Guidelines for the management of acute paracetamol overdose in Ethiopia. Colour lithograph by DACA, ca. 2000.

GUIDELINES FOR THE MANAGEMENT OF ACUTE PARACETAMOL OVERDOSE
(Adults & children)

Paracetamol overdose may result in severe centrilobular hepatic necrosis. Renal tubular necrosis may also develop. Hepatic and renal failure typically manifest only after 2-5 days

A SUBSTANTIAL PARACETAMOL OVERDOSE IS DEFINED AS:

- **>150mg/kg body weight in children**
- **> 125mg/kg body weight or 7.5g, whichever is the smaller, in adults**

Section 1: MANAGEMENT

STEP 1

After paracetamol overdose, perform GASTRIC LAVAGE if LESS than 2 hours have elapsed since ingestion.

STEP 2

Give ACTIVATED CHARCOAL if patient presents before 4-6 hours after ingestion, UNLESS the antidote has to be administered orally. (See Section 2 for activated charcoal dose)

STEP 3

TAKE BLOOD for urgent estimation of the plasma paracetamol level as soon as 4 hours or more have elapsed since ingestion. Levels taken under 4 hours may not represent peak concentrations.

- Specifically request paracetamol level as some toxicology screens do not include this.

STEP 4

a) Get paracetamol LEVEL back.

- If the patient presents after 8 hours and a substantial overdose has been taken, the antidote should be administered **immediately, without waiting for plasma levels.** The antidote may be discontinued if the levels are subsequently found to be in the non-toxic range.

b) ASSESS RISK by using the Treatment Nomogram. Remember to make adjustments for high risk patients. (See Section 3)

- Delayed gastric emptying, e.g. from concomitant ingestion of dextropropoxyphene or codeine, will render a less reliable level at 4 hours post ingestion. Under such circumstances, a further reading should be obtained at ≥ 6 hours.
- If an extended-release preparation has been taken obtain an additional sample 4-6 hours after the initial sample. If both or either one of the levels is on or above the relevant treatment line, full therapy is indicated.
- The Treatment Nomogram is not reliable for blood levels taken **after** 24 hours.

DO NOT use the Nomogram and administer acetylcysteine immediately if:

- A patient **presents 24 hours or later** after a substantial or unknown dose or has detectable plasma levels or biochemical evidence of hepatotoxicity.
- There is **any** doubt about the time interval since ingestion.
- A patient has ingested repeated large amounts of paracetamol **over a period longer than 4 hours.**

STEP 5

If the patient is at risk of developing liver damage START IV ACETYLCYSTEINE (See Section 4)

- If the initial paracetamol level is in the toxic range, **full dose and duration** of antidote therapy is necessary.
- Pregnant patients are treated in the same way as non-pregnant patients.

STEP 6

If paracetamol levels are in the potentially toxic range, liver and kidney function TESTS should be performed daily until discharge. Also monitor blood glucose, electrolytes and INR.

- If the INR continues to rise on day 3-4 post ingestion refer patient to a major centre urgently.

BEFORE DISCHARGE:

- Consider social and/or psychological assessment of the patient.
- Advise ALL patients to return to the hospital if vomiting or abdominal pain develops or recurs.

STEPWISE APPROACH FOR MANAGING A PARACETAMOL OVERDOSE

(See specific steps in section 1 for explanation of procedures)

< 8 HRS AFTER INGESTION

Perform GASTRIC LAVAGE if less than 2 hours have elapsed since ingestion (Step 1)

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Give ACTIVATED CHARCOAL if patient presents before 4-6 hours (Step 2)

↓

TAKE BLOOD (Step 3)

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Get the LEVEL back and ASSESS THE RISK (Step 4)

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If the patient is at risk of developing liver damage START IV ACETYLCYSTEINE (Step 5)

If the paracetamol level is not available within 8 hours of ingestion, and a substantial overdose has been ingested, start acetylcysteine without awaiting the level. Stop treatment if level is non-toxic.

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Perform special TESTS daily until discharge (Step 6)

8-24 HRS AFTER INGESTION

In substantial overdoses or if ingested amount is unknown START IV ACETYLCYSTEINE immediately (Step 5)

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TAKE BLOOD (Step 3)

↓

Get LEVEL back and ASSESS THE RISK (Step 4)

↓

Level below treatment line and INR, plasma creatinine or ALT/AST normal and patient asymptomatic → Stop acetylcysteine

Level above treatment line or INR, plasma creatinine or ALT/AST abnormal or patient symptomatic → Continue acetylcysteine

Perform special TESTS (Step 6)

Patients who have symptoms or an abnormal INR and/or plasma creatinine require further monitoring

