Management of paracetamol overdose using 12 Hour SNAP regime

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Based on Tox Base protocols
Approved by: UHSussex MGG August 2023. Use of SNAP protocol approved by RACH Gastroenterology Teams and Kings Paediatric Liver team
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Background

- The main effects of paracetamol poisoning are delayed- onset liver and kidney damage
- Treatment with N-Acetylcysteine (NAC) is very effective but efficacy declines if administered >8 hours post ingestion
- Refer to ToxBase for most up to date advice UN: H3538 PW: NAB55P

Definitions

Significant ingestion: >75 mg/kg in >6 years or >150 mg/kg in <6 years

Staggered ingestion: dose taken over longer than 1 hour. Includes therapeutic excess

Single ingestion: dose taken all in one go or within 1 hour

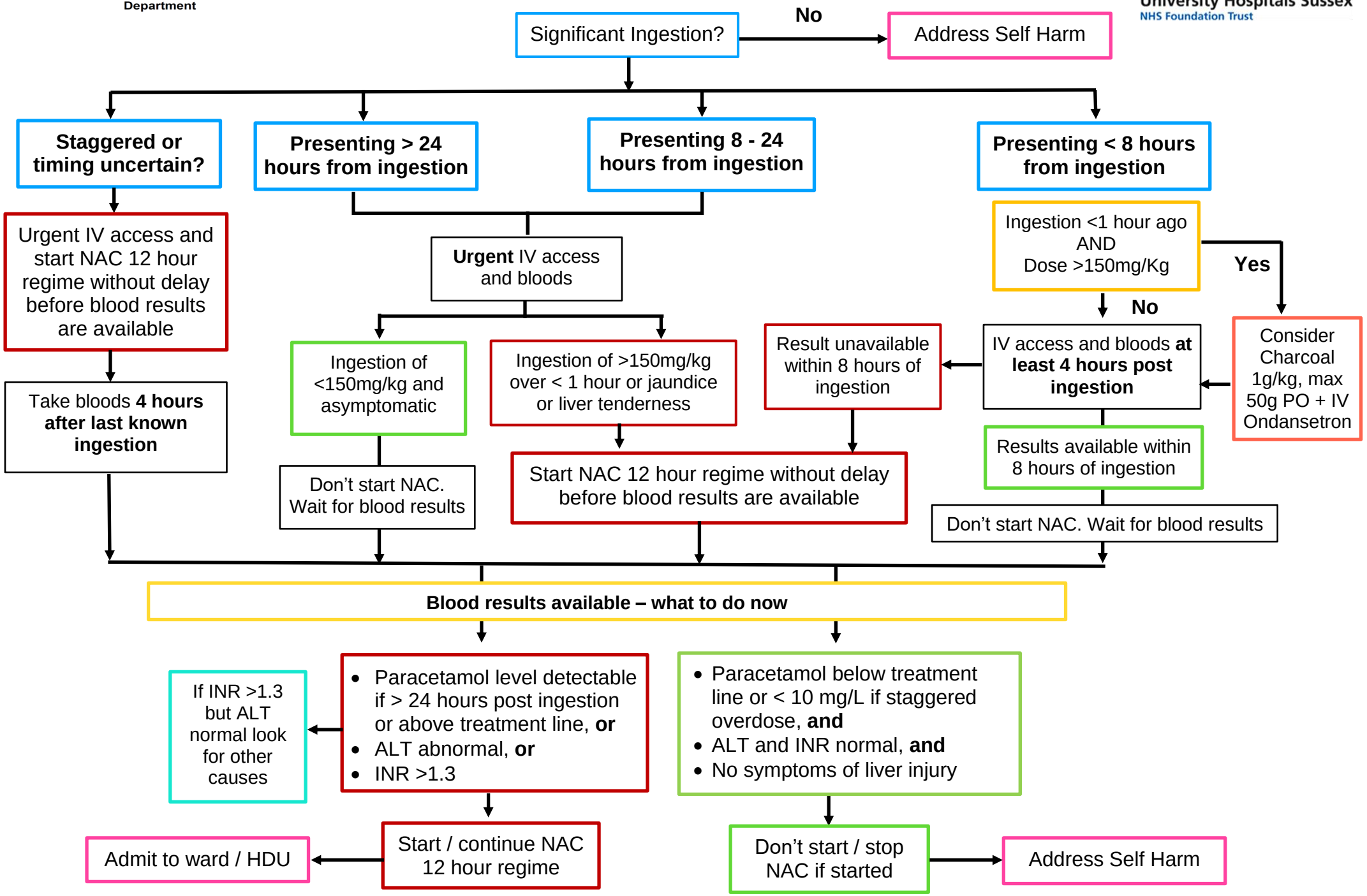
What bloods to take?

