
# PARACETAMOL POISONING

# TOXIC DOSE


- More than 200 mg/kg as a single ingestion or over 24 hours

  (for a person over 50 kg of weight, > 10 gram - toxic dose)

- More than 150 mg/kg over 2 consecutive days

  (for a person > 50 kg, > 7.5 g ingestion over 2 consecutive days)

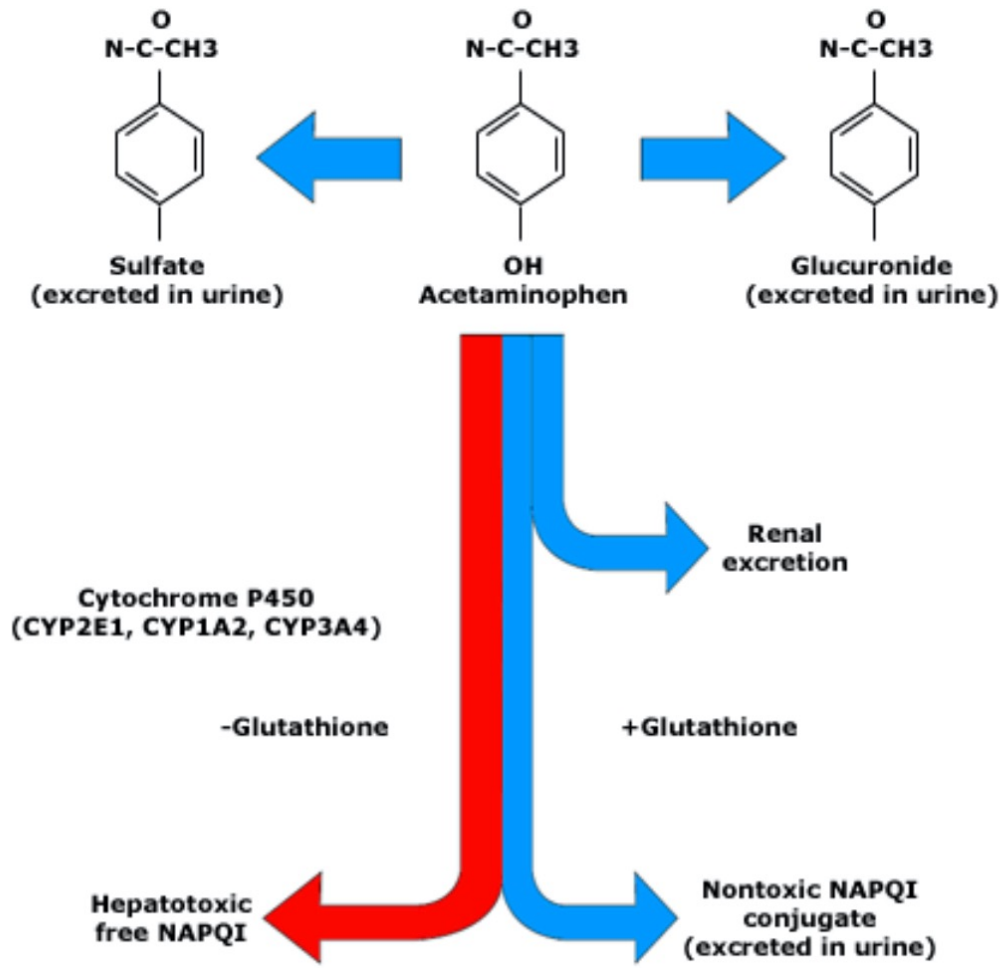

- Serum concentration peaks at 4 hours after ingestion

- Food, opioids, anticholinergics - delays absorption

# MECHANISM OF TOXICITY



**Acetaminophen metabolism**



- Therapeutic dose : 90% of acetaminophen is metabolized in liver to sulfate and glucuronide conjugates

  excreted in urine

- In the remaining 10%,

  5% is excreted unchanged in urine

  5% is metabolized via hepatic cytochrome P450 to NAPQI

  (N-acetyl p- benzoquinoneimine) - hepatotoxic


- With normal doses , NAPQI is rapidly conjugated to hepatic glutathione, forming nontoxic cysteine and mercaptate compounds that are excreted in the urine

- With toxic doses, the sulfate and glucuronide pathways become saturated, resulting in an increased fraction of acetaminophen being metabolized by cytochrome P450 enzymes. Once glutathione stores are depleted, NAPQI begins to accumulate - hepatotoxicity

