ED QUICK QUIZ
WHAT IS THE DIAGNOSIS?

BACKGROUND

A 23 year old female presents to ED after taking a paracetamol overdose. She was found by her flatmate acting unusually and admitted that she had taken multiple handfuls of paracetamol 2 hours previously. She is asking you to leave her alone and tells you that she just wants to die. There is no history of mental health issues and no previous episodes of self-harm. She tells you that she has been thinking about doing this for months and had ensured everybody was out of her flat before taking the tablets. A note has been written to her parents. She tells you that she split up with her boyfriend 3 months ago and she doesn't want to go on living without him. There is no concurrent alcohol use. She lost her job as an air stewardess 4 months ago.
She is asymptomatic. On assessment she is GCS 15 with no obvious head injury and a soft, non-tender abdomen.
Observations are:
Pulse 114
BP 116/84
RR 21
Oxygen sats 98% in RA
Temp 36.8
Weight 55kg

You manage to talk to her and convince her to have her bloods taken.
Her bloods show:
Paracetamol 240
Salicylate <50
Urea 5.2
Creatinine 84
Bilirubin 32
ALT 56
AST 42
PT 12
APTT 28

QUESTIONS

1. What immediate management is required?
2. When should she have her initial bloods taken?
3. Should she be referred to psychiatry?
4. What are the risk factors for paracetamol toxicity?
5. What are the indications for consideration of liver transplantation?

ANSWER & DISCUSSION

1. Immediate management

Parvolex (Acetylcysteine) is indicated if the paracetamol level is above the treatment line. It acts by binding to the toxic metabolite NAPQI and preventing hepatic necrosis. The paracetamol level in this case is 240 mg/l, which is above the treatment line on the normogram. The Parvolex dose is calculated based on weight and 3 infusions are given. For a weight of 55kg, as per NHS GGC, the 1st infusion should contain 42ml in 200ml, the 2nd 14ml in 500ml and the 3rd 28ml in 1000ml. The concentration is 200mg/ml per ampoule. The duration of infusions are 1 hour, 4 hours and 16 hours respectively. The normogram is shown at the bottom of the section. If the patient presents after 4 hours following a potentially toxic overdose then parvolex should be started immediately. The toxic dose of paracetamol is >150mg/kg (or >75mg/kg in high risk patients).

Acetylcysteine can cause side effects. These include erythema and urticarial around the injection site, nausea, angioedema, generalised urticarial, bronchospasm and hypotension. They often occur during the first infusion and are dose related. If these occur the infusion should be stopped, chlorphenamine given and the infusion restarted at the slowest infusion rate.

2. Blood timing

Bloods should be taken 4 hours after the time of ingestion, if known. The normogram is inaccurate before 4 hours.
Bloods that should be taken include:

- Paracetamol levels
- Salicylate levels – in case there is co-ingestion.
- LFTs – these may not be abnormal until >18 hours post ingestion.
- INR – sensitive marker of liver damage and the best prognostic marker.
- U&Es – creatinine is a useful prognostic marker. A low urea may indicate malnutrition.
- Glucose – hypoglycaemia may occur.
- VBG - metabolic acidosis may occur and is a poor prognostic sign.

3. Referral

The SADS PERSONS score is a useful aid memoir for the risk factors of self-harm and may be used to identify high risk patients.

Sex – Male
Age - <19 or >45 years
Depression/hopelessness
Previous attempt/psychiatric care
ETOH/Drug abuse
Rational thinking loss
Separated/divorced/single
Organised or serious attempt
No social support
Stated future attempt

1 point is gained for each positive answer, except 2 points for depression, rational thinking loss, organised or serious attempt and stated future intent.

A risk assessment scale is then calculated:

0-5 : may be safe to discharge
6-8: may require psychiatric consultation
>8: may require psychiatric hospital admission

In this case she would require psychiatric assessment and in practice all patients that have taken a large overdose should be referred to psychiatry. Her score would be 7 with hopelessness, an organised and serious attempt, stated future intent and single.

4. Risk factors

Paracetamol is normally conjugated in the liver to inactive substrates. A small amount (1%) is metabolised by the cytochrome P450 system producing a toxic metabolite, NAPQI, which is then inactivated by conjugation with glutathione. In overdose the normal conjugation pathway in the liver becomes saturated and a greater proportion is metabolised by the cytochrome P450 system. The reserves of glutathione may become depleted and the toxic metabolite NAPQI builds up causing liver necrosis.
Patients taking medications that induce the cytochrome P450 system or those with glutathione depletion are at increased risk of hepatic toxicity.

Risk factors

Induction of P450 system	**Depletion of glutathione**
Chronic alcoholics	Malnutrition
Phenytoin	Anorexia
Carbamazepine	Cachexia
Barbiturates	HIV
Rifampicin	Cystic fibrosis
St John's wort	Alcoholism

5. Liver transplantation

The patients that have any criteria for liver transplantation require an urgent referral to the liver unit in Edinburgh.
Criteria for liver transplantation in paracetamol toxicity:

- pH <7.3
- PT >100 secs
- Creatinine >300
- Lactate >3.5 on admission or >3 24hours post ingestion or after adequate fluid resuscitation.
- Grade 3 or 4 hepatic encephalopathy.