- Paracetamol level
- FBC, U&Es, LFTs, INR
- venous blood gas for glucose and bicarbonate

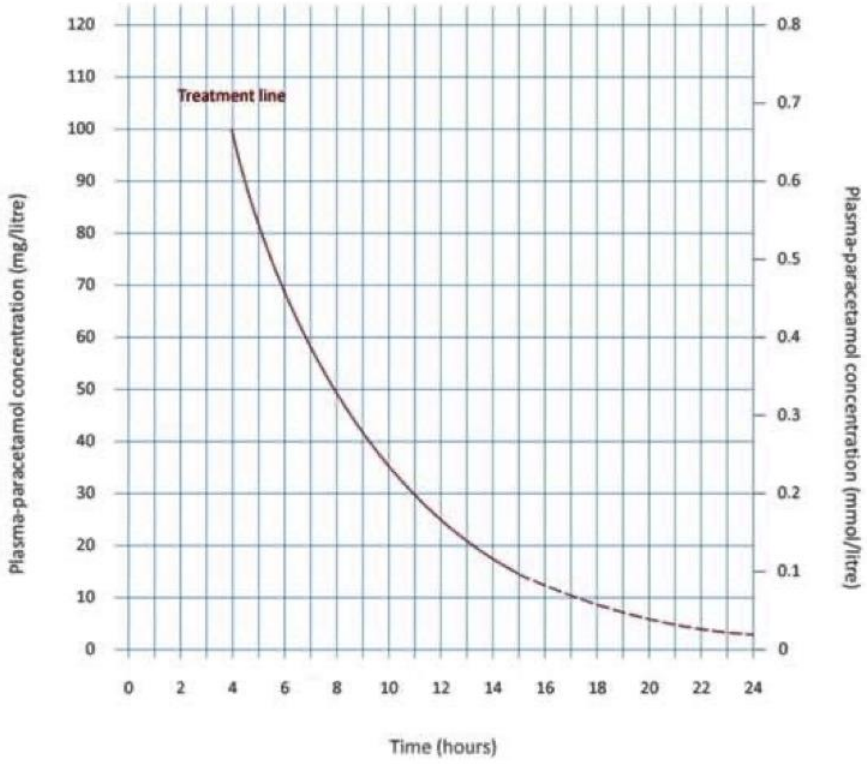
Management

See management pathway on next page

Paracetamol overdose management pathway



Paracetamol concentration treatment line – NB check units



Prescribing NAC

Dosing in obese patients

- Use actual weight for calculating **BOTH** paracetamol toxic dose and acetylcysteine dose (up to a maximum of 110 kg).

Dosing in Pregnancy – see Tox Base

- Please be aware Toxbase uses volumes >500mL for infusions of acetylcysteine. This is not trust policy at RACH and the table below has been produced for prescription and administration of acetylcysteine in volumes ≤500mL
- For all patients ≥40kg whereby total infusion volume of acetylcysteine is 1000mL, this will need to be split into TWO separate infusions of 500mL as below
- For all patients ≥25kg but ≤39kg whereby total infusion volume of acetylcysteine is >500mL, please prescribe TWO separate infusions as below
- Acetylcysteine should always be infused in 5% glucose in the first instance
- For information around reconstitution and infusing acetylcysteine, please refer to Medusa

See next page for prescribing guides

Children weighing 39kg or less

Acetylcysteine prescription for children weighing 39kg or less									
12 - Hour Regimen	First Infusion			Second Infusion					
Drug	Acetylcysteine 200mg / mL for infusion (10 mL ampoule)								
Infusion Fluid	5% glucose or 0.9% sodium chloride								
Duration of Infusion	2 Hours			10 Hours OR two separate infusions of 5 hours (total 10 hours)					
Drug dose	100mg / kg Acetylcysteine			200mg / kg Acetylcysteine					
Concentration of infusion	50 mg/mL			10 mg/mL					
Patient weight	Acetylcysteine Dose	Total Infusion Volume	Infusion Rate	Acetylcysteine dose	Multiple Infusions needed?	Acetylcysteine dose per bag (if 2 bags required)	Total Infusion Volume	Infusion Volume per Bag (if 2 bags required)	Infusion Rate
kg	mg	mL	mL / Hr	mg	Y/N	mg	mL	mL	mL / Hr
1	100	2	1	200	N		20		2
2	200	4	2	400	N		40		4
3	300	6	3	600	N		60		6
4	400	8	4	800	N		80		8
5	500	10	5	1000	N		100		10
6	600	12	6	1200	N		120		12
7	700	14	7	1400	N		140		14
8	800	16	8	1600	N		160		16
9	900	18	9	1800	N		180		18
10 - 14	1200	24	12	2400	N		240		24
15 - 19	1700	34	17	3400	N		340		34
20 - 24	2200	44	22	4400	N		440		44
25 - 29	2700	54	27	5400	Y	2700	540	270	54
30 - 34	3200	64	32	6400	Y	3200	640	320	64
35 - 39	3700	74	37	7400	Y	3700	740	370	74

