Case: Delayed Presentation of Acute Acetaminophen Toxicity
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Target Audience: Emergency Medicine Resident, PGY-2 and above

Primary Learning Objectives:

1. Identify the primary treatment for acetaminophen toxicity, N-acetylcysteine (NAC).
2. Describe the four stages of acute acetaminophen toxicity, and determine which stage the patient is in.
3. Generate a differential diagnosis for a patient with an increased anion gap metabolic acidosis.
4. Interpret acetaminophen concentrations in the setting of an acute ingestion with a delayed presentation of greater than 24 hours.

Secondary Learning Objectives: Detailed technical and behavioral goals, and didactic points

1. Recognize the indications for liver transplant evaluation in acute acetaminophen toxicity.
2. Apply crisis resource management principles, including role assignment, closed-loop communication, and situational awareness, throughout the care of a critically ill patient
3. Communicate a patient's critical condition with appropriate consulting specialists and family members.

Critical Actions Checklist:

1. Perform an appropriate initial assessment for a critically ill patient with altered mental status.
2. Obtain fingerstick glucose levels.
3. Perform an endotracheal intubation.
4. Calculate an anion gap and determine if it is normal or increased. Generate a differential for increased anion gap metabolic acidosis.
5. Initiate NAC therapy.
6. Consult Medical Toxicology/Poison Center.
7. Consult the transplant team.

Environment:

1. Room Set Up – ED acute care area
    a. Manikin Set Up – high-fidelity simulator
        i. Female manikin, pediatric adolescent/young adult
        ii. Include vital signs monitor
    b. Props: Standard ED equipment
        i. Intubation materials, including laryngoscope, ETT sizes starting at 5.0 cuffed and up to 7.5 cuffed
        ii. Bag valve mask
        iii. Nasal cannula

SYNOPSIS OF CASE

Setting: Academic university hospital emergency department

History of Presenting Illness: The patient is a 16-year-old female with a history of depression and prior suicide attempt by naproxen ingestion 2 years prior. The patient is brought into the emergency department (ED) via EMS with a chief complaint of altered mental status after mother couldn't wake her up this morning. En route, the patient was found to be hypoglycemic to 54; EMS established IV access and administered D50. She went to an outside ED 3 days ago for a chief complaint of abdominal pain, where they obtained a complete blood count, complete metabolic panel and lipase. All labs obtained were unremarkable. They also obtained an ultrasound of the right upper quadrant and CT abdomen-pelvis. Both were negative for acute abnormalities. She was discharged with a diagnosis of gastritis. Her symptoms improved with sucralfate and ondansetron, and she was discharged with tolerable abdominal pain. Since discharge she complained of persistent abdominal pain and decreased PO intake, this morning it was hard to arouse per mother.

The patient is triaged, found to have abnormal vitals (see below) and sent to the resuscitation bay.

PMHx: Depression
Medications: Citalopram 20mg daily (ran out 2 weeks ago)
Surgical History: none
Family History: None
Social History: No observed tobacco use, drug use, or alcohol use.

SYNOPSIS OF PHYSICAL

Initial Vital Signs: HR 126/min, BP 79/35, RR 22/min, O2 sat: 95%RA, T 98.6 F (37 C)
General: Ill appearing
CNS: Doesn't open eyes to pain, groaning to pain, withdraws to pain bilaterally, GCS 10 (E1, V2, M4).
HEENT: Scleral icterus, PERRLA
CVS: Tachycardia normal heart sounds
Resp: Tachypneic, equal breath sounds bilaterally, no rhonchi, rales or wheezing
Abdo: Abdomen is soft and flat. Moans when palpating abdomen diffusely without guarding or rebound.
MSK: Back and extremities are atraumatic, lower extremities without edema, no clonus or rigidity present
Skin: Jaundiced, cool and dry, capillary refill > 3 seconds

IDEAL FLOW OF CASE

In the resuscitation bay:

