

# Acute Liver Failure

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## Definition

- Liver injury that impairs the ability of the liver to synthesize proteins and detoxify by-products of metabolism
- No history or physical evidence of pre-existing liver disease
- Sudden onset, life threatening condition

## Clinical Features

- Onset after flu-like illness common
- Yellow eyes and skin, abdominal pain, dark urine, lethargic or inappropriate behavior
- Bleeding complications and secondary bacterial infection
- Elevated liver enzymes, bilirubin and prolonged clotting studies
- Coma in late stages

## Coma Staging

Stage	Clinical Signs of Encephalopathy	EEG changes
I (Prodrome)	Slowness of mentation; mild disturbed sleep wake cycle	Minimal
II	Drowsiness, confusion, inappropriate behavior, disorientation, mood swings	Generalized slowing of rhythm
III	Very sleepy, but arousable, unresponsive to verbal commands, increased reflexes	Grossly abnormal
IV (Coma)	Unconscious, abnormal posture in response to pain, or no response at all	Appearance of d waves, decreased amplitudes

## Clinical Presentation Infants

- Lethargy, poor feeding following viral type illness
- Bilirubin elevation not pronounced in metabolic diseases
- Encephalopathy manifest by irritability to unresponsiveness

## Mechanisms of Hepatic Injury

- Initial injury
  - Direct injury
    - Viral infection
    - Drug toxicity
  - Immune mediated injury
    - Autoimmune hepatitis
- Inflammatory response
  - Cytokine release
  - Mediators of regeneration

## Epidemiology of Acute Liver Failure in North America

- Indeterminate 50 %
- Acetaminophen 15 %
- Autoimmune 8 %
- Other drugs/toxins 7 %
- Metabolic 7 %
- Viral hepatitis 1 %
- Other identifiable causes 12 %

TABLE 4.1. CAUSES OF FULMINANT HEPATIC FAILURE IN CHILDREN

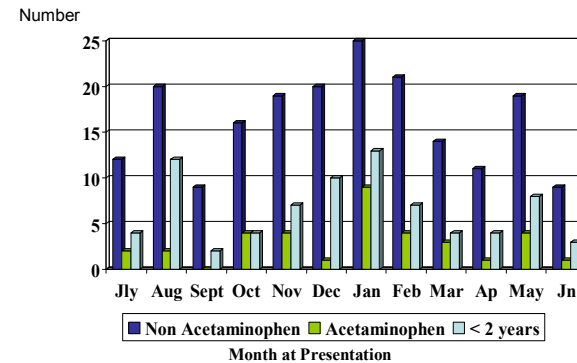
	Disease	Incidence
<b>Neonates</b>		
Infectious	Herpes viruses, echovirus, adenovirus, hepatitis B virus	Frequent
Inborn errors of metabolism	Hereditary fructose intolerance, <sup>a</sup> galactosemia, <sup>a</sup> tyrosinemia, <sup>a</sup> neonatal hemochromatosis <sup>b</sup>	Moderately frequent
Ischemia and abnormal perfusion	Congenital heart disease, cardiac surgery, myocarditis, severe asphyxia	Rare
<b>Infants</b>		
Infectious	Hepatitis A virus, hepatitis B virus, non A, non B hepatitis, herpes viruses, sepsis <sup>a</sup>	Frequent
Drugs and toxins	Valproate, isoniazid, acetaminophen, Amanita	Moderately frequent
Inborn errors of metabolism	Hereditary fructose intolerance, <sup>a</sup> others	Rare
Ischemia and abnormal perfusion	Congenital heart disease, cardiac surgery, myocarditis, severe asphyxia	Rare
Other	Malignancy	Rare
<b>2- to 10-yr-olds</b>		
Infectious	Non A, non B hepatitis, others same as infants	Frequent
Drugs and toxins	Same as infants	Moderately frequent
Ischemia and abnormal perfusion	Budd-Chiari syndrome, other same as infants	Rare
Other	Malignancy, hyperthermia	Rare
<b>10- to 18-yr-olds</b>		
Infectious	Same as 2-10 yr	Frequent
Drugs and toxins	Same as 2-10 yr	Moderately frequent
Ischemia and abnormal perfusion	Same as 2-10 yr	Rare
Metabolic	Wilson's disease, Fatty liver of pregnancy	Rare
Other	Same as 2-10 yr	Rare

Adapted from Sokol RJ. Fulminant hepatic failure. In: Balistreri WF, Stocker JT, eds. *Pediatric Hepatology*. New York: Hemisphere Publishing, 1990:315-362, with permission.

