

Author: LEE-WM.

Article title: ACUTE LIVER FAILURE.

Source (journal):

AMERICAN-JOURNAL-OF-MEDICINE. 1994, JAN 17, V96, S1A, P3-9. ISSN 0002-9343

Abstract: Acute liver failure is a multiorgan syndrome with dramatic clinical features and, often, a fatal outcome. It is characterized by the onset of coma and coagulopathy within 6 months, and usually in <6 weeks, from onset of illness. Viral hepatitis, **drug-related liver injury**, and the **alcohol-acetaminophen syndrome** are the most common etiologies. Altered mental status accompanied by jaundice is a hallmark of acute liver failure. A unique feature is the evolution of increased intracranial pressure due to cerebral edema. The resulting cerebral ischemia and brainstem herniation account for approximately 50% of deaths in patients with acute liver failure. Mannitol therapy may successfully treat most patients with high intracerebral pressure. Most patients demonstrate features of the multiple organ failure syndrome, including a **shock-like state, renal failure, and occasionally respiratory distress** syndrome. Close monitoring of volume status is necessary, since administration of large quantities of fluid may be required. Infection is also common; most pathogens are gram-positive, and fungal infections are also seen. Because an optimum therapy for acute liver failure does not yet exist, liver transplantation should be considered early, before advanced levels of coma develop. Alternative, experimental treatment modalities include heterotopic liver grafting, administration of hepatocyte growth factor, use of an extracorporeal liver-assist device, and liver cell transplantation, but none of these has attained widespread use.

Author: CRIPPIN-JS.

Article title: ACETAMINOPHEN HEPATOTOXICITY - POTENTIATION BY ISONIAZID.

Source (journal):

AMERICAN-JOURNAL-OF-GASTROENTEROLOGY. 1993, APR, V88, N4, P590-592

Abstract: Potentiation of **acetaminophen** hepatotoxicity has previously been associated with a history of alcohol abuse. Presented here is the case of a 21-yr-old Philippino female with rapidly deteriorating hepatic functions. She had been on isoniazid, 300 mg daily, as prophylaxis against tuberculosis due to a positive tuberculin skin test. She took 3.25 g of acetaminophen for abdominal cramping and subsequently had rapid deterioration of liver function manifested by **prolongation of the prothrombin time, elevated ammonia, marked elevation of transaminases, and hyperbilirubinemia**. Over the course of 1 wk, these values essentially normalized and she was discharged. **Isoniazid induces the cytochrome P-450 system**, resulting in increased metabolism of acetaminophen, formation of **toxic metabolites, depletion of glutathione stores**, and subsequent hepatocellular injury. Patients on isoniazid should use caution when taking acetaminophen since the potentially hepatotoxic effects may be amplified due to induction of the cytochrome P-450 system.

Author: WHITCOMB-DC. BLOCK-GD.

Article title: ASSOCIATION OF ACETAMINOPHEN HEPATOTOXICITY WITH FASTING AND ETHANOL USE.

Source (journal):

JAMA-JOURNAL-OF-THE-AMERICAN-MEDICAL-ASSOCIATION. 1994, DEC 21, V272, N23, P1845-1850. ISSN 0098-7484.

**Abstract:** Objectives.-To evaluate the association of fasting and alcohol use with hepatotoxicity from acetaminophen ingested for therapeutic reasons. Design.-Retrospective case series. Setting.-Hospitals of the University of Pittsburgh (Pa) Medical Center. Patients.-A total of 126779 discharge summaries from January 1987 to July 1993 were reviewed using a comprehensive, whole-text-indexed medical database to identify all patients with acetaminophen ingestion and hepatotoxicity. These patients were categorized according to the intended acetaminophen use and dose of acetaminophen ingested. Main Outcomes Measured.-The independent variables of chronic alcohol use, recent alcohol use, and recent fasting were determined for all patients. Results.-Forty-nine patients with acetaminophen hepatotoxicity (**aspartate aminotransferase > 1000 U/L**) were identified. Twenty-one patients (43%) ingested acetaminophen for therapeutic purposes. All patients with hepatotoxicity took more than the recommended limit of 4 g/d. Recent fasting was more common than recent alcohol use among those who suffered hepatotoxicity after a dose of 4 to 10 g of acetaminophen per day ( $P=.02$ ). Recent alcohol use was more common in the group who took more than 10 g/d than in those who took 4 to 10 g/d ( $P=.004$ ). Conclusion.-Acetaminophen hepatotoxicity after a dose of 4 to 10 g/d was associated with fasting and less commonly with alcohol use. Patients who developed hepatotoxicity after taking acetaminophen doses of greater than 10 g/d for therapeutic purposes were alcohol users. Acetaminophen hepatotoxicity after an overdose appears to be enhanced by fasting in addition to alcohol ingestion.