1. Team lead goes over initial assessment of airway, breathing, circulation
2. Team lead requests that patient be placed on pads, pulse oximetry and two large bore IV
3. Team lead orders fingerstick glucose

    a. Found with a glucose of 120
4. Team lead orders IVF and recycling the blood pressure
    a. Blood pressure improves
5. Team lead to obtain history from mother and perform physical examination
6. Patient starts vomiting and needs to be intubated w/ RSI
7. Laboratories/imaging should be ordered and returned
8. Laboratories show severe acidosis, which may or may not include tox labs (ie. acetaminophen, salicylates, VBG). The following information should be given:
    a. EKG
    b. BMP
    c. PT/INR
    d. VBG/Lactic Acid
    e. Acetaminophen/salicylates/alcohol
    f. Rest of labs (except LFTs)
    g. CTH
9. Calculate the anion gap and discuss a list of differentials for an increased anion gap metabolic acidosis with the team
10. Liver panel returns
11. NAC is ordered
12. Resident to consult toxicology
    a. Toxicology stimulus – consideration of fomepizole, hemodialysis
    b. +/- recommend transplant service consult

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CRITICAL ACTIONS

1. **Perform primary survey in critically ill patients**
   In critical patients, a primary survey should be performed as soon as possible to determine what other critical actions might need to be taken before further assessment can occur.
   Cue Guidelines: Mother will ask, “how is she doing doctor? Will she be okay?”
2. **Obtain fingerstick glucose levels**
   Consider that hyperglycemia or hypoglycemia can point out additional etiologies that can be addressed.
   Cue Guidelines: Mom to say, “She hasn't really been eating since her stomach has been hurting, do you think her blood sugar is okay?”
3. **Endotracheal intubation**
   This should occur after GCS is determined to be low and there’s concern for airway protection.
   Cue Guidelines option 1: Patient starts vomiting non-bilious non-bloody emesis.
   Cue Guidelines option 2: Nurse states, “I think the patient is more lethargic now, what’s her GCS?”
4. **Calculate an anion gap and determine if it is normal or increased. Generate a differential for increased anion gap metabolic acidosis**
   Cue Guidelines: Nurse will say, “wow, I have never seen a bicarbonate that low in my life”
5. **Initiate NAC therapy**
   This should be prompted after significant elevation of liver enzymes with detectable APAP.
   Cue Guidelines: Nurse, “Do you think she took something? Mom did say she overdosed two years ago”
6. **Consult medical toxicology/Poison Center**
   By this point, acetaminophen toxicity should be recognized as a possibility within the differential diagnosis for drug-induced acute liver failure.
   ***Key: If the learner has not initiated NAC by this time, have the PC/Tox recommend NAC.**
   Cue Guidelines: Nursing to say, "do you want me to call anyone?”
7. **Consult transplant team**
   This could be either prompted from Medical Toxicology/Poison Center, Intensivist or determined by the resident/medical student running the case upon recognition of acute liver failure.
   Cue Guidelines: Medical Toxicology/Poison Center or Intensivist (whoever gets called first): “this patient appears to be in liver failure; do you think they’ll need liver transplant?”.

Critical Actions Checklist[1]								
Resident Name								
Case Description								
Skills Measured **Core competencies:** **PC** patient care, **MK** medical knowledge, **IC** interpersonal and communication skills, **P** professional, **PBI** practice-based learning and improvement, **SB** system-based practice	Very Unacceptable		Unacceptable		Acceptable		Very Acceptable	
Data Acquisition (D) PC MK I	1	2	3	4	5	6	7	8
Problem Solving (S) PC MK PB	1	2	3	4	5	6	7	8
Patient Management (M) PC MK IC P PB SB	1	2	3	4	5	6	7	8
Resource Utilization (R) PC PB SB	1	2	3	4	5	6	7	8
Health Care Provided (H) PC SB	1	2	3	4	5	6	7	8
Interpersonal Relations (I) IC P	1	2	3	4	5	6	7	8
Comprehension of Pathophysiology (P) MK PB	1	2	3	4	5	6	7	8
Clinical Competence (C) PC MK IC P PB SB	1	2	3	4	5	6	7	8

