Chapter 97
Approach to Paracetamol Poisoning in the ICU

97.1 Introduction

Paracetamol (acetaminophen) poisoning is a prevalent medical emergency worldwide and a leading cause of acute liver failure. Overdose can result from a single acute ingestion, repeated supratherapeutic doses, or chronic exposure. The risk of significant morbidity and mortality increases if not managed promptly and appropriately. Early recognition, risk stratification, and timely intervention are crucial. The cornerstone of management includes thorough patient assessment, application of the Rumack-Matthew nomogram (with revisions for high-risk populations), and administration of acetylcysteine. Recent advancements have led to updated guidelines and protocols, emphasizing considerations for special populations, modified-release formulations, and resource-limited settings [1, 2]. [Ref: Algorithm 97.1].

97.2 Risk Assessment

Effective management begins with a comprehensive risk assessment to determine the likelihood of hepatotoxicity and guide treatment decisions.

97.2.1 Patient History and Time of Ingestion

Key Actions

- Determine the Time and Circumstances of Ingestion:
- Establish the exact time of ingestion to apply the Rumack-Matthew nomogram accurately.

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- In cases of staggered or repeated ingestions, assess the duration and total amount consumed.
- Identify the Type of Formulation:
- Recognize if modified-release (MR) paracetamol was ingested, as it affects absorption and management.
- Assess Co-ingested Substances:
- Identify substances like anticholinergics or opioids that may delay gastric emptying and paracetamol absorption.
- Evaluate Symptoms and Clinical Status:
- Look for signs such as nausea, vomiting, abdominal pain, or altered mental status indicating toxicity or complications.

Paracetamol dosing may be associated with acute liver injury.
Acute single ingestion: ≥ 10 g or ≥ 200 mg/kg (whichever is less)
Repeated Supratherapeutic Ingestion:

≥ 10 g or ≥ 200 mg/kg (whichever is less) over a single 24-h period
≥ 12 g or ≥ 300 mg/kg (whichever is less) over a single 48-h period or ≥ a daily therapeutic dose (e.g., ≥4 g/day in adults) per day for more than 48 h in patients who also have abdominal pain or nausea or vomiting

Rationale
Understanding the type of ingestion (acute, staggered, or repeated supratherapeutic), the formulation involved, and any co-ingested substances is pivotal for determining hepatotoxicity risk and guiding timely intervention.

97.2.2 Populations with Altered Metabolism

Considerations for High-Risk Groups:

- Chronic alcoholics
- Patients with preexisting liver disease
- Malnourished individuals
- Patients taking enzyme-inducing medications

Rationale
These populations may have depleted glutathione stores or enhanced production of the toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI), increasing their susceptibility to hepatotoxicity even at lower paracetamol doses.

97.3 Laboratory Tests

Recommended Tests
- Serum Paracetamol Concentration:
- Essential for applying the Rumack-Matthew nomogram in acute ingestions.
- Liver Function Tests (ALT/AST):
- Assess for hepatic injury; rising levels indicate hepatocellular damage.
- Coagulation Profile (PT/INR):
- Elevated INR may indicate progression to hepatic failure.
- Renal Function Tests (Serum Creatinine, BUN):
- Evaluate for potential acute kidney injury.
- Electrolytes and Glucose Levels:
- Identify metabolic derangements, such as hyponatremia.
- Arterial Blood Gas (ABG):
- Assess for acid-base disturbances.
- Additional Toxicology Screens:
- If co-ingestion is suspected.

Rationale
These investigations help stratify patients into low or high risk for hepatotoxicity, guide treatment decisions, and monitor for complications.

97.4 Management Pathways

Management should be tailored based on the type of ingestion, time since ingestion, patient-specific factors, and the presence of co-ingestants.

97.4.1 Acute Single Ingestion (<24 H)

Use of Rumack-Matthew Nomogram
- Standard Application:
- Plot serum paracetamol concentration against time since ingestion.
- If the level is above the treatment line (typically 150 μg/mL at 4 h), initiate acetylcysteine.
- Revised Nomogram for High-Risk Patients:
- For populations with altered metabolism, use a lower treatment threshold (e.g., 100 μg/mL at 4 h).

Rationale
The nomogram helps identify patients at risk of hepatotoxicity. Adjustments for high-risk populations ensure timely intervention.

97.4.2 Modified-Release Paracetamol Overdose

Challenges
- Extended Absorption Window:
- Peak serum levels may be delayed beyond 4 h.
- Potential for Double Peaks:
- Due to delayed and prolonged absorption.

Management Strategies
- Activated Charcoal:
- Administer up to 4 h post-ingestion, or later if delayed absorption is suspected.
- Serial Serum Paracetamol Levels:
- Measure at 4, 6, and 8 h post-ingestion.
- Initiate Acetylcysteine:
- Do not wait for levels if modified-release overdose is confirmed.
- Prolonged Acetylcysteine Administration:
- Extend treatment duration beyond standard protocols.

Rationale
Due to unpredictable absorption, early and prolonged treatment mitigates the risk of delayed hepatotoxicity.

