

PedsCases Podcast Scripts

This is a text version of a podcast from PedsCases.com on “[Acetaminophen overdose in pediatric populations.](#)” These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedsCases.com/podcasts.

Acetaminophen overdose in pediatric populations

Developed by Parker Vandermeer and Dr. Melanie Lewis for PedsCases.com.

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Introduction:

Hi everyone, my name is Parker Vandermeer and I am a third year medical student at the University of Alberta. This podcast was developed in conjunction with Dr. Melanie Lewis, a general pediatrician and associated professor at the University of Alberta and Stollery Children's Hospital in Edmonton, Alberta. Today we are going to take a look at Acetaminophen overdose in pediatric populations. We will focus on the following 5 questions:

1. What tests are included in the initial workup of a suspected overdose?
2. What are the typical causes of drug overdose in pediatric populations?
3. How does acetaminophen overdose present?
4. Which patients are at increased risk of hepatotoxicity with acetaminophen overdose?
5. How is acetaminophen overdose managed medically?

Early one morning while on your emergency medicine rotation a 3-year-old girl, Carla, is rushed into the emergency department by EMS. The paramedic takes you aside and quickly explains that the child was found by her parents in the bathroom unconscious. Beside her lay a large empty bottle of Tylenol. They are unsure of how much was left in the bottle, or exactly how long ago she had taken it – though it must have been in the last 2 hours. GCS at presentation is 10 (E2-M4-V4) and Carla is medically stable. How are you going to manage this?

Let's start by discussing **acetaminophen**, which is one of the most commonly used analgesics and is easily available in numerous over the counter medications. Though relatively safe in low, therapeutic, doses it can be potentially lethal in overdose due to its hepatotoxicity in higher doses. Fortunately, there is a readily accessible antidote for acetaminophen toxicity: **N-acetylcysteine (NAC)**. If given within the first 8 – 10 hours following ingestion outcomes are quite good, especially in pediatric populations in which proper treatment results in very low mortality rates. However, to treat for acetaminophen overdose you first must know that overdose is the diagnosis and that your patient is stable! ABC's must be taken care of first. Ensure that your patient has a patent airway and is hemodynamically stable. After this, the initial workup for a suspected overdose should include at least: Ethanol, ASA, Acetaminophen, Cr, LFT, Osmol Gap, Electrolytes, ABG, Glucose, as well as other tests determined by the history and clinical scenario. Remember that overdose frequently occurs with multiple substances simultaneously.

Acetaminophen overdose may be intentional, unintentional, or iatrogenic. We will discuss the former two here. **Intentional overdose** is more common in older children and adolescents.

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They usually involve a *single, large dose* of acetaminophen and may be disclosed on presentation or detected with a toxicology screen. Intentional over dose rarely occurs in by the actions of younger children, though on occasion caregivers will intentionally give high doses of acetaminophen in an attempt to poison infants and young children. **Unintentional overdose** is more common with younger children. It may be the result of exploratory accidental ingestion of acetaminophen by young children who like to put everything they find into their mouth, or inappropriate dosing by caregivers who were trying to treat symptoms and who were *not* trying to harm the child. These unintentional overdoses may be caused by frequent dosing, doses which are too high, consumption of multiple acetaminophen containing products, “intentional” overdosing due to the perceived lack of improvement on pediatric doses, or by two caregivers unknowingly both treating the child among other things. Unfortunately, the signs and symptoms of overdose may mimic the symptoms which the caregivers were trying to treat – propagating the issue and delaying treatment. Caregivers may also be hesitant to admit their mistake while underestimating the potential toxicity of overdose. In general, younger children are less susceptible to developing hepatotoxicity. Though age may be used to dose acetaminophen in pediatrics, it is better to dose by weight. The maximum daily dose of acetaminophen for children under 50kg or 12 years of age should not exceed 75mg/kg/day, and is generally prescribed as 10 – 15mg/kg q4-6h PRN.

After a thorough history you discover that Carla and both of her parents have been suffering from an uncomplicated cough with headaches and rhinorrhea for the past two days. Carla had been given Tylenol in the past by her parents for headaches, and was heard earlier this morning complaining that “her head was hurting”. Carla’s father tells you that he is concerned she had taken a large amount of the Tylenol thinking that it would stop her headache.

Carla is otherwise healthy, has NKDA, no PMHx, and takes no medications regularly – other than 800UI of Vitamin D daily.