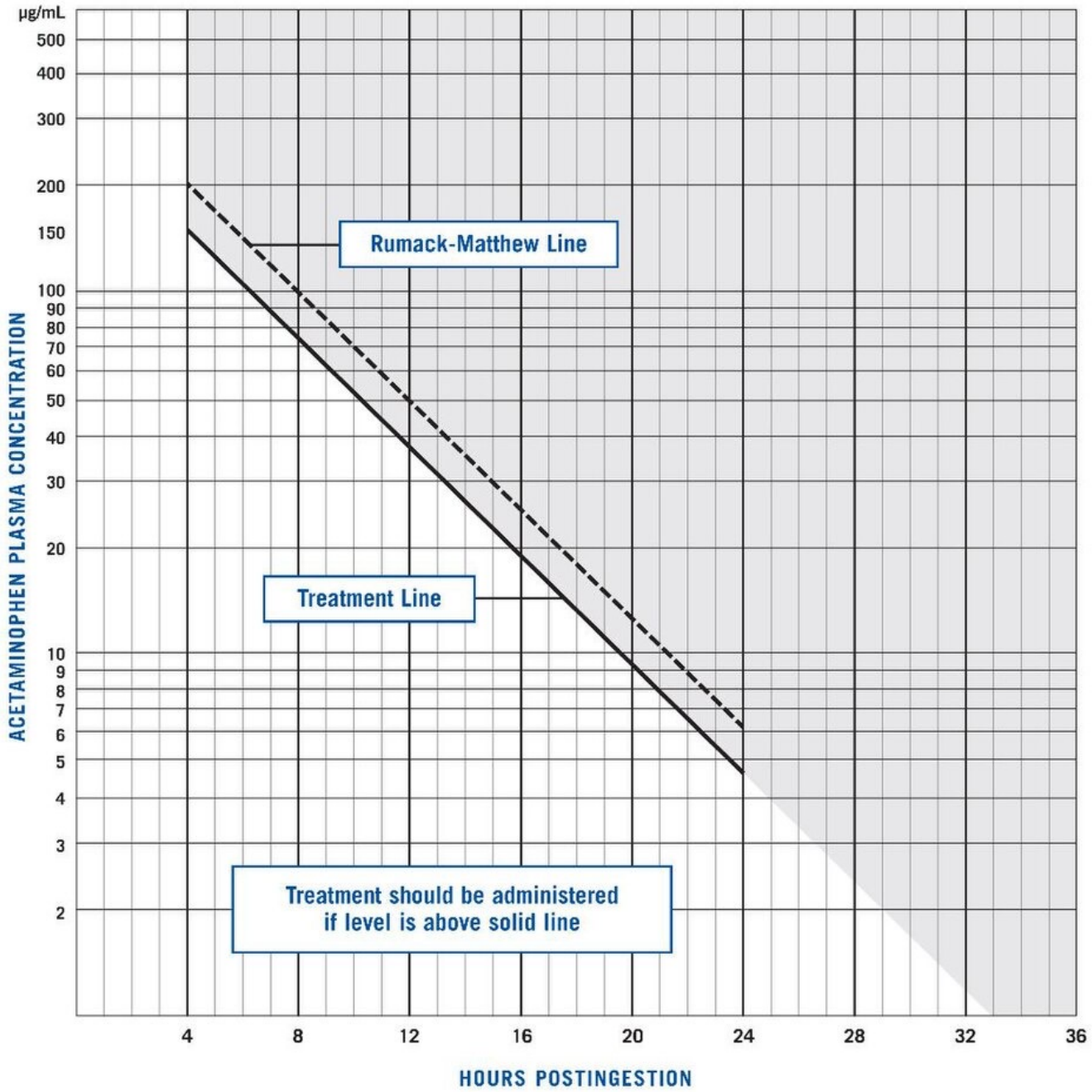
# STAGES OF ACETAMINOPHEN INTOXICATION


| Stage | Hours after ingestion | Clinical features |
|---|---|---|
| I | 0.5 to 24 hours | Nausea, vomiting, diaphoresis, pallor, lethargy, and malaise |
| | | Some patients remain asymptomatic |
| | | Laboratory studies are typically normal |
| II | 24 to 72 hours | Stage I symptoms resolve |
| | | Hepatotoxicity and nephrotoxicity become evident |
| | | Right upper quadrant pain, liver enlargement and tenderness |
| | | Elevation of aminotransferases occurs within 36 hours of ingestion in patients with hepatic injury |
| | | Elevation of prothrombin time (PT) and internationalized ratio of PT |
| | | Oliguria, abnormalities of renal function |
| | | Elevation of serum amylase with or without clinical pancreatitis may occur |
| III | 72 to 96 hours | Liver enzyme and function abnormalities peak (enzymes may be >10,000 IU/L) |
| | | Recurrence of Stage I symptoms |
| | | Jaundice, hepatic encephalopathy, hyperammonemia, bleeding diathesis, hypoglycemia, lactic acidosis |
| | | Renal failure, the incidence of which is related to the severity of intoxication |
| | | Death, from multi-organ failure, occurs most commonly in this stage |
| IV | 4 to 14 days | Recovery phase |
| | | Symptoms and laboratory values may not normalize for several weeks |
| | | Histologic recovery lags behind clinical recovery and may take up to three months |

# MANAGEMENT


- Stabilize ABC
- Gastric lavage (within 1 hour)
- Activated charcoal (1g/kg) may be used in patients presenting within 2-4 hours
- Antidote : NAC (N-acetyl cysteine). Replenishing hepatic glutathione
- Basis for determining treatment - Serum paracetamol levels

  Sample to be sent 4 hours after ingestion or immediately if time not known



# Laboratory Tests


- LFT
- PT-INR
- RFT
- Serum electrolytes
- ABG
- Serum amylase
- Serum lactate

# NAC PROTOCOL


- **Oral regimen**

  140 mg/kg followed 4 hours later by 70 mg/kg every 4 hours

  for a total of 17 doses

- **IV regimen**

  150 mg/kg of NAC diluted in 200 ml of 5% dextrose IV over 15-60 minutes, followed by

  - 50 mg/kg NAC diluted in 500 ml of 5% dextrose IV over 4 hours, followed by

  - 100 mg/kg NAC diluted in 1000 ml of 5% dextrose IV over 16 hours

- NAC may be discontinued if patient is clinically well and ALT is decreasing and PT-INR <2
- NAC should be continued (at 6.25 mg/kg/hr) in patients with persistently high paracetamol concentration > 10mg/l or ALT > 50 U/L and is increasing

# Kings College Criteria for Liver Transplantation


- pH < 7.3 or arterial serum lactate > 3 mmol/l

  OR

- All the following

  PT-INR > 6

  Serum creatinine > 3.4 mg/dl

  Grade III or IV encephalopathy