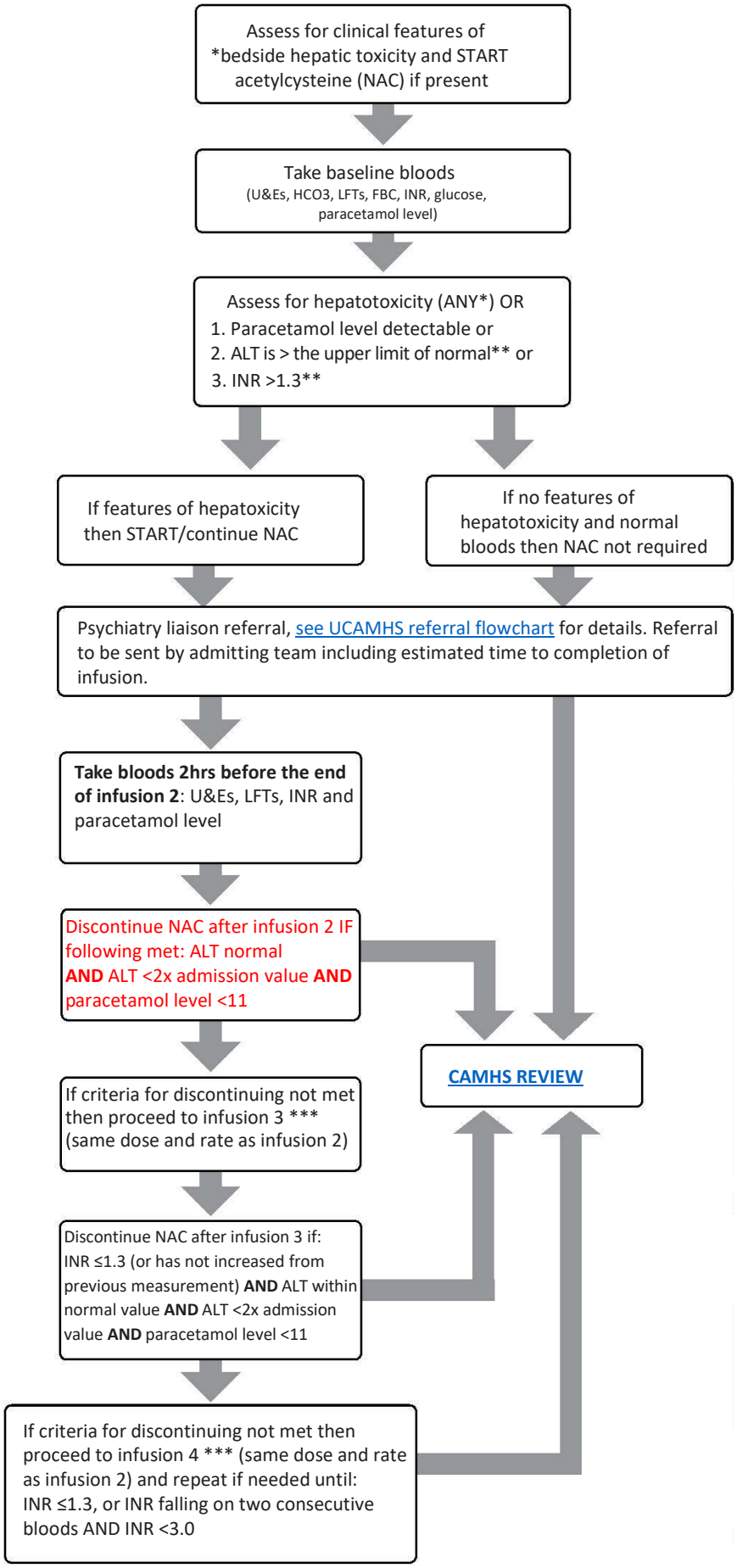
Paracetamol overdose presenting >24hrs

(Ingested total overdose in ≤1 hour time period)



*Clinical judgement required

- Bedside hepatic toxicity: Jaundice, tender liver, hypoglycaemia, encephalopathy, unexplained lactic acidosis.
- Ensure no doubt about time of ingestion or type.
- If uncertainty then treat and review with bloods.

**Clinical judgement required

- Some patients have a chronically raised ALT/INR.
- Review old LFTs/INRs and if chronic derangement discuss with a senior clinician before proceeding to NAC.