Acute acetaminophen overdose can be divided into four stages. In the first 24 hours it is common for pediatric patients to be asymptomatic. However, nausea and vomiting; diaphoresis; lethargy; and malaise may be present. This early on laboratory tests may be relatively normal. Remember that you want to treat within the first 8 – 10 hours, so these are the symptoms and signs to watch for! 1 – 3 days following ingestion signs of hepatorenal toxicity start to appear and most of the initial symptoms have improved. In those who have sustained organ damage laboratory results will be abnormal. RUQ pain and an enlarged liver may be found on physical exam. 3 – 4 days following ingestion the initial symptoms may start to reappear. If the overdose did damage, this is when your lab tests will peak. There are very few things that can elevate ALT and AST above 10 000. Acetaminophen is one of them! Stigmata of liver dysfunction will appear at this stage, and in severe overdose renal failure may also occur. If the patient is going to die from their overdose, it is generally during this 3 – 4 day post ingestion window. 4 days to 2 weeks following ingestion shows clinical recovery, followed by some histologic recovery and normalizing of laboratory values over the following weeks. If, after assessment, you have reason to believe that the amount of acetaminophen ingested was not significant enough to cause serious toxicity no treatment is necessary.

There are several conditions which increase an individual’s susceptibility to developing hepatic toxicity. Patients who are elderly, have restricted diets, lack the building blocks necessary for

¹ <http://emedicine.medscape.com/article/820200-overview>

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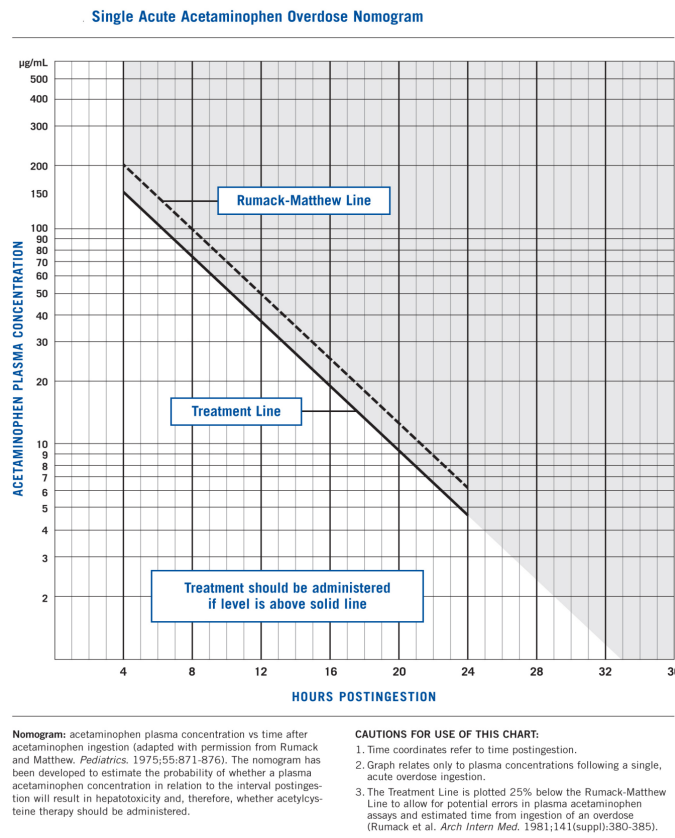
glutathione synthesis, have underlying hepatic or renal disease, or have a compromised nutritional status a number of conditions including HIV, alcoholism, cystic fibrosis, or eating disorders are at increased risk and may not require as high of doses to reach toxic levels. In addition to these conditions, medications and drugs which are metabolized by CYP450 also increase the risk of hepatocellular injury. Some common examples include: alcohol, tobacco, phenytoin, carbamazepine, TMP-SMX, and barbiturates.

Carla appears ill and lethargic; she is quiet sweaty but has not vomited. You order liver and kidney function tests, ALT, AST, an acetaminophen level, electrolytes, blood glucose, and an ABG in addition to starting an IV and giving a bolus of normal saline, followed by maintenance fluids. Although you know that it is unlikely that accidental overdose will cause serious toxicity, you order that NAC be started as well as activated charcoal, as it has been less than 4 hours since ingestion.