NHSGGC Adult Acetylcysteine Prescribing and Administration Chart

NHS Greater Glasgow and Clyde

Name: .....

Address: .....

.....

DoB: .....

CHI number: .....

Affix patient data label

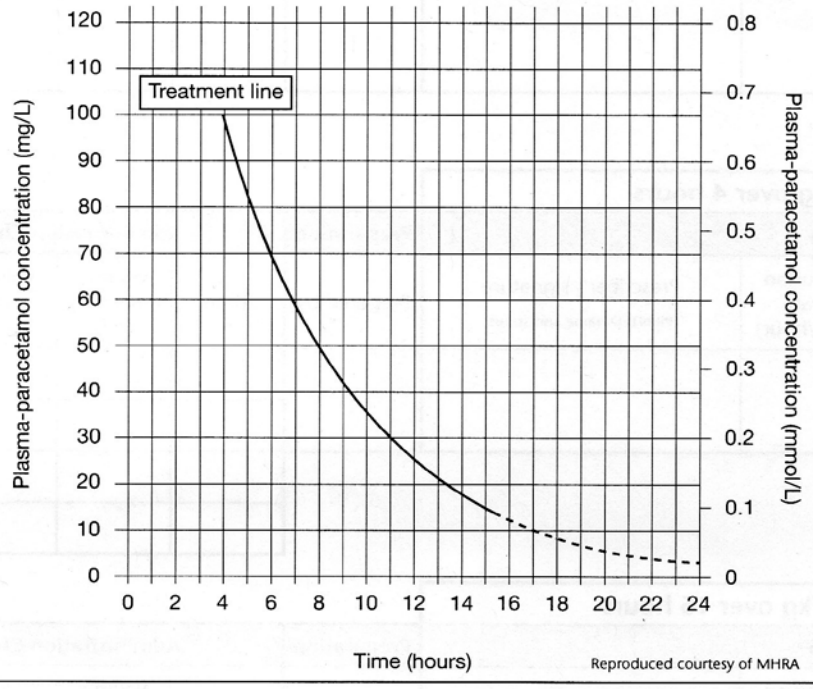
Important: Refer to the NHS GGC Therapeutics Handbook for further information on the management and biochemical monitoring of paracetamol overdose.

Weight:

Plasma paracetamol level: mg/L

Hours between sample and ingestion of paracetamol (if known): hours

Figure 1. Acetylcysteine Treatment Nomogram



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- Determine the need for acetylcysteine by plotting the measured plasma paracetamol level (in mg/L) against the time since ingestion. If plasma level falls above the line then give acetylcysteine as detailed in Table 1 below.
- If timing of ingestion is unreliable then treat with acetylcysteine regardless of whether the plasma level is above or below the treatment line.
- If overdose is staggered (taken over longer than 1 hour) then the nomogram is unreliable; see Therapeutics Handbook for management.

N.B. In NHSGGC paracetamol plasma levels reported in mg/L.

Table 1. Acetylcysteine IV adult dosing and administration

Each ampoule = 200 mg/ml

Regimen	1st infusion		2nd infusion		3rd infusion	
Infusion fluid	200 ml 5% glucose or sodium chloride 0.9%		500 ml 5% glucose or sodium chloride 0.9%		1000 ml 5% glucose or sodium chloride 0.9%	
Preparation	Use a 250 ml infusion bag and remove 50 ml prior to adding in the required volume of acetylcysteine		Add the required volume of acetylcysteine to the 500 ml infusion bag		Add the required volume of acetylcysteine to the 1000 ml infusion bag	
Duration of infusion	1 hour		4 hours		16 hours	
Drug dose	150 mg/kg acetylcysteine		50 mg/kg acetylcysteine		100 mg/kg acetylcysteine	
Patient weight[1] (kg)	Ampoule volume[2] (ml)	Infusion rate (ml/hour)	Ampoule volume[2] (ml)	Infusion rate (ml/hour)	Ampoule volume[2] (ml)	Infusion rate (ml/hour)
40 - 49	34	234	12	128	23	64
50 - 59	42	242	14	129	28	64
60 - 69	49	249	17	129	33	65
70 - 79	57	257	19	130	38	65
80 - 89	64	264	22	131	43	65
90 - 99	72	272	24	131	48	66
100 - 109	79	279	27	132	53	66
≥ 110	83	283	28	132	55	66

[1] Dose calculations are based on the weight in the middle of each band.

[2] Ampoule volume has been rounded up to the nearest whole number.

Important notes

1. Prescribe the acetylcysteine on the kardex "As per chart".
2. **Patients < 40 kg – access paediatric dosing table through TOXBASE www.toxbase.org (password required).**
3. Hypersensitivity and anaphylaxis reactions with acetylcysteine are **not contraindications** as the benefits of treatment still outweigh the risk. True anaphylaxis is rare with acetylcysteine but can be managed by stopping the infusion and then re-starting at a slower rate (e.g. give infusion 1 over 2 hours and infusion 2 over 8 hours). See Therapeutics Handbook for management of anaphylaxis
4. 1000ml bags of glucose 5% or sodium chloride will be available in Accident and Emergency Units or Medical Receiving.

Approved by NHSGGC Acute Medicine | Date of review November 2013