Overview and Diagnosis

While acute liver failure (ALF) remains a relatively rare event, estimated at approximately 2,000 cases per year, the mortality associated with this disease is staggering. At California Pacific Medical Center, only 5 percent of over 1,300 liver transplants since 1988 have been due to ALF, however many more patients are admitted annually for this syndrome.

It is important to distinguish between acute hepatitis or hepatic injury and ALF:

- **Acute hepatic injury**: elevated transaminases, bilirubin, and/or INR without evidence of altered mental status (hepatic encephalopathy, HE)
- **Acute liver failure (fulminant)**: severe acute hepatic injury accompanied by coagulopathy and altered mental status (HE)

Cerebral edema with subsequent herniation or sepsis with multiorgan failure are the most lethal complications of ALF. These outcomes may be prevented with earlier diagnosis and effective management. Current therapies have evolved in an effort to allow sufficient time for hepatic recovery or to perform liver transplantation if spontaneous recovery remains unlikely.

Causes of Acute Liver Failure

Most frequently, ALF is the result of acetaminophen poisoning, either intentional, or often unintentional: the so-called “therapeutic misadventure.” ALF also occurs following ingestion of medications with idiosyncratic hepatotoxicity (see listing). Other less common causes of ALF include acute viral hepatitis (A, B, D, E, HSV, EBV, CMV), Budd-Chiari syndrome (hepatic vein occlusion), *Amanita* mushroom poisoning, Wilsons disease, or autoimmune hepatitis. Many cases remain a mystery and are classified as “seronegative” or cryptogenic.

### Medications or Supplements Implicated in ALF

- Allopurinol
- Alpha-methyldopa
- Amiodarone
- Amphetamines/Ecstasy
- Dapsone
- Diclofenac
- Didanosine
- Disulfiram
- Efavirenz
- Etoposide
- Flutamide
- Gemtuzumab
- Halothane, Isoflurane
- Imipramine
- Isoniazid*
- Ketoconazole
- Labetalol
- Lisinopril
- Metformin
- Nefazodone
- Nicotinic acid
- Nitrofurantoin*
- Phenytoin*
- Propylthiouracil*
- Pyrazinamide
- Quetiapine
- Statins
- Sulfasalazine
- Sulonamides
- *continued
Supplements implicated in ALF, continued

- Tolcapone
- Troglitazone
- Valproic acid*

* denotes more common causes

Enhanced Toxicity:
- Amoxicillin-clavulanate
- Rifampin-isoniazid
- Trimethoprim-sulfamethoxazole

Herbal products/dietary supplements:
- Bai-Fang herbs
- Camelia Sinensis (green tea)
- Chaparral
- Comfrey
- Germander
- Greater celandine
- Gum Thistle
- He Shon Wu
- Heliotrope
- Impila
- Jin Bu Huan
- Kava kava
- LipoKinetix
- Ma Huang
- Pennyroyal
- Rattleweed
- Senecio
- Skullcap
- Sunnhemp

Early Management
- Begin treatment immediately with N-acetylcysteine (Mucomyst®) for known or suspected ingestion of Tylenol (acetaminophen). Consider Mucomyst for all patients with ALF with grade 1-2 HE *

Avoid sedatives if possible

Assess severity/prognosis: acetaminophen level, toxicology screen/BAL, Factor V level, arterial: lactate, pH, and ammonia, AFP, phosphate, INR

10% Dextrose infusion should be considered, especially for transport or documented hypoglycemia

Activated charcoal is recommended if within 4 hours of ingestion (1gm/kg orally). This will not interfere with N-acetylcysteine absorption.

Endotracheal intubation for grade 4 hepatic encephalopathy (HE) (consider for grade 3 with poor airway protection)

Measure serum osmolarity if HE or cerebral edema present or suspected. Then elevate head of bed to 30 degrees and give Mannitol 1 gm/kg IV.

Advanced Management

(Not recommended without prior expertise or outside of a transplant center)

- Intracranial pressure (ICP) monitor for known or suspected cerebral edema or intracranial hypertension (ICH)

- Active cooling to 33-34°C C with cooling blankets and ventilator for ICH not responsive to Mannitol

- Hypertonic saline (3% NaCl) to target serum sodium to 145-150 for refractory ICH

- Continuous renal replacement therapy (CRRT) if evidence of renal insufficiency and/or refractory ICH

- Liver support devices—California Pacific is active in this area of research

- Liver transplantation