In those patients in which there is a risk of serious toxicity treatment needs to be started ASAP. Unintentional overdose, especially exploratory, is less likely to be in doses high enough to cause serious toxicity. However, it is still important to do your initial workup, including an acetaminophen level. An acetaminophen level should also be taken if either the dose, or the time of ingestion, are unknown. For any overdose presenting within 4 hours of ingestion activated charcoal should be considered to decrease the amount of acetaminophen available to be absorbed into the blood. There is little evidence to support giving activated charcoal after 4 hours unless medications which slow gastric motility were also ingested at the same time. A serum acetaminophen level must be ordered 4 or more hours following ingestion. If extended release acetaminophen was taken a second level should be taken 4 hours after the first. This value can then be plotted on the acetaminophen nomogram to aid in determining if treatment is necessary. Keep in mind that this nomogram can only be used for single dose ingestions, and is useless if ingestion took place more than 24 hours ago. Remember that treatment should not be delayed waiting around for lab results. If you do not know how much was ingested, or know that it was a potentially toxic amount, start treatment with activated charcoal (if within 4 hours of ingestion) and NAC before lab values return! INR, PTT, ALT, AST, and CR should be monitored throughout treatment.

³ http://www.uptodate.com/contents/management-of-acetaminophen-paracetamol-poisoning-in-children-and-adolescents?source=search_result&search=Acetaminophen+Overdose&selectedTitle=2~50

Acetaminophen Nomogram:*



In patients presenting more than 24 hours post ingestion with signs and symptoms of liver failure are still potential candidates for NAC. These patients may have nausea, vomiting, signs of liver failure, hypotension, hepatic encephalopathy, cerebral edema, among other symptoms. They may require urgent resuscitation or care in an Intensive Care Unit, which will not be discussed here.

As a rule of thumb you should be concerned about acetaminophen toxicity in pediatric patients when the single dose exceeds 7.5g or 150mg/kg. If presenting within 4 hours activated charcoal should be given at a dose of 1g/kg up to 50g PO. Contraindications to activate charcoal include altered mental status with an unprotected airway and gastrointestinal obstruction. Around 30% of patients will develop nausea and vomiting with oral activated charcoal so consider giving an antiemetic, like Ondansetron or Metoclopramide, with it.

NAC should be given within 8 – 10 hours following ingestion, but still shows benefit if given after this period. Consider NAC when the dose exceeds 7.5g or 150mg/kg; the time of ingestion is unknown and acetaminophen plasma concentrations are $\geq 10\text{mg/L}$; serum acetaminophen

* https://upload.wikimedia.org/wikipedia/commons/9/9b/Rumack_Matthew_nomogram_with_treatment_line.pdf

levels are above the treatment line on the nomogram; and in patients presenting more than 24 hours after ingestion with either symptomatic or laboratory signs of hepatotoxicity. While NAC can be given PO -- at a loading dose of 140mg/kg followed by 70mg/kg q4h x 17 doses – this is rarely done in pediatrics as NAC tastes horrible! More commonly in pediatrics NAC is given IV. The dosing and administration is complicated and beyond the scope of this podcast, but it is important to remember that it should be done in conjunction with a physician who has experience administering NAC IV. Potential complications of NAC include hyponatremia, seizures, and death. In children over 40kg NAC can be prescribed as per adults, in children less than 40kg a total dose of 300mg/kg should be given over 21 hours. As mentioned, this is not a simple infusion, and requires special monitoring to reduce the risk of adverse events.

It is now around 9 hours post ingestion and Carla's 8 hour acetaminophen level has just arrived. At 47µg/mL she falls below the line of treatment on the nomogram and you decided to discontinue the NAC while continuing the maintenance fluids. You order ALT, AST, LFT, Cr, Acetaminophen level, and Electrolytes to be completed in 4 hours and then go to see Carla and her parents.

Carla is looking significantly better than when she first presented. You let Carla and her parents know that the recent lab work shows that we are likely out of the danger zone for toxicity, but that you would like to keep an eye on everything for a few more hours just to make sure. You then briefly discuss how important it is to “always ask mom and dad about taking medicine” with Carla as well as options for keeping medications safe from children with her parents. Carla is sent home in the morning healthy and happy.

In summary, acetaminophen is an easily accessible and commonly used analgesic. In overdose, it has the potential to prove lethal if not treated with NAC and supportive care quickly. With treatment, outcomes improve significantly and fatalities are rare. As such, it is important to always keep in mind the possibility of acetaminophen overdose in patients presenting after a known or suspected suicide attempt. In patients in which accidental ingestion is suspected, education on proper medication storage is vital. Today, we have briefly gone over the work up, etiologies, presentation, and management of acetaminophen overdose in a pediatric population. Hopefully you have found this podcast helpful and informative, thanks for listening!