Critical Actions					
Yes	**No**		**Comments:**		
		Perform initial assessment			
		Obtain fingerstick glucose level			
		Perform an endotracheal intubation			
		Recognize anion gap metabolic acidosis			
		Medical Toxicology/Poison Center Consult			
		Initiate N-acetylcysteine therapy			
		Consult transplant team	**Yes**	**No**	
		Admit to PICU			**Dangerous Actions**

[1]Modified ABEM Oral Certification Examination on checklist and scoresheet

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HISTORY

Age:	16-year-old
Sex:	Female
Name:	Jane Porter
Method of Transportation:	EMS
Person Giving Information:	Mother
Chief Complaint:	Altered mental status
HPI:	The patient is a 16-year-old female with a history of depression and prior suicide attempt by naproxen ingestion 2 years prior. The patient is brought into the emergency department (ED) via EMS with a chief complaint of altered mental status after mother couldn't wake her up this morning. En route, the patient was found to be hypoglycemic to 54; EMS established IV access and administered D50. She went to an outside ED 3 days ago for a chief complaint of abdominal pain, where they obtained a complete blood count, complete metabolic panel and lipase which were unremarkable. They also obtained an ultrasound of the right upper quadrant and CT abdomen-pelvis which were negative for acute abnormalities. She was discharged with a diagnosis of gastritis. Her symptoms improved with sucralfate and ondansetron, and she was discharged with tolerable abdominal pain. Since discharge she complained of persistent abdominal pain and decreased PO intake. This morning it was hard to arouse per mother. **If asked**: Mother will disclose that there's acetaminophen ibuprofen and prescribed medications available at home. Maybe she took some when her stomach hurt the other day. **If asked**: Mother will state that she ran out of her antidepressant medications in two weeks (two weeks ago or in two weeks instead of the intended time to take them, 1 month, 3 months etc?)
Past Medical Hx:	Depression, Suicide Attempt with naproxen (2yrs ago)
Family Medical Hx:	None
Social Hx:	No observed tobacco use, drug use, or alcohol use. No disclosed relationships or sexual activity to mother.
Medications:	Citalopram 20mg QD

Required Actions within the First Three Minutes

- Perform primary survey (ABCs), obtain GCS.
- Establish IV access, place on monitor, capnography and order labs
- Check fingerstick glucose to evaluate correction of hypoglycemia
- Addressing the abnormal vital signs
    - Hypotension – 20 cc/kg of crystalloid IV fluids should be given and improvement of vitals

Branch Points (EMESIS)

- If not intubated for GCS of <8, the patient will have emesis which should cue learner of having airway compromise.
- RSI will occur from poor mentation leading to airway compromise.

POST INITIAL RESUSCITATION

- Re-assessment of vital signs after intubation.
- EKG, Post-Intubation CXR and Post-intubation sedation should be ordered

Branch Points

- IF no post-intubation sedation is ordered, cue with RT/nursing: “Hey do you want to give anything for the patient, she seems to be bucking the tube”
- If no post intubation CXR is ordered, cue with nursing: “should we get a CXR to confirm the tube?”

Labs Return

- Learner receives BMP, notices low bicarb and will calculate anion gap
- List differential for anion gap metabolic acidosis
- Learners receive PT/INR, blood gas, lactic acid, APAP and ASA levels, they should initiate NAC therapy
- Learner receives LFTs, which should cue to NAC initiation

Consults and Disposition

- Calling Medical Toxicology/Poison Center
    - Med Tox/PC to recommend NAC if the learner did not give it, case ends.
- Calling Transplant

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STIMULUS INVENTORY

1. Complete Blood Count
2. Venous Blood Gas
3. Lactic acid
4. TSH
5. Osmolarity
6. Liver Profile (not available until ICU consult)
7. CT Head (delayed until patient is intubated and hemodynamically stable)
8. Basic Metabolic Panel
9. Other electrolytes (Ca, Mg, Phos)
10. Toxicology (ASA, APAP, Alcohol)
11. Coagulation studies
12. Beta-hCG
13. Lipase
14. CXR
15. CT abdomen-pelvis (delayed until patient is intubated and hemodynamically stable)
16. POCUS: heart, lungs and abdomen