## Indeterminate Cases

- Presumed to be viral infection
- Most common cause of liver failure in school aged children
- Low rate of spontaneous recovery
- One year survival 50-60% with transplant
- Aplastic anemia in 30%
  - Can develop prior to transplant

## Pediatric ALF: Seasonal Variation



## Acetaminophen Toxicity

- 95% of drug metabolized to non-toxic by-product
- 5% metabolized by a different pathway which forms toxic intermediate compound
  - This fraction increases dramatically in overdose
- Toxicity may result from inadvertent overdose
  - Different concentrations in liquid formulations
  - Included in cold and flu preparations
- Potential for toxicity increased by fasting and alcohol ingestion
  - Depletion of anti-oxidant defense in the liver

## Acetaminophen Toxicity

- May respond well to anti-oxidant therapy with NAC
- Few patients require transplantation
- Risk for recurrent suicide attempts should be addressed

## Infectious Hepatitis

- Liver failure occurs in approximately 1% of acute Hepatitis A and B
- Consider Hepatitis E in travelers
  - Average case fatality rate 1%
  - Case fatality rate 12% in pregnant patients
- Systemic viral infections
  - Usually in immunocompromised hosts
  - EBV, HSV

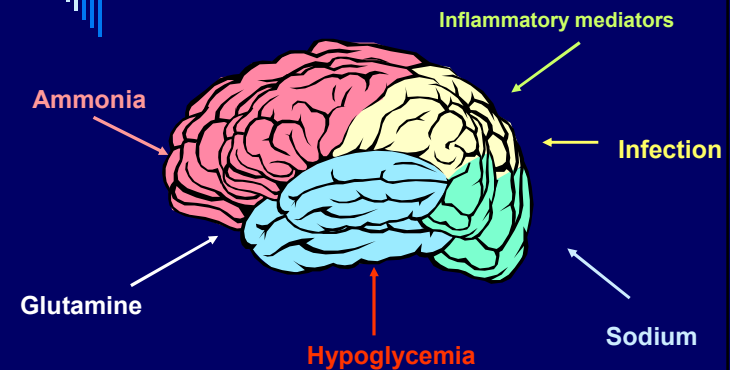
## Complications of Acute Liver Failure in Children

<u>Complication</u>	<u>Frequency</u>
Encephalopathy	++++
Altered Clotting	++++
Cerebral Edema	+++
Renal Dysfunction	++
Secondary Infections	++
Low blood sugar	++
Bone Marrow suppression	++

## Support of Altered Clotting

- Fresh frozen plasma infusions
- Plasma exchange
- Artificial clotting factor replacement
- Bio-artificial Assist devices
  - Clinical trials mixed results
  - Not widely available for children

## Cerebral Edema



## Prognosis

- Spontaneous recovery more common in Acetaminophen injury
  - 91% vs. Others 45%
- Laboratory predictors
  - Higher bilirubin
  - Longer clotting studies
  - Abnormal acid-base status
- Spontaneous recovery lower in younger children
  - < 3 yrs 48% vs. ≥ 3 yrs 55%

## Outcome

- 70% mortality in pretransplant era
  - Contributing causes
    - Cerebral edema 56%
    - Bleeding 50%
    - Renal failure 30%
    - infection 15%
- Patients with spontaneous recovery have excellent long-term prognosis

## Liver Transplantation

- Long term survival 50%
- Failure of other organs not uncommon
- Permanent neurologic injury or progression of cerebral edema in some survivors
- Diminished organ availability increases mortality risk
  - LRD may improve survival

## Summary

- Causes vary with age
- Majority of cases are indeterminant
- Survival without transplant 20%
- Multi-system injury common
- Skilled medical management may improve survival