Criteria for Liver Transplant (King's College Criteria)

I. Persistent acidosis (pH < 7.3) despite fluid resuscitation.

or

II. INR > 6 and creatinine >300 mmol/L with grade III or IV encephalopathy.

97.4.3 Massive Overdose

Criteria
- Ingestion of ≥30 g or ≥ 500 mg/kg (whichever is less).
- Serum paracetamol concentrations > double the nomogram line.

Management Strategies
- Higher-Dose Acetylcysteine Regimens:
- Increase the dose and duration.
- Consider Extracorporeal Elimination:
- Initiate hemodialysis in cases of mitochondrial dysfunction or persistent lactic acidosis.

Rationale
Massive overdoses may overwhelm detoxification mechanisms, necessitating aggressive interventions.

97.4.4 Staggered and Repeated Supratherapeutic Ingestions (>24 H)

Criteria
- Total dose >150 mg/kg over 24 h.
- Elevated ALT/AST levels.
- Serum paracetamol concentration > 20 μg/mL.

Management Strategies
- Initiate Acetylcysteine:
- Start treatment regardless of serum levels if clinical suspicion is high.
- Monitor Liver Function:
- Continue acetylcysteine until ALT/AST levels normalize.

Rationale
In repeated ingestions, toxicity may not correlate with serum levels, so clinical judgment is paramount.

97.4.5 Management of High-Risk and Special Populations

Pediatric Patients
- Adjusted Acetylcysteine Protocols:
- Use weight-based dosing to prevent adverse effects like hyponatremia.
- Monitoring:
- Close observation for fluid overload and electrolyte imbalances.

Pregnant Patients
- Safety of Acetylcysteine:
- Safe in all trimesters; treatment benefits outweigh risks.
- Fetal Monitoring:
- Consider obstetric consultation for fetal assessment.

Rationale
Tailoring treatment minimizes risks and maximizes benefits in vulnerable populations.

97.5 Treatment Protocol

97.5.1 Activated Charcoal

Indications
- Administer within 2–4 h of ingestion:

- Consider beyond 4 h for modified-release formulations or delayed gastric emptying.

Dosage
- Adults:
- 50 g orally
- Children:
- 1 g/kg orally (maximum 50 g).

Rationale
Activated charcoal reduces paracetamol absorption, decreasing the amount available for hepatotoxic metabolism.

97.5.2 Acetylcysteine Administration

Updated Two-Bag Protocol
- Bag 1:
- 200 mg/kg IV over 4 h.
- Bag 2:
- 100 mg/kg IV over the next 16 h.
- Total Dose:
- 300 mg/kg over 20 h.

Advantages over Traditional Three-Bag Protocol
- Simplifies Dosing:
- Reduces complexity and potential for errors.
- Reduces Adverse Reactions:
- Lower incidence of anaphylactoid reactions.

Higher Doses for Massive Ingestions
- Consider Increasing Dose:
- For ingestions >30 g or serum levels > double the nomogram line.
- Monitor Closely:
- Adjust based on clinical response and laboratory values.

Rationale
The two-bag regimen improves patient compliance and reduces side effects while ensuring effective detoxification.

97.5.3 Extracorporeal Techniques

Indications
- Massive Overdose:

- Extremely high serum paracetamol levels.
- Mitochondrial Dysfunction:
- Severe lactic acidosis unresponsive to standard therapy.

Methods
- Hemodialysis:
- Preferred method for extracorporeal elimination.

Rationale
Dialysis can remove paracetamol and its metabolites, particularly when hepatic metabolism is overwhelmed.

97.6 Monitoring and Criteria for Discontinuation

97.6.1 Ongoing Monitoring Protocols

Frequency of Measurements
- ALT/AST and INR:
- Every 12 h during acetylcysteine treatment.
- Serum Paracetamol Levels:
- As needed to assess ongoing absorption, especially in modified-release overdoses.
- Renal Function and Electrolytes:
- Regularly monitor for nephrotoxicity and electrolyte imbalances.

Rationale
Continuous monitoring detects worsening hepatic function and guides treatment adjustments.

97.6.2 Criteria for Discontinuation of Acetylcysteine

Stopping Criteria
- Decrease in ALT/AST:
- Levels falling by 25%–50% from peak values.
- Normalizing INR:
- Indicates improving liver function.
- Serum Paracetamol Concentration:
- Undetectable or < 10 μg/mL.
- Clinical Stability:
- No signs of hepatic failure or encephalopathy.

Rationale
Meeting these criteria indicates recovery, allowing safe cessation of acetylcysteine.

97.7 Special Considerations in Rural and Resource-Limited Settings

Simplified Management Protocols
- Empirical Treatment:
- Initiate acetylcysteine when paracetamol overdose is suspected.
- Use of Flowcharts:
- Provide visual aids for decision-making without extensive laboratory data.
- Community Education:
- Train healthcare workers on recognition and initial management.

Rationale
In the absence of laboratory testing, empirical treatment prevents delays that could worsen outcomes.

97.8 Algorithmic Approach

97.8.1 Decision-Making Flowchart for Paracetamol Poisoning

Step 1: Assess the Type of Ingestion
- Acute Single Ingestion.
- Modified-Release Formulation.
- Staggered or Repeated Supratherapeutic Ingestions.