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LAB DATA AND IMAGING RESUTS

Stimulus #1		**Stimulus #9**
Complete Blood Count		**Other electrolytes**
WBC 11.5 /mm^3		Ca (ionized) 0.83 mmol/L
Hgb 14 g/dL		Mg 3.5 mEq/L
Hct 38%		PO_4 12.5 mEq/L
Plt 253 /mm^3		
		Stimulus #10
Stimulus #2		**Toxicology**
Venous Blood Gas		ASA < 2.1 mg/dL
pH 7.05		Acetaminophen (APAP) 18 mcg/mL
pCO2 19 mmHg		Alcohol < 0.05 mg/L
pO2 38 mmHg		
HCO_3 5.1 mEq/L		**Stimulus #11**
		Coagulation Studies
Stimulus #3		PT >100 sec, INR >12.4
Lactic Acid 14 mmol/L		PTT 40 sec
Stimulus #4		**Stimulus #12**
TSH 0.4 (normal)		Qualitative beta-hCG negative
Stimulus #5		**Stimulus #13**
Osm 300 mOsm/kg (Normal: 275-295 mOsm/kg)		Lipase 10 U/L (normal 5-60 U/L)
Stimulus #6		**Stimulus #14**
Liver Profile (not available until ICU consult)		**CXR**
AST > 7500 U/L		Post-intubation: ETT in appropriate placement
ALT > 7500 U/L		
D. bili 15		
T. Bili 20 mg/dL		**Stimulus #15**
Albumin 2.0 mg/dL		CT abdomen-pelvis: no acute intraabdominal abnormalities to explain symptoms.
T. protein 7 mg/dL		
ALP 120 U/L		**Stimulus #16**
		Point-of-care-ultrasound
Stimulus #7		Heart: tachycardia, hyperdynamic, preserved EF, no pericardial effusion
CT Head: no acute intracranial abnormalities		Lung: lung sliding present bilaterally, no B-lines, no evidence of pleural effusion
		Abdomen: negative for intraperitoneal free fluid, no gallstones/sludge, no gallbladder wall thickening, no pericholecystic fluid
Stimulus #8		
Basic Metabolic Panel		
Na 132 mEq/L		
K 5.5 mEq/L		
Cl 94 mEq/L		
HCO_3 5 mEq/L		
BUN 10 mg/dL		
Cr 3.6 mg/dL		
Gluc 120 mg/dL		
AG 33		

LAB DATA AND IMAGING RESUTS

Stimulus #1

Complete Blood Count
WBC 11.5 /mm^3
Hgb 14 g/dL
Hct 38%
Plt 253 /mm^3

Stimulus #2

Venous Blood Gas
pH 7.05
pCO2 19 mmHg
pO2 38 mmHg
HCO_3 5.1 mEq/L

Stimulus #3

Lactic Acid 14 mmol/L

Stimulus #4

TSH 0.4 (normal)

Stimulus #5

Osm 300 mOsm/kg (Normal: 275-295 mOsm/kg)

Stimulus #6

Liver Profile
AST > 7500 U/L
ALT > 7500 U/L
D. bili 15
T. Bili 20 mg/dL
Albumin 2.0 mg/dL
T. protein 7 mg/dL
ALP 120 U/L

Stimulus #7

CT Head

Stimulus #8

Basic Metabolic Panel
Na 132 mEq/L
K 5.5 mEq/L
Cl 94 mEq/L
HCO_3 5 mEq/L
BUN 10 mg/dL
Cr 3.6 mg/dL
Gluc 120 mg/dL
AG 33