Children weighing 40kg or more

Acetylcysteine Prescription for children weighing 40 kg or more (Each Ampoule = 200mg / mL Acetylcysteine)								
12 - Hour Regimen	First Infusion			Second Infusion				
Infusion Fluid	200 mL 5% glucose or 0.9% sodium chloride			2 x SEPARATE infusions of 500 mL 5% glucose or 0.9% sodium chloride				
Duration of Infusion	2 Hours			5 Hours per 500mL bag (Total 10 hours / 1000mL)				
Drug Dose	100mg / kg Acetylcysteine			200mg / kg Acetylcysteine				
Patient Weight	Acetylcysteine Dose	Ampoule Volume	Infusion Rate	Acetylcysteine Dose per 1000mL	Acetylcysteine dose per 500mL	Ampoule Volume mL	Ampoule volume per 500mL	Infusion Rate
kg	mg	mL	mL/Hr	mg	mg	mL	mL	mL/Hr
40 - 49	4600	23	112	9000	4500	45	22.5	105
50 - 59	5600	28	114	11000	5500	55	27.5	106
60 - 69	6600	33	117	13000	6500	65	32.5	107
70 - 79	7600	38	119	15000	7500	75	37.5	108
80 - 89	8600	43	122	17000	8500	85	42.5	109
90 - 99	9600	48	124	19000	9500	95	47.5	110
100 - 109	10600	53	127	21000	10500	105	52.5	111
≥110	11000	55	128	22000	11000	110	55	111

Adverse Effects

- NAC is more likely to cause adverse effects if paracetamol concentrations are low or absent. Adverse effects are also more likely in females, asthmatics, and in patients with a family history of allergy.
- Nausea, vomiting, flushing, urticarial rash, angioedema, tachycardia, bronchospasm are relatively common. Hypotension and collapse are uncommon. Anaphylactoid reactions are dose-related and most commonly occur during or soon after the initial (high dose) NAC infusion ('first bag').
- A history of anaphylactoid reactions is **NOT** a contraindication to NAC in patients with paracetamol overdose when antidote treatment is clinically indicated
    - Before starting a NAC infusion consider prophylactic treatment with antihistamines
    - Pretreatment with nebulised salbutamol may be considered if previous history of bronchospasm following NAC
    - Systemic corticosteroids have no role in the treatment or prevention of anaphylactoid reactions.

Management of patients experiencing an adverse reaction to NAC

1. Temporarily stopping the acetylcysteine may be all that is required.
2. Consider an H_1 antihistamine (e.g. chlorphenamine) and nebulised salbutamol if bronchospasm is present.

It is essential that the acetylcysteine infusion is restarted once the reaction has settled. Consider slowing the infusion rate (e.g. administer the first bag over twice as long as usual. The normal infusion rate can be used for subsequent bags).

What to do at the end of treatment
= at the end of 2nd treatment bag of NAC (12-hours after starting acetylcysteine)

1. In all patients re-check the plasma paracetamol concentration, INR, U&Es, and ALT at, or just before, the end of the 2nd treatment bag (12-hour infusion).

2. Patients who do not meet the criteria for continuing acetylcysteine and have no symptoms suggestive of liver injury can be considered for discharge

3. NAC should be continued if ANY of the following criteria are met:

- The ALT is above the upper limit of the normal range, OR
- The ALT has doubled or more from admission (even within the normal range), OR
- The paracetamol concentration is greater than 10 mg/L

Continue at the dose and infusion rate used in the 2nd treatment bag (10-hour).
It is not necessary to give a further loading dose unless a second overdose has been taken.

NB. The decision regarding whether more NAC is required at end of 12-hours is dependent on the ALT and paracetamol.

The INR does not influence this decision. If ALT does rise however, INR is needed as a marker of severity.

If the ALT is normal but INR has increased, or in patients with chronically high ALT (e.g. chronic liver disease) consult Tox Base for further guidance.

For advice regarding stopping NAC after the third bag (i.e. second 10 hour treatment bag) and beyond, please refer to Tox Base advice here: **Paracetamol - Guidance for the end of the modified 12-hour IV acetylcysteine regimen (SNAP) (toxbase.org)**

Discharge advice

Come back to hospital if any vomiting, abdominal pain, or jaundice.

NAC therapy not started
Following single acute ingestions of paracetamol where patients did not meet the criteria for NAC treatment, but had an initial paracetamol concentration above 20 mg/L, advise to avoid paracetamol for the next 12 hours.

NAC therapy given
When NAC therapy has been stopped, but the patient has ongoing abnormal liver function, the patient would be expected to have normal liver function within 2 weeks, and should therefore be advised to avoid paracetamol for this 2 week period.

Patients with normal liver function following treatment with acetylcysteine can have therapeutic paracetamol.