# TYLENOL OVERDOSE

(*Last updated October 2020; Reviewers: Tabinda Jawaid, MBBS, Aysun Tekin, MD; Ognjen Gajic, MD)*

**PRESENTING COMPLAINT:** History of ingestion, nausea, abdominal pain, sweating.

**FINDINGS**

- **A** Check airway
- **B** ↑ RR
- **C** ↓/↑/N BP, ↑/N HR
- **D** Initially normal (A) , later variable (V,P,U,D)*
- **E** Pallor, diaphoresis, right upper quadrant pain
- **$U_{PC}$** mild hepatic enlargement
- **$L_{PC}$** ABG: ↓ pH, ↓ $HCO_3$, ↓ $CO_2$ ,

*V (verbal), **P** (Pain), **U** (unconsciousness), **D** (delirious)

**$L_{PC}$** (point-of-care labs), **$U_{PC}$** (point-of-care ultrasound)

**OTHER HISTORY**

1. **0-24 hours:** Possibly asymptomatic, general malaise, nausea, vomiting, diffuse abdominal pain, fatigue, anorexia
2. **24-72 hours:** Right upper quadrant pain.
3. **72-96 hours:** Jaundice, vomiting, GI upset, coagulopathy, encephalopathy, metabolic acidosis, pancreatitis, possible acute renal failure.
4. **>96 hours:** Full resolution of hepatotoxicity (OR) multi-organ failure and death.

## DIFFERENTIAL DIAGNOSIS

- Alcoholic hepatitis
    - Other drug or toxin-induced hepatitis
- Viral hepatitis
- Hepatobiliary disease
- Reye's syndrome
- Ischemic hepatitis ("shock liver")

## OTHER INVESTIGATIONS

**Monitoring:**

- If ALT elevation present:
    - ALT and INR to be checked every 12 hours.
- If ALT > 1000 IU/L, INR >1.5, OR encephalopathy:
    - ALT, INR, bicarbonate, glucose, creatinine to be checked every 12 hours.
- Prior to ending treatment:
    - Acetaminophen level, INR, bicarbonate, creatinine
    - Continue treatment if any results are abnormal

- Refer for emergent liver transplant:

  Kings College Criteria

    - Arterial pH <7.3 OR
    - INR >6.5 AND Cr > 3.4 mg/dl AND grade 3 or 4 hepatic encephalopathy

        - Grade 3 hepatic encephalopathy: marked confusion, incoherent speech, sleeping but arousable
        - Grade 4 hepatic encephalopathy: comatose

- Rumack-Matthew nomogram: https://en.wikipedia.org/wiki/Rumack-Matthew_nomogram
    - Initiation of treatment is based on the Acetaminophen level drawn 4 or more hours after a single Acetaminophen ingestion
    - If multiple ingestions occurred initiate treatment regardless of level
    - If long-acting formula ingested get a level 4 hours after ingestion and then again 8 hours after ingestion to make sure a peak was reached

- **Additional tests:** serum salicylate levels, pregnancy test in women of childbearing age, AST, ALT, serum BUN and creatinine, glucose, serum total bilirubin level, PT, INR, NH3, urine screening for other drugs or toxins, lipase, amylase, ammonia, and urinalysis.

- **Imaging:** Abdominal CT (hepatotoxicity)

**THERAPEUTIC INTERVENTIONS**

- **Medications:**
    - Activated charcoal 50 grams
        - Only in patients presenting within first 4 hours of acute overdose
        - Contraindications: airway compromise, sedated, gastrointestinal tract injury

- **N-Acetylcysteine**
  - Indications:
    - Serum acetaminophen concentration is above the treatment line on the Rumack-Matthew nomogram
    - Serum acetaminophen level is not available
    - Time of ingestion is unknown
    - Staggered overdose
    - Ingestion of >150 mg/kg or 7.5 g
    - Evidence of hepatotoxicity
  - Oral
    - Can only be used if: not pregnant, no liver toxicity, functional GI tract
    - Dosage: 140 mg/kg loading dose, followed by 17 doses of 70 mg/kg every 4 hours
    - Duration: 24-36 hours if no signs of liver failure and acetaminophen level <10 mcg/mL
  - IV
    - 21 hour IV protocol
      - 150 mg/kg loading dose over 60 minutes followed by 50 mg/kg infused over 4 hours, then 100 mg/kg for 16 hours
      - No liver failure evidence: 21 hour protocol only
      - Evidence of liver failure: 21 hour protocol followed by 6.25 mg/kg/hr until INR <2
- Anti-emetics
  - Ondansetron or metoclopramide

- **Contact/Consult:**

  Liver transplant team if the patient is in liver failure

    - Liver failure is differentiated from liver injury by the presence of encephalopathy.

## ONGOING MANAGEMENT

- **Manage Complications:**
  - Hypotension: Fluid resuscitate, initiate pressor if MAP <65 after adequate fluid resuscitation
    - Be careful to not over fluid resuscitate: will increase cerebral edema
  - Coagulopathy: Fresh frozen plasma and cryoprecipitate only if actively bleeding
  - Avoid sedatives: will not be cleared by the liver and can accumulate

## CAUTION

- **Complications:**
  - Cerebral herniation
  - N-acetylcysteine is generally safe.
    - Rarely non IgE mediated anaphylaxis can occur.
    - Vomiting from oral formula may occur.

## REFERENCES & ACKNOWLEDGMENTS

- This card was reviewed by Reviewers: Gwen Thompson, MD; Namita Jayaprakash, MD in 2019.

- Castaldo ET, Chari RS. Liver transplantation for acute hepatic failure. HPB : The Official Journal of the International Hepato Pancreato Biliary Association. 2006;8(1):29-34. doi:10.1080/13651820500465741.

- Lancaster EM, Hiatt JR, Zarrinpar A. Acetaminophen hepatotoxicity: An updated review. Arch Toxicol 2015; 89:193-199.

- Heard K, Dart R. Acetaminophen (paracetamol) poisoning in adults: Treatment. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on April 18, 2016.)