Stimulus #9

Other electrolytes
Ca (ionized) 0.83 mmol/L
Mg 3.5 mEq/L
PO_4 12.5 mEq/L

Stimulus #10

Toxicology
ASA < 2.1 mg/dL
Acetaminophen (APAP) 18 mcg/mL
Alcohol < 0.05 mg/L

Stimulus #11

Coagulation Studies
PT >100 sec, INR >12.4
PTT 40 sec

Stimulus #12

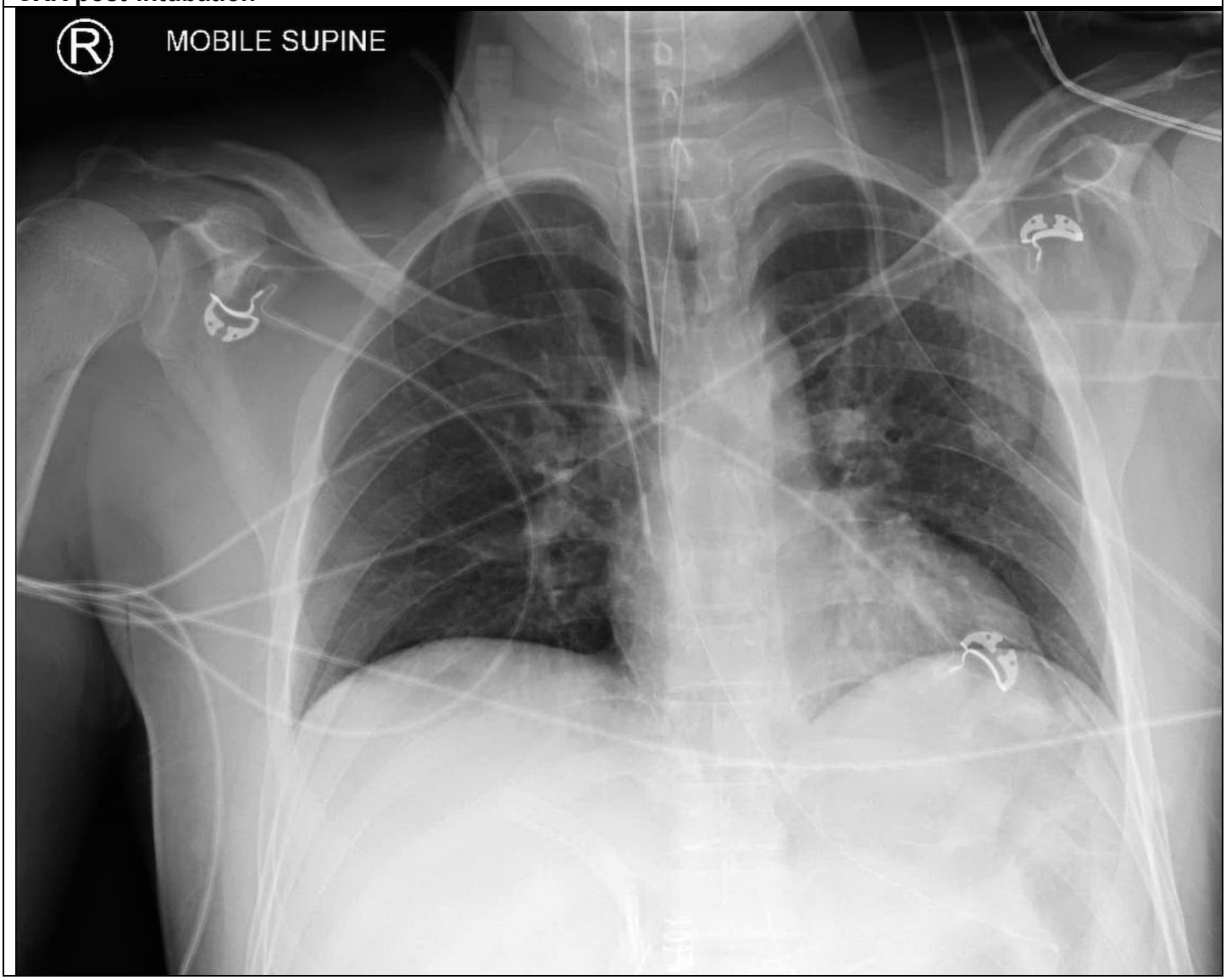
Qualitative beta-hCG negative

Stimulus #13

Lipase 10 U/L (normal 5-60 U/L)

Stimulus #14

CXR post-intubation



Stimulus #15

CT abdomen-pelvis: no acute intraabdominal abnormalities to explain symptoms.