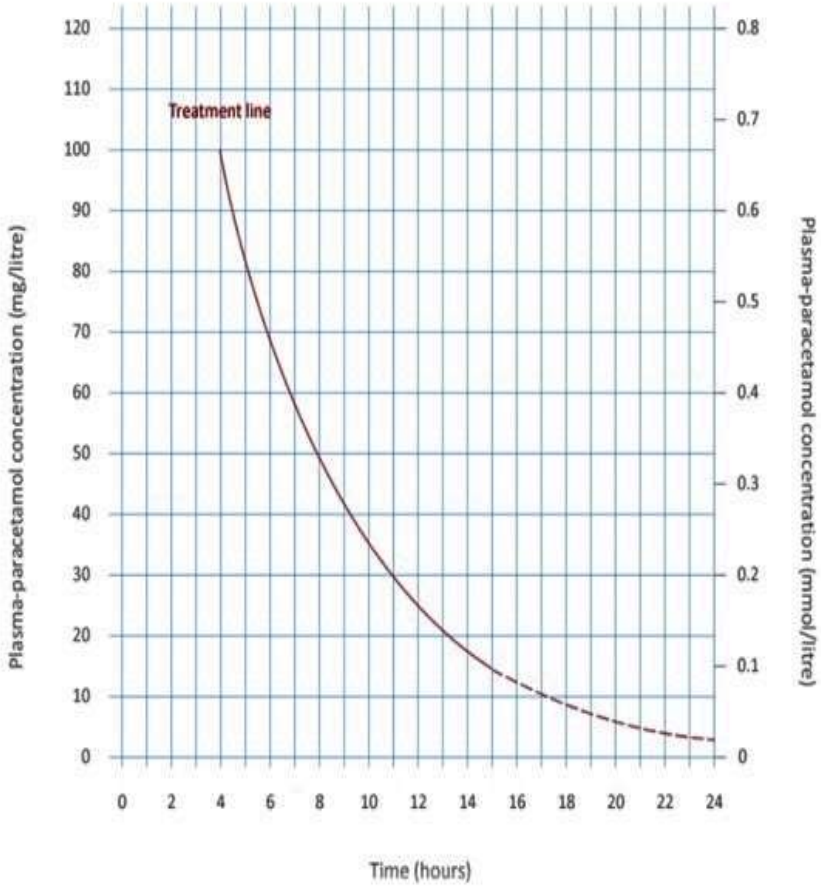
Blood monitoring

- Checking a paracetamol level 2hrs before the end of bag 2 is NEW for this protocol.
- U&E, LFTs and INR should be done 2 hours before the end of infusion 2. Ensure results are READY for the end of the infusion
- If unable to achieve blood sampling at the correct time and a delay of >90 minutes is predicted then proceed to the next infusion to avoid prolonged omission of NAC. Bloods should be checked at the earliest opportunity and discontinuation criteria referred to.
- Capillary Blood Glucose (CBG) 6 hourly while on NAC.
- If rapid or progressive biochemical deterioration then discuss with senior and consider referral to regional transplant centre.

For patients with an increase in INR and normal ALT see NAC prescribing sheet or full SNAP guideline for clinical guidance

*** **Bloods should be done 2 hours before the end of infusion 3 and 4.**

Paracetamol treatment nomogram and 12-hr shortened N-acetylcysteine dosing schedule (SNAP protocol)



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If unclear which of the five paracetamol overdose protocols to follow, discuss with ED / paeds Reg / Cons.

In situations where paracetamol levels will be used to determine need for acetylcysteine (refer to appropriate protocol), plot the measured plasma concentration (in mg/L) against the time since ingestion. If plasma level falls above the line then give acetylcysteine as detailed below.

The nomogram is less accurate between 15-24 hours and accurate ingestion time is even more vital.

Actual weight should be used for calculating both the toxic dose and the acetylcysteine dose - up to a **maximum of 110 kg**

Reactions to acetylcysteine include flushing, nausea & vomiting.
Please use 'Acetylcysteine Antidote Adverse Effects – Features & Management' guidance to document any adverse events and guide further management.

Hypersensitivity and anaphylactoid reactions with acetylcysteine are not contraindications as the benefit of treatment still outweighs the risk of not treating.

True anaphylaxis is rare with acetylcysteine but can be managed by stopping the infusion and then restarting at a slower rate.

Table 1. 12-hr shortened N-acetylcysteine dosing schedule (SNAP protocol).

Regimen	First infusion		Second (& extended) infusion	
Infusion fluid	200mL sodium chloride 0.9% or 5% glucose		1000mL sodium chloride 0.9% or 5% glucose	
Preparation	Use 250mL infusion bag and remove 50mL and add required volume of acetylcysteine		Add required volume of acetylcysteine to 1000mL infusion bag	
Duration of infusion	2 hours		10 hours	
Drug dose	100mg/kg acetylcysteine		200mg/kg acetylcysteine	
Weight (kg)	Ampoule volume (mL)	Infusion rate (mL/h)	Ampoule volume (mL)	Infusion rate (mL/h)
30-39	18	109	35	104
40-49	23	112	45	105
50-59	28	114	55	106
60-69	33	117	65	107
70-79	38	119	75	108
80-89	43	122	85	109
90-99	48	124	95	110
100-109	53	127	105	111
≥ 110	55	128	110	111

Each ampoule = 200mg/mL acetylcysteine. Dose calculation based on weight in middle of band. Ampoule rounded up to nearest whole number.

