ACETAMINOPHEN TOXICITY

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Introduction

- Acetaminophen (Anacin-3, Liquiprin, Panadol, Paracetamol, Tempra, Tylenol, and many other brands) is a widely used drug

Mechanism of toxicity

- **A. Hepatic injury**
- **B. Renal**

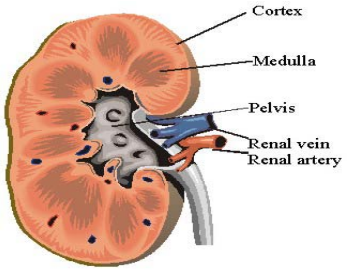


Figure 1: Anatomy of Normal Kidney

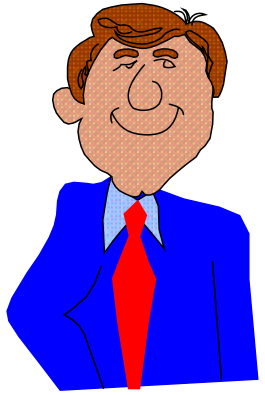
- **C. Overdose during pregnancy**

pharmacokinetic

- Onset (hr): 0.5
- Peak (hr): 0.5--2
- Half-life (hr): 1--3
- Active Metabolite: -
- Half-life of active metabolite (hr): -
- Vd (L/kg): 0.8--1
- % Protein Binding: 10--30
- Enhanced Elimination: HP
- Comments: Sustained release

Clinical presentation

- Clinical manifestations depend on the time after ingestion.
- A. Early after acute acetaminophen overdose,
- B. After 24-48 hours, (AST and ALT)



Toxic dose

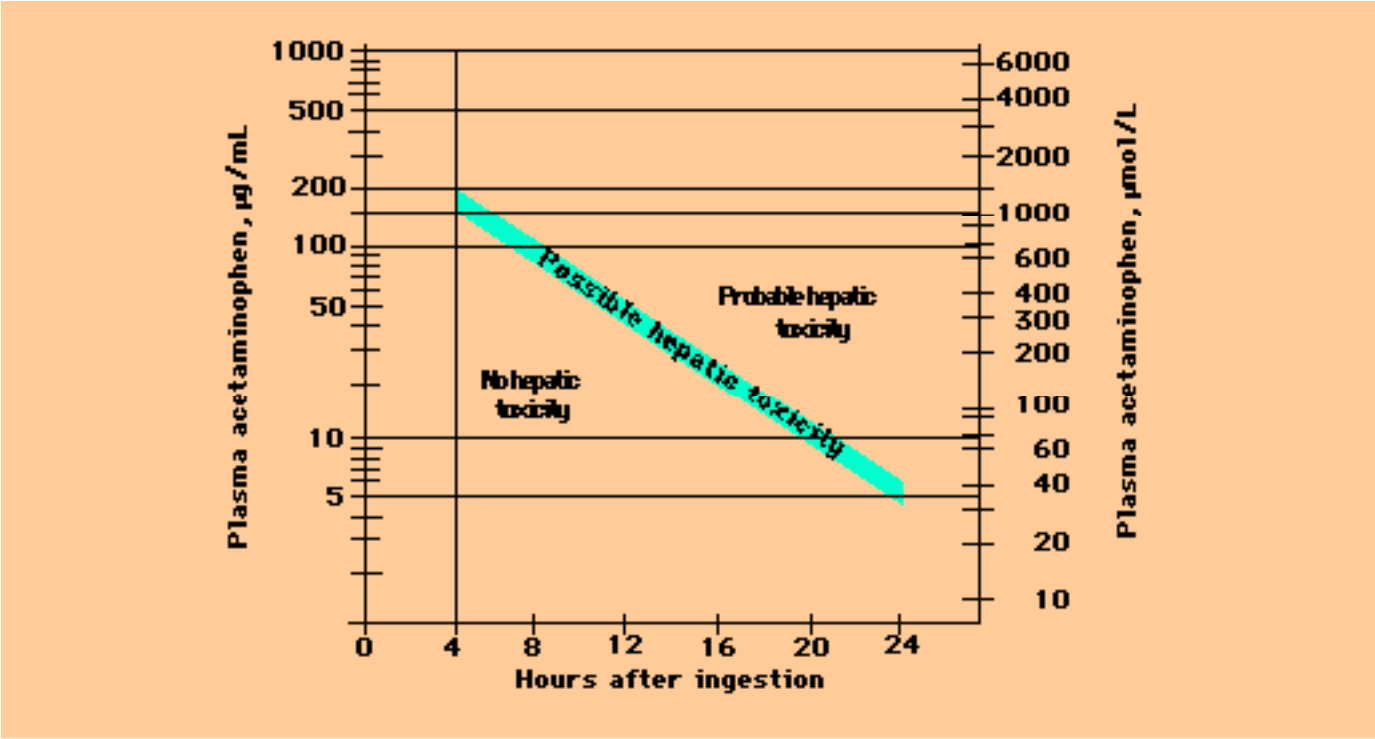
- A. Acute ingestion of more than 150-200 mg/kg in children or

- B- 6-7 g in adults is potentially hepatotoxic.

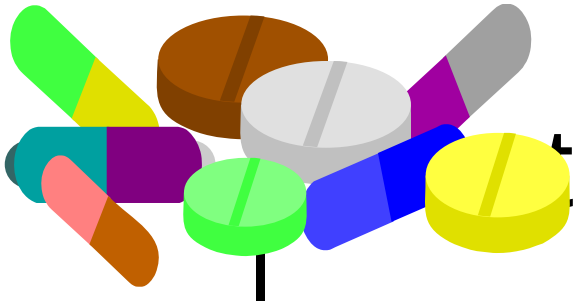
Diagnosis

- Specific levels

- Other useful laboratory studies (figure 1)



Severity of acetaminophen intoxication Relationship between plasma acetaminophen concentration (in µg/mL or µmol/L), the time after drug ingestion, and the risk of hepatic toxicity. The thick diagonal line of possible hepatic toxicity represents a 25 percent likelihood of disease. A relatively low level (such as 10 µg/mL) is safe soon after ingestion, but associated with appreciable risk at 24 hours since it reflects a high initial load which has now distributed into the tissues. (Redrawn from Rumack, BH, Matthews, H, Pediatrics 1975; 55:873.)



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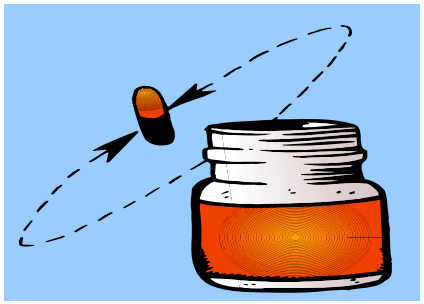

- Emergency and supportive measures

- Specific drugs and antidotes

References

- Boutis K, Shannon M: Nephrotoxicity after acute severe acetaminophen poisoning in adolescents. J Toxicol Clin Toxicol 2001;39(5):441-445. [PMID: 11545233] (Nephrotoxicity occurred in about 9% of adolescents with severe acetaminophen poisoning.)
- Brok J et al: Interventions for paracetamol (acetaminophen) overdoses. Cochrane Database Syst Rev 2002;(3):CD003328. [PMID: 12137690] (There are few randomized controlled trials of treatment, but oral activated charcoal and use of N-acetylcysteine is recommended, with no NAC regimen proven more effective than any other.)


THANK YOU