Stimulus #16

Point-of-care-ultrasound
Heart: tachycardia, hyperdynamic, preserved EF, no pericardial effusion
Lung: lung sliding present bilaterally, no B-lines, no evidence of pleural effusion
Abdomen: negative for intraperitoneal free fluid, no gallstones/sludge, no gallbladder wall thickening, no pericholecystic fluid

Debriefing Notes: **Delayed Presentation of Acute Acetaminophen Overdose**

Educational Goals: Review the key principles of the diagnosis and management of delayed presentation of acute acetaminophen toxicity

Acetaminophen (Tylenol) is a commonly used analgesic and antipyretic that is widely available as an over-the-counter product. Deliberate or unintentional overdose can result in acute liver injury or failure, acute kidney injury, and death. It remains one of the leading causes of acute liver failure in North America, Europe and Australia.

Upon suspicion of acute ingestion, patients will have absorption within hours and have a maximum serum concentration within 4 hours. Around this maximum concentration is when the Rumack-Matthew Nomogram was built to better risk stratify patients that may develop hepatotoxicity with further concerns of deteriorating into liver failure. It's important to note that there are other factors that might influence blood acetaminophen concentration levels such as repeated supratherapeutic dosing, bezoar formation, bowel obstruction, individual genetics, and underlying liver pathologies, among others. Outside of the acetaminophen levels, it is essential to inquire about the patient's clinical course, which is generally established within stages relative to patient's time of ingestion (Table 1).

Table 1. Stages of Acute Acetaminophen Poisoning

Stage	Time Post ingestion	Description
I	0-24 hours	Anorexia, Nausea, vomiting
II	24-72hours	Right upper quadrant abdominal pain (common), transaminitis and, if severe, bilirubin and PT sometimes elevated
III	72-96 hours	Vomiting and symptoms of liver failure. Peaking of liver enzymes, bilirubin, and INR. Sometimes renal failure and pancreatitis
IV	> 5 days	Resolution of hepatotoxicity or progression to multi-organ failure (sometimes fatal)

Liver enzymes = alanine aminotransferase (ALT) and aspartate aminotransferase (AST); INR: international normalized ration; PT: prothrombin time

Mechanism of Toxicity

Acetaminophen is largely metabolized by the liver and largely conjugated to nontoxic metabolites such as APAP sulfate (20-46%) and APAP glucuronide (40-67%). However, around 5% and up to 50% (when other routes have been saturated) will be metabolized by CYP2E1 to produce N-acetyl-p-benzoquinone imine (NAPQI) that leads to toxicity.

Pharmacokinetics

Oral bioavailability	60% - 98%
Volume distribution	1 L/kg
Half-life	2-3 hours (nontoxic doses)
Peak plasma concentrations time	4 hours

Toxic Dose

Adults: 7-10 g/dose
Children: 150 mg/kg

Clinical Presentation

Many physicians have clinical experience with patients who acutely overdose on acetaminophen-containing products and present to healthcare facilities shortly after, fewer have encountered a scenario where a patient presents during stage III of acetaminophen toxicity.

In this case, the patient's history reveals that she presented with similar symptoms 3 days ago to an outside hospital. What is not known is that she had an acute ingestion of acetaminophen prior to that ER visit, but she did not tell anyone. After symptomatic relief, she felt improved and went home. However, as the acetaminophen was absorbed and created toxic amounts of NAPQI over the next 1-3 days, she became more ill, prompting the emergency department visit with her mother.

By this time, she has developed acute liver failure from the build-up of toxic acetaminophen byproducts, leading to liver failure, as seen on the diagnostics tests (Liver panel, PT/INR, Cr, hypoglycemia) and as defined by the King's College Criteria.

