using lean body weight.

Side effects of NAC therapy:

- **Gastrointestinal upset** – nausea, vomiting, abdominal pain, diarrhoea
- **Anaphylactoid reactions** – rash, itch, wheeze, shortness of breath (SOB), hypotension – most commonly occur during the 2nd infusion. In the event of an anaphylactoid reaction, NAC therapy should be ceased for 1hr and the patient treated as per standard management (e.g. anti-emetics, antihistamines, steroids, adrenaline). The 2nd infusion may be recommenced at half the rate or, if on the 3rd 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 NAC infusion should have cardiorespiratory monitoring in Emergency Department or high dependency area 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 NAC 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 NAC infusion:

- Observe for any side effects or allergic reaction to the NAC 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 2nd infusion is started at half the rate (or same rate for 3rd infusion).
- After the first 2 hours of the infusion the child can be transferred to the ward if medically stable. Patients on NAC 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. Therapeutic Guidelines : http://etg.hcn.com.au/desktop/tgc/twg/5599.htm?acc=36422
2. Daly FFS et al. Guidelines for the management of paracetamol poisoning in Australia and New Zealand – explanation and elaboration (consensus statement) MJA 2008; 188 (5): 296-301. https://www.mja.com.au/system/files/issues/188_05_030308/dal10916_fm.pdf
3. NSW MoH Safety Information SI:001/08: http://www.health.nsw.gov.au/sabs/Documents/2008-si-001.pdf