PAEDIATRIC ACUTE CARE GUIDELINE	
Poisoning – Paracetamol	
Scope (Staff):	All Emergency Department Clinicians
Scope (Area):	Emergency Department

This document should be read in conjunction with this DISCLAIMER
http://kidshealthwa.com/about/disclaimer/

Poisoning – Paracetamol

Poisons Information Centre: 131126

Background

- Paracetamol overdose can occur as either a single large ingestion, usually as a deliberate self-poisoning, or as an accidental supra-therapeutic ingestion over days.
- Morbidity and mortality is from hepatic injury. Life-threatening liver failure is rare.
- An effective and well-tolerated antidote is available (N-Acetyl Cysteine (NAC)), and if given within 8 hours of ingestion, carries a 100% survival rate.

Limitations of this Guideline:

- This guideline will cover single overdoses, or staggered ingestions over a period of less than 8 hours of the immediate-release preparation of paracetamol.
- Supra-therapeutic overdoses of >60mg/kg/day in children (>4g/day in adults), or those involving modified release preparations (*Panadol Osteo*, *Duatrol SR*) cannot be interpreted using the Rumack-Matthew nomogram, and advice should be sought from the Toxicology Handbook[1], **Poisons information Service on 13 11 26**, or local Toxicology Services.

Approach to Paracetamol Toxicity

Resuscitation

- Resuscitation is only required in the event of co-ingestion of other agents, or in the rare event of massive acute ingestions causing coma, severe lactic acidosis and

hypoglycaemia.

Risk Assessment

- The threshold for hepatic injury following an acute ingestion varies, but is generally around 200mg/kg.
- The risk of hepatotoxicity (without treatment with NAC) can be determined by plotting the post-ingestion paracetamol level on the Rumack-Matthew nomogram below
- Time of ingestion:
    - If time of ingestion is unknown, assume that it took place at the earliest possible time, to give the worst-case scenario.
    - Patients presenting over 8 hours after ingestion with elevated transaminases are assumed to have early toxicity.
    - Patients presenting over 24 hours post ingestion with no elevated transaminases and a negative paracetamol level have a negligible risk of toxicity.

Clinical Features

- Most patients will initially present with no symptoms, or only mild gastrointestinal symptoms.
- Massive overdose is rare, but may cause coma and metabolic acidosis.
- Four chronological phases are described in cases of significant acute overdose:
    - Under 24 hours:
        - Asymptomatic
        - Mild nausea and vomiting
    - 1-3 days:
        - Right upper quadrant tenderness
        - Hepatotoxicity
    - 3-4 days (severe cases):
        - Fulminant hepatic failure and/or death
        - Acidosis
        - Renal failure
    - Day 4 to 2 weeks:
        - Recovery

Supportive Care and monitoring

- General supportive care, such as IV fluid, antiemetics, thromboembolic prophylaxis should be given as required on a case by case assessment.
- Patients with rising transaminases or INR>2.5 should have four hourly observations and BSL monitoring.

Investigations

- Screening tests in deliberate paracetamol overdoses should include an ECG and BSL.

- When a patient has taken an overdose of another agent, screening paracetamol levels should be taken anytime after 30 minutes post-ingestion. Four hour levels do not need to be done unless screening indicates a detectable level which may represent a potentially toxic overdose of paracetamol.
- Specific tests, including paracetamol levels, transaminases, INR, renal function, glucose, blood gases and platelets should be done only according to the time of presentation post-ingestion and / or concerning clinical features.

Test	**Time after paracetamol ingestion**[1]		
	< 8 hours	8-24 hours	> 24 hours
Serum paracetamol	At 4 hours post ingestion or as soon after as possible	At presentation	At presentation
Transaminases (ALT, AST)	Not indicated	At presentation and at end of 20 hour NAC infusion	At presentation
INR	Not indicated	Not indicated	At presentation
Creatinine and urea	Not indicated	Not indicated	At presentation
Blood glucose	Not indicated	Not indicated	At presentation
Blood gas	Not indicated	Not indicated	At presentation

Decontamination

- Activated charcoal is never indicated in small children with isolated paracetamol overdose.

