

# ACETAMINOPHEN

N-acetyl-p-aminophenol or (APAP) or paracetamol (PARA)

## Mechanism of Action

1. COX-associated peroxidase hypothesis  
A reducing agent inhibiting a step in prostanoid synthesis by COX enzymes
2. Cannabinoid Hypothesis  
Acetaminophen metabolite (AM404) inhibits COX, activates TRPV1 and TRPA1 channels, pain receptors that are also sensitive to cannabinoids

**25 Billion** doses used annually as a non-prescription medication

## Dosing

- <50 kg: 12.5 mg/kg every 4 hours or 15 mg/kg every 6 hours; maximum daily dose: 75 mg/kg/day ( $\leq 3.75$  g/day)
- $\geq 50$  kg: 650 mg every 4 hours or 1,000 mg every 6 hours; maximum single dose: 1,000 mg/dose; maximum daily dose: 4 g/day
- **Caution in hepatic disease/cirrhosis, limit therapy to  $\leq 2$  g/day**

## IV vs. Oral?

- 2015 Meta-analysis of 6 randomized clinical trials comparing IV and oral acetaminophen
- No clinically significant difference in efficacy between the two formulations
- These studies however looked at patients who could tolerate oral formulation. IV acetaminophen may be best used for our patients with poor GI absorption at baseline or post-surgically.

**181,640** adults who underwent colectomy at 602 hospitals, retrospective between 2011 and 2016

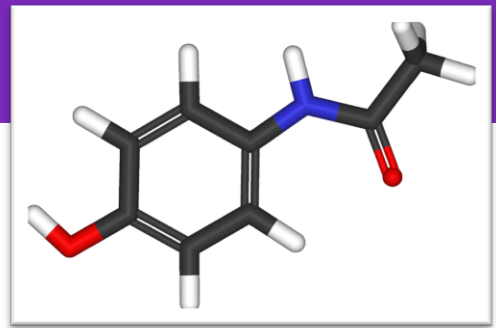
## POD#1 Opioid decrease



IV – 12.4%



Oral – 22.6%



## Pharmacokinetics

- Excellent bioavailability (98%)
- Onset 30 mins
- Peak plasma concentrations 30-60mins
- Crosses both BBB and placenta
- Half-life 1.5-2hrs
- Excretion: Hepatic conjugation by glucuronidation/sulfation and subsequent renal excretion

Caffeine accelerates absorption and decreases its clearance (increased analgesia effect when taken together)



## U.S. Lexi-comp Drug Pricing

\$52

IV Acetaminophen

\$0.55

Oral Acetaminophen

\$119

2ml vial Sugammadex (For comparison only!)

\*Pricing from UCSF lexi-comp however may not reflect current formulary pricing

## References:

1. Politi JR, Davis RL 2nd, Matka AK. Randomized Prospective Trial Comparing the Use of Intravenous versus Oral Acetaminophen in Total Joint Arthroplasty. J Arthroplasty. 2017 Apr;32(4):1125-1127. doi: 10.1016/j.arth.2016.10.018. Epub 2016 Oct 21. PubMed PMID: 27839957.
2. Jibril F, Sharaby S, Mohamed A, Wilby KJ. Intravenous versus Oral Acetaminophen for Pain: Systematic Review of Current Evidence to Support Clinical Decision-Making. Can J Hosp Pharm. 2015 May-Jun;68(3):238-47. doi: 10.4212/cjhp.v68i3.1458. Review. PubMed PMID: 26157186; PubMed Central PMCID: PMC4485512.

Wasserman et.al Anesthesiology July 2018