

# Acetaminophen Overdose

## Acetaminophen General Information

Litovitz TL et al. 2001 Annual Report of the American Association of Poison Control Centers. Toxic Exposure Surveillance System. *Am J Emer Med.* Sept 2002;20(5):391-452. **LOE = E**

Lee WM. Drug-induced Hepatotoxicity. *N Engl J Med* 1995;333:1118. **LOE = E**

Davidson DG, Eastham WN. Acute liver necrosis following overdose of paracetamol. *Br Med J.* 1966;2:497. **LOE = E**

## Laboratory Testing

O'Grady JG et al. **Early Indicators of Prognosis in Fulminant Hepatic Failure.** *Gastroenterology* 1989;97:439-45 **LOE = B**

### King's College Hospital Criteria

- ◆ arterial pH < 7.30
- ◆ peak prothrombin time > 100 sec
- ◆ serum creatinine > 300 Mmol/L

Shakil A et al. Acute liver failure: clinical features, outcome analysis and applicability of prognostic criteria. *Liver Transplant* 2000;6:163-69.

Makin A et al. A 7 year experience of severe acetaminophen induced hepatotoxicity. *Gastroenterology* 1995;109:1907-16.

Mitchell I et al. Earlier identification of patients at risk from acetaminophen induced acute liver failure. *Crit Care Med* 1997;26:279-84.

Bernal W et al. Blood lactate as an early predictor of outcome in paracetamol-induced acute liver failure: a cohort study. *Lancet* 2002;359:558-63. **LOE = B**

- ◆ measured lactate level at 4 hrs and 12 hrs.
- ◆ > 3.5 mmol/L at 4hrs identified as earlier predictor of need for transplant
- ◆ > 3.0 mmol/L at 12hrs identified as earlier predictor of need for transplant

## Gastric Lavage and Activated Charcoal

Pond SM et al. Gastric emptying in acute overdose: A prospective randomized controlled trial. *Med J Aust* 1995;163:345-349. **LOE=A**

- ◆ gastric lavage added no difference in clinical outcome than charcoal alone

Buckley NA et al. Activated charcoal the need for NAC treatment after acetaminophen overdose. *Clin Tox.* 1999;37(6):753-57. **LOE=C**

- ◆ charcoal administration decreased likelihood of patient having high risk acetaminophen level

Kulig et al. Management of acutely poisoned patients without gastric emptying. *Ann Emer Med.* 1985;14:562-7. **LOE = A**

Rose et al. Simulated acetaminophen overdose: pharmacokinetics and effectiveness of activated charcoal. *Ann Emer Med.* 1991;20:1064-8. **LOE = B**

- ◆ charcoal administration decreased likelihood of patient having high risk acetaminophen level  
best results when given two hours within time of ingestion

## Gastric Lavage and Activated Charcoal cont.

Spiller et al. A prospective evaluation of the effect of activated charcoal before oral NAC in acetaminophen overdose. *Ann Emer Med.* 1994;23:519-23. **LOE = C**

- ◆ Activated charcoal does not reduce efficacy of N-acetylcysteine Treatment with N-acetylcysteine

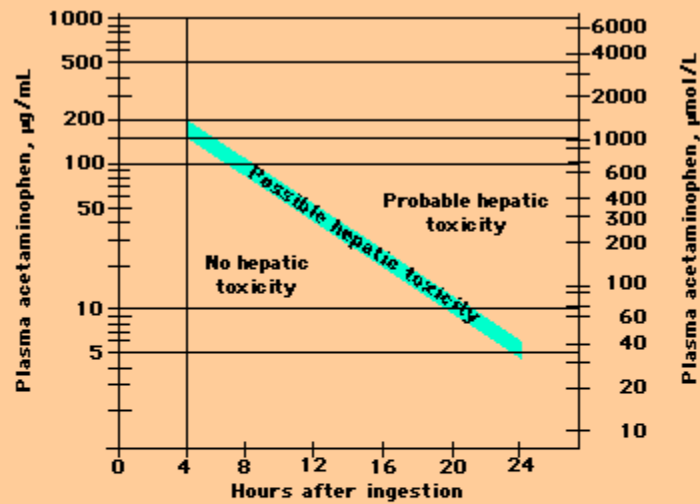
#### Articles 1-4

◆ **lower nomogram threshold when any following present:** medications in use ( carbazepine, phenobarbital, phenytoin, TMP-SMZ, and zidovudine) fasting, malnourished state, and chronic alcoholism.

1. Bray et al. Long-term anticonvulsant therapy worsens outcome in paracetamol-induced fulminant hepatic failure. *Human and Experimental Toxicol.* 1992;11:265-270. **LOE = C**
2. Shriner K, Goetz M. Severe hepatotoxicity in a patient receiving both acetaminophen and zidovudine. *Am J of Med.* 1992;93:94-6. **LOE = F**
3. Whitcomb D, Block G. Association of Acetaminophen hepatotoxicity with fasting and ethanol use. *JAMA* 1994;272:1845-50. **LOE= C**
4. Rumack et al. Acetaminophen overdose. *Arch Int Med.* 1981;141:380-5. **LOE=C**

#### Articles 5- 11

- ◆ Oral and IV delivery is equally efficacious when delivered within 10 hours of ingestion
  - ◆ > 10 hours post ingestion : 72 hour oral regimen superior to 20 hr IV regimen
  - ◆ **N-acetylcysteine is approved by FDA for oral use only**
  - ◆ IV indications only if absolute contraindications exist for oral form, pregnancy, or fulminant hepatic failure ( not to be used if just tastes bad)
5. Prescott LF et al. Intravenous N-acetylcysteine: the treatment of choice for paracetamol poisoning. *Br Med J.* 1979;2:1097. **LOE=C**
  6. Smilkstein MJ et al. Efficacy of oral N-acetylcysteine in the treatment of acetaminophen overdose. Analysis of the national multicenter study (1976-1975). *NEJM* 1988;319:1557-62. **LOE=C**
  7. Smilkstein MJ et al. Acetaminophen overdose: a 48 hour intravenous N-acetylcysteine treatment protocol. *Ann Emerg Med* 1991;20:1058-63. **LOE=B**
  8. Perry HE et al. Efficacy of oral versus intravenous N-acetylcysteine in acetaminophen overdose: results of an open label clinical trial. *J Pediatrics* 1998;132:149. **LOE = C**
  9. Holdiness MR. Clinical pharmacokinetics of N-acetylcysteine. *Clin Pharmacokin* 1991;20:123-34. **LOE = E**
  10. Keays R et al. Intravenous acetylcysteine in paracetamol induced fulminant hepatic failure: a prospective controlled trial. *Br Med J.* 1991;303:1026-9. **LOE=A**
  12. Makin A, Williams R. The current management of paracetamol overdosage. *Br J Clin Pract.* 1994;48:144-8. **LOE = E**



**Severity of acetaminophen intoxication** Relationship between plasma acetaminophen concentration (in  $\mu\text{g}/\text{mL}$  or  $\mu\text{mol}/\text{L}$ ), 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  $10 \mu\text{g}/\text{mL}$ ) 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. (Adapted from Rumack, BH, Matthews, H, Pediatrics 1975; 55:873.)