Enhanced Elimination

- Not clinically useful

Antidote – N-Acetyl Cysteine

- Intravenous NAC is indicated in all patients who have a risk assessment suggesting the potential for hepatotoxicity or who present with clinical symptoms of hepatic injury
- Management and use of NAC in patients with a known time of overdose is shown in the flow chart below

Management Flowchart for Acute Paracetamol Exposure with Known Time of Ingestion[2]

- Patients who present with an unknown time of ingestion should have NAC commenced on arrival. It may be ceased if and when history or laboratory testing confirms a non-

toxic overdose or on advice from toxicology services.

- Patients presenting over 24 hours post ingestion should only be given NAC in the event that serum paracetamol is detectable, or hepatic transaminases are elevated. Guidance from toxicological services is recommended in these cases.
- Continuation of the infusion beyond 20 hours may be indicated in patients with delayed presentations, repeated supra-therapeutic ingestions, or those with evidence of hepatotoxicity. The third infusion dose should be repeated until transaminase levels are falling and the patient is clinically improving.

- NAC is known to cause an anaphylactoid reaction in 10-50% of patients, with symptoms including hypotension, flushing, rash and angio-oedema. This typically occurs after the first bag. It can be treated using an oral antihistamine such as loratadine or promethazine. Cessation of the infusion should only occur in severe reactions and should be restarted once the reaction is settling. This reaction does not indicate anaphylaxis.
- Patients should be cardiac monitored for the first infusion bag, and can be discontinued after this time unless an anaphylactoid reaction has occurred.
- The dosage of NAC in children is the same as in adults, but should be infused in smaller volumes of 5% dextrose (5% dextrose with 0.45% NaCl can be used if hyponatraemia is of concern)

Infusion Protocol for N-Acetyl Cysteine in Acute Paracetamol Overdose			
	Child < 20kg	**Child > 20kg**	**Adolescent > 50kg**
First infusion	NAC 150mg/kg in 3mL/kg 5% glucose over 30 minutes	NAC 150mg/kg in 100mL 5% glucose over 30 minutes	NAC 150mg/kg in 200mL 5% glucose over 15 minutes
Second infusion	NAC 50mg/kg in 7mL/kg 5% glucose over 4 hours	NAC 50mg/kg in 250mL 5% glucose over 4 hours	NAC 50mg/kg in 500mL 5% glucose over 4 hours
Third infusion	NAC 50mg/kg in 7mL/kg 5% glucose over 8 hours	NAC 50mg/kg in 250mL 5% glucose over 8 hours	NAC 100mg/kg in 1000mL 5% glucose over 16 hours
Fourth infusion	NAC 50mg/kg in 7mL/kg 5% glucose over 8 hours	NAC 50mg/kg in 250mL 5% glucose over 8 hours	

Disposition and Follow-up

- Medical discharge can be given in the following scenarios:
  - Patients with a four-hour paracetamol level below 150mg/L
  - Patients presenting within 8 hours with a level below the treatment threshold.
  - All patients who have received NAC within 8 hours of ingestion (except for those with massive overdoses) at the end of the infusion
  - Patients who have received NAC whose transaminases are improving and who are clinically well
- All cases of deliberate poisoning should be assessed psychiatrically

When to seek additional advice

- Overdose of modified release preparations
- Repeated supra-therapeutic overdoses
- Massive overdoses (>500mg/kg)
- Delayed presentations with elevated transaminases

Nursing

- Baseline observations include temperature, heart rate, respiratory rate, oxygen saturation, blood pressure and neurological observations
- Minimum of hourly observations should be recorded whilst in the emergency department
    - Any significant changes should be reported immediately to the medical team
- Apply Emla® approximately 1 hour prior to expected time of blood collection

Patient's requiring IV N-acetylcysteine

- 30 minutely heart rate, respiratory rate, blood pressure, oxygen saturation for first 2 hours then hourly if stable
- Observe for localised reaction and anaphylactoid reactions as per above medical guidelines

References

1. Murray L, Little M, Pascu O, Hoggett K. Toxicology Handbook 3rd Churchill Livingston 2015.
2. Management Flowchart for Acute Paracetamol Exposure with Known Time of Ingestion – Guidelines for the management of paracetamol poisoning in Australia and New Zealand – explanation and elaboration. Medical Journal of Australia. 2008; 188 (5); 298.
3. Chiew AL, Fountain JS, Graudins A, et al. Summary statement. New guidelines for the management of paracetamol poisoning in Australia and New Zealand. Med J Aust 2015; 2013: 215-218.doi:10.5694/mja15.00614.

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