Step 2: Determine Time since Ingestion
- <24 h: Use Nomogram for Acute Ingestions.
- >24 h: Consider Risk Factors and Clinical Presentation.

Step 3: Obtain Baseline Laboratory Tests
- Serum Paracetamol Concentration.
- ALT/AST Levels.
- INR and Renal Function.

Step 4: Apply Appropriate Guidelines
- Use Standard or Revised Nomogram for Acute Ingestions.
- Follow Modified-Release Protocols as Needed.
- Initiate Treatment in Repeated Ingestions if Criteria Met.

Step 5: Initiate Treatment
- Activated Charcoal if Within Timeframe.
- Acetylcysteine Using Updated Protocols.

Step 6: Monitor Patient
- Regular Laboratory Testing.
- Clinical Observations.

Step 7: Adjust Treatment
- Increase Acetylcysteine Dose for Massive Overdoses.
- Consider Extracorporeal Techniques if Indicated.

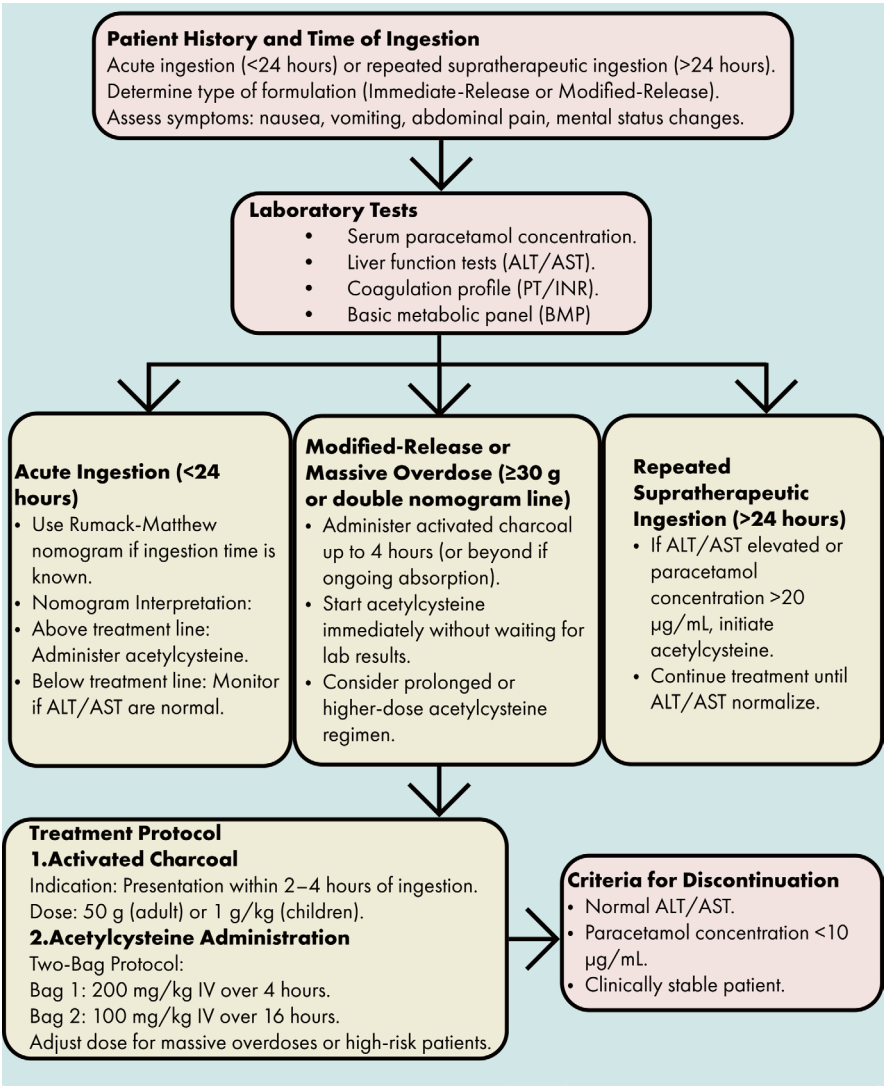
Step 8: Determine when to Discontinue Treatment
- Based on Clinical Improvement and Laboratory Criteria.

Rationale
An algorithmic approach ensures systematic assessment and management, improving patient outcomes by reducing the likelihood of oversight.

97.9 Conclusion

Management of paracetamol poisoning in the ICU requires a structured and comprehensive approach that accounts for the type of ingestion, patient-specific factors, and available resources. Early risk assessment using the standard or revised Rumack-Matthew nomogram guides timely initiation of acetylcysteine. Updated two-bag acetylcysteine protocols simplify dosing and reduce adverse reactions. Special considerations for high-risk populations, modified-release formulations, massive overdoses, and resource-limited settings enhance the effectiveness of interventions. Continuous monitoring and clear criteria for treatment discontinuation ensure patient safety. Utilizing algorithmic decision-making tools aids clinicians in providing optimal care across diverse clinical scenarios.

Algorithm 97.1: Approach to paracetamol poisoning in the ICU



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