Acetylcysteine Prescribing and Administration Chart for 12-hr shortened N-acetylcysteine dosing schedule (SNAP protocol) – **RHC Glasgow**

Name: _____
Address: _____
DoB: _____
CHI: _____
Affix patient data label

Infusion 1 & 2 only

Please ensure that acetylcysteine is also prescribed on the patient's HEPMA Kardex.

Weight:……kgs
(NO NOT USE If patient <6 years of age)

Infusion 1	**Acetylcysteine 100mg/kg over 2 hours**									
Prescription						Preparation	Administration checks			
Date	Time	Dose (mL)	Diluent (200mL)	Infusion rate (mL/hr)	Prescriber's signature	Prepared/ Checked by	Date Time	Volume remaining (mL)	Volume infused (mL)	Checked by
Comments:			Stopped by:							
			Date:	Time	Signature					

Infusion 2	**Acetylcysteine 200mg/kg over 10 hours**									
Prescription						Preparation	Administration checks			
Date	Time	Dose (mL)	Diluent (1000mL)	Infusion rate (mL/hr)	Prescriber's signature	Prepared/ Checked by	Date Time	Volume remaining (mL)	Volume infused (mL)	Checked by
Comments:			Stopped by:							
			Date:	Time	Signature					

EXTENDED TREATMENT

- If extended treatment with acetylcysteine is required (see clinical guideline) then continue at the dose and infusion rate used for the infusion 2 and prescribe on the infusion 3 & 4 chart.
- Recheck bloods as per guideline 2hrs before the end of the infusions and refer to guideline regarding discontinuation of extended treatment.

Patients with an increase in INR and normal ALT

Both paracetamol and acetylcysteine treatment may cause an increase in INR in the absence of liver injury.

Patients who do not meet any of the criteria for continuation of acetylcysteine treatment but have an increase in INR of 0.4 or less (e.g. 1.1 to 1.5) AND have a normal ALT do not require further acetylcysteine.

Patients who have an increase in INR of 0.5 or more (e.g. 1.1 to 1.6) **without** an ALT rise - **STOP** acetylcysteine & recheck INR and ALT **after 4 - 6 hours**. If bloods show INR is unchanged or falling **AND** ALT is less than two times the upper limit of normal then no further treatment is required.

If the criteria above are not met - restart acetylcysteine at the dose and infusion rate used in the last treatment bag.

Acetylcysteine Antidote Adverse Effects – Features & Management

REACTION to acetylcysteine				COMPLICATIONS of paracetamol ingestion			
None ☐ Flushing ☐ Vomiting ☐ Rash ☐		Wheeze ☐ Hypotension ☐ Other: ☐ Specify.....		Abnormal liver function ☐ Acute kidney injury ☐ Hypoglycaemia ☐ Acidosis ☐		Encephalopathy ☐ Haemorrhage ☐ Other: ☐ Specify.....	
Date and time of reaction		Initial		Date and time of reaction		Initial	

MANAGEMENT OF SIDE EFFECTS

- N-acetylcysteine may cause anaphylactoid reactions in 2% of cases with this protocol. Flushing, pruritus, rash, hypotension, angioedema, bronchospasm and vomiting are most common.
- Reactions can be managed by stopping the infusion. Consider chlorphenamine for flushing/itch, nebulised salbutamol if there is bronchospasm and ondansetron if there are GI side effects.
- **Restart the infusion once the reaction has resolved at half the rate to completion of infusion.**
- Previous reaction is **NOT** a contra-indication to N-acetylcysteine and cases should receive treatment if indicated. Reactions are now considerably less common with the 12-hour SNAP protocol compared to standard regimes.

Ondansetron oral or IV slow (over 2mins) injection (Nausea and vomiting) - Age 6 months-16 years

Body weight	Dose
Up to 10kg	2mg three times daily
10 - 40kg	4mg three times daily
41kg and above	8mg three times daily

Chlorphenamine ORAL (Rash and itch)

Age	Dose
1-23 months	1mg twice per day
2-5 years	1mg 4-6 hourly (maximum 6mg per day)
6-11 years	2mg 4-6 hourly (maximum 12mg per day)
12-16 years	4mg 4-6 hourly (maximum 24mg per day)

Chlorphenamine IV INJECTION (Rash and itch)

Age	Dose
1-5 months	250 micrograms/kg (maximum four times daily)
6 months - 5 years	2.5mg (maximum four times daily)
6 - 11 years	5mg (maximum four times daily)
12 - 16 years	10mg (maximum four times daily)