Diagnosis

The diagnosis of delayed presentation of acute acetaminophen ingestion should not rely on the Rumack-Matthew Nomogram. The nomogram is helpful in determining whether an acetaminophen concentration obtained 4-24 hours post ingestion will lead to possible liver toxicity. In patients who are undifferentiated and do not have a clear etiology of their illness, a detectable acetaminophen concentration outside the nomogram's timeframe should lead the physician to consider acetaminophen toxicity, and there should be a low threshold to initiate treatment with NAC.

This clinical case was built on a real patient encounter. The patient remained critically ill for 1-2 months. Once she was extubated and able to provide a history, she admitted to overdosing on acetaminophen a few hours prior to her initial healthcare facility visit.

Decontamination

Gastrointestinal decontamination could be considered for ingestion cases, however, there is always a risk of aspiration with GI-decontamination products such as activated charcoal. Initially, with a somnolent/lethargic patient with a low GCS and seizures, activated charcoal would be contraindicated.

If an orogastric tube was placed following intubation, then activated charcoal can be considered if ingestion was high on the differential, and there would be no absolute contraindications to that form of gastrointestinal decontamination.

Interventions: Emergency care, Supportive measures, and antidotal therapy

1. Naloxone: opioid reversal should be considered for acutely ill patients with altered mental status
2. Dextrose check and administration: hypoglycemia should be ruled out in emergency department patients with altered mental status
3. IV fluids resuscitation for hypotension
4. N-Acetylcysteine should be initiated for patients who are undifferentiated and may have drug induced liver injury. While N-Acetylcysteine is helpful in the treatment of drug induced liver injury from acetaminophen, there is growing literature that NAC has overall hepatoprotective effects. Given its safety profile with low risk of adverse effects, NAC should be considered for critically ill patients with signs of liver injury.
    a. Mechanism of Action:
    NAC acts primarily as a precursor for the synthesis of glutathione (GSH) and replenishes cysteine, the rate-limiting step in GSH synthesis. Additional minor mechanisms are that it prevents hepatotoxicity by acting as a substrate for sulfation, intracellular GSH substitute by directly binding to NAPQI, and by enhancing the reduction of NAPQI to APAP.
    b. Dosing (21-hour or "three-bag" protocol):
        i. 150 mg/kg IV over 1 hour
        ii. 50 mg/kg IV over 4 hours
        iii. 100 mg/kg IV over 16 hours

- Acetaminophen levels and liver enzymes should be repeated 1-2 hours prior to the end of the 16-hour therapy to determine if it should be discontinued or should be repeated with another 16-hour therapy regimen.
- Criteria for discontinuation:
    - Acetaminophen levels are undetectable
    - No consensus about liver enzyme levels (either one is acceptable):
        - liver enzymes are 50% of its peak value
        - liver enzymes less than AST 1000
        - significant decrease in AST with two consecutively decreasing
        - AST/ALT ratio 0.4
    - For hepatic failure (all have to be met):
        - Normal mental status (or recovery from hepatic encephalopathy)
        - INR < 2

c. Adverse reactions:
    i. Anaphylactoid reactions (14%-18%)
    ii. Stomach upset: nausea, vomiting, flatus, diarrhea
    iii. Severe reactions (1%): bronchospasm, hypotension, and angioedema

5. Fomepizole can be considered in this patient: This undifferentiated patient had an increased anion gap metabolic acidosis; the differential includes methanol and ethylene glycol, toxic alcohols which may cause end organ damage. Additionally, there is growing literature to support the use of fomepizole for severe acetaminophen toxicity. Fomepizole has been demonstrated to be an effective adjunct to standard therapy; it inhibits the CYP2E1 pathway, leading to decreased NAPQI production. It is also postulated to decrease mitochondrial injury via the JNK-pathway.
6. Vitamin K can be considered in this patient as well, given the coagulopathy reflected by PT/INR values being extremely elevated.
7. Antibiotics should be considered in an undifferentiated patient with leukocytosis, hypotension, lactic acidosis, and vital signs meeting SIRS criteria.