> 24 HRS AFTER INGESTION

In substantial overdoses or if ingested amount is unknown START IV ACETYLCYSTEINE immediately (Step 5)

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Monitor INR, plasma creatinine, arterial pH, LFTs and paracetamol level

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Only stop acetylcysteine if the INR and AST/ALT are normal or both falling, the paracetamol level is undetectable and the patient is asymptomatic

If FAST becomes elevated by 96 hours after ingestion, hepatotoxicity is present and the full course of acetylcysteine is indicated

Section 2: ACTIVATED CHARCOAL DOSAGE

Infants: 1g activated charcoal per kg in 50-100ml water Children: 15-30g activated charcoal as a single dose mixed with 100-300ml water

Adults: 50-100g activated charcoal as a single dose mixed with 400-750ml water

Section 3: HIGH RISK PATIENTS

High risk patients include:

- Alcohol abusers
- Patients with conditions causing glutathione depletion (e.g. malnutrition and HIV infection)
- Patients taking enzyme inducing drugs e.g. barbiturates, phenytoin, carbamazepine, rifampicin and meprobamate

High risk patients may develop paracetamol toxicity at lower plasma concentrations, and a lower threshold for instituting specific antidote therapy should be used **(50% of the potential toxic levels)**. SEE DOTTED LINE ON NOMOGRAM

Section 4: HOW TO USE ACETYLCYSTEINE

Dose for Adults

a) By IV infusion, initially 150mg/kg in 200ml of 5% dextrose over 15-60 minutes;
b) then 50 mg/kg in 500ml of 5% dextrose over the next 4 hours by continuous infusion;
c) followed by 100mg/kg in 1 litre of 5% dextrose over 16 hours.

Dose for Children (<12 years)

Body weight 20kg and over:

a) By IV infusion, initially 150mg/kg in **100ml** of 5% dextrose over 15-60 minutes;
b) then 50mg/kg in **250ml** of 5% dextrose over the next 4 hours by continuous infusion;
c) followed by 100mg/kg in **500ml** of 5% dextrose over 16 hours.

Body weight less than 20kg:

a) By IV infusion, initially 150mg/kg in **3ml/kg body weight** of 5% dextrose over 15-60 minutes;
b) then 50mg/kg in **7ml/kg** of 5% dextrose over the next 4 hours by continuous infusion;
c) followed by 100mg/kg in **14ml/kg** of 5% dextrose over 16 hours.

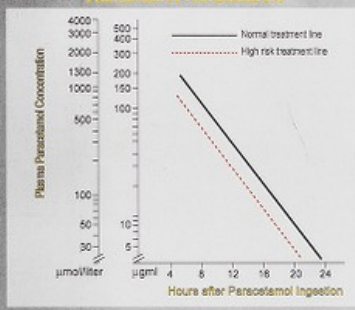
There are **strong indications that a 44-hour regimen is superior to a 20-hour regimen,** especially if treatment was started late or in seriously intoxicated patients. If AST/ALT/INR and/or plasma creatinine are elevated, then administer acetylcysteine for another 24 hours.

d) The recommended dose for the **second 24 hours** is 150mg/kg in 1 litre of 5% dextrose water over 24 hrs in adults.

Precautions:

- Volume of IV fluids should be modified for children. (As above)
- Use with caution in patients with asthma or a history of asthma
- Observe patients carefully for the emergence of hypersensitivity reactions. These reactions are often due to histamine release and not necessarily true allergic reactions. Mild reactions may be overcome by temporary cessation of the infusion. IV administration of an antihistamine, followed by a slower initial infusion rate of acetylcysteine.
- Incompatible with rubber and metals; silicone and plastic should be used.
- Plasma potassium should be monitored; hypokalaemia and ECG changes have been associated with paracetamol overdose

TREATMENT NOMOGRAM



- Patients with plasma levels above or on the normal treatment line should be treated with acetylcysteine.
- High risk patients (See section 3) should be treated if their paracetamol concentrations are above or on the high risk treatment line.
- The graph should only be used in relation to a single acute ingestion.
- Plasma paracetamol levels taken before 4 hours may not represent peak concentrations.

ALTERNATIVES TO IV ACETYLCYSTEINE

Oral acetylcysteine has proven effective in the treatment of paracetamol overdose. Oral preparations may cause nausea and vomiting, however they may be the only alternative in patients presenting with severe reactions to IV acetylcysteine. An antiemetic is indicated if vomiting is persistent. Activated charcoal should **NOT** be given if an oral antidote is used.

Dose: (oral acetylcysteine)

Oral, loading dose of 140mg/kg followed by 70mg/kg 4 hourly for 17 doses (over 72 hours). Powder should be taken with adequate amounts of fluid (250ml).

FOR FURTHER INFORMATION CONTACT

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