Prognosis

Patients who present with acute liver failure from acetaminophen are critically ill and may have poor prognosis. Following stage III of acetaminophen toxicity, patients may recover or may develop multi-system organ failure, which will require a liver transplantation. The King's College Criteria may be utilized to see which patients will require liver transplant evaluation. The criteria are seen below, and a patient meeting any of the requirements should be evaluated by a liver transplant service. In this case, the patient met all 4 criteria; she was evaluated by the local transplant team but luckily did not need a transplant and survived.

King's College Criteria:

1. pH < 7.3 after fluids resuscitation
   Or in a 24h period, all 3 of the following:
1. INR > 6 (PT > 100s)
2. Cr > 300mmol/L
3. grade III or IV encephalopathy

Do's and Don'ts

DO start NAC if you have a critically ill patient and drug induced liver toxicity is on the differential diagnosis.
DO involve poison center/medical toxicology on critically ill patients in whom ingestion is suspected.
DON'T assume that a normal value on labs that is not highlighted is normal. 'Clinically correlate'
DON'T forget to check sugar

References

- *Acetaminophen Poisoning - Injuries; Poisoning - Merck Manual Professional Edition*. (n.d.). Retrieved May 11, 2025, from https://www.merckmanuals.com/professional/injuries-poisoning/poisoning/acetaminophen-poisoning#Symptoms-and-Signs_v8343411
- Dart, R. C., Mullins, M. E., Matoushek, T., Ruha, A. M., Burns, M. M., Simone, K., Beuhler, M. C., Heard, K. J., Mazer-Amirshahi, M., Stork, C. M., Varney, S. M., Funk, A. R., Cantrell, L. F., Cole, J. B., Banner, W., Stolbach, A. I., Hendrickson, R. G., Lucyk, S. N., Sivilotti, M. L. A., … Rumack, B. H. (2023). Management of Acetaminophen Poisoning in the US and Canada: A Consensus Statement. *JAMA Network Open*, *6*(8), e2327739–e2327739. https://doi.org/10.1001/JAMANETWORKOPEN.2023.27739
- Chiew, A. L., Wood, D. M., Cao, D., Overberg, A., Faber, K., Wong, A., Thanacoody, R., Pomerleau, A. C., Gosselin, S., Bhalla, A., Lonati, D., & Bateman, D. N. (2025). Paracetamol (acetaminophen) poisoning; consensus definitions of poisoning types and outcomes to be used in the clinical toxicology recommendations collaborative systematic review. *Clinical Toxicology*. https://doi.org/10.1080/15563650.2025.2479721;WGROUP:STRING:PUBLICATION
- Tan, H., Stathakis, P., Varghese, B., Buckley, N. A., & Chiew, A. L. (2022). Delayed Acetaminophen Absorption Resulting in Acute Liver Failure. *Case Reports in Critical Care*, *2022*. https://doi.org/10.1155/2022/3672248
- Hendrickson, R. G., & McKeown, N. J. (2022). Acetaminophen. In Goldfrank's Toxicologic Emergencies (11th ed., pp. 472–491). McGraw Hill Medical. https://accessemergencymedicine.mhmedical.com/content.aspx?bookid=2569&sectionid=210270383
- Hendrickson, R. G., & Howland, M. A. (2022). N-Acetylcysteine. In *Goldfrank's Toxicologic Emergencies* (11th ed., pp. 492–500). McGraw Hill Medical. https://accessemergencymedicine.mhmedical.com/content.aspx?bookid=2569&sectionid=210261914
- Ogilvie JD, Rieder MJ, Lim R. Acetaminophen overdose in children. CMAJ. 2012 Sep 18;184(13):1492-6. doi: 10.1503/cmaj.111338. Epub 2012 Jun 4. PMID: 22664763; PMCID: PMC3447018.
- Pourbagher-Shahri, A. M., Schimmel, J., Shirazi, F. M., Nakhaee, S., & Mehrpour, O. (2022). Use of fomepizole (4-methylpyrazole) for acetaminophen poisoning: A scoping review. In Toxicology Letters (Vol. 355, pp. 47–61). Elsevier Ireland Ltd. https://doi.org/10.1016/j.toxlet.2021.11.005