

# Acute Liver Failure: What's the Cause and How Do I Keep Them Alive?

## Acute Liver Failure: What's the Cause and How Do I Keep Them Alive?

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## Acute Liver Failure, Background

- Trey and Davidson first definition
- < 24 weeks duration, INR > 1.5, encephalopathy
- < 2000 cases per year US
- Key components: Etiology  
Prognosis estimate  
Transplant candidate?
- Acute liver Failure Study Group (ALFSG)  
[www.acuteliverfailure.org](http://www.acuteliverfailure.org)

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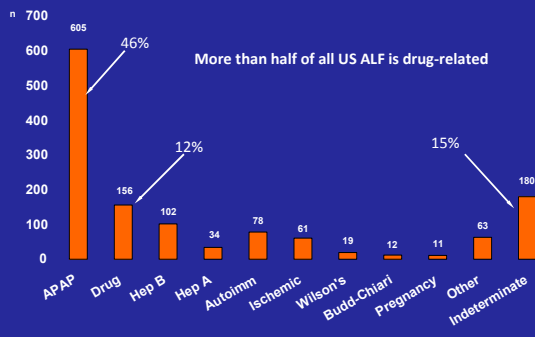
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## Etiology of ALF in the USA

Adult Registry (n = 1,321)



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**Comparison of Different ALF Etiology Groups**

N = 1,033

	ACM n=475	Drug n=119	Indeterminate n=151	HepA/HepB n=31/75	All Others n=182
Age (median)	36	43	37	47/41	41.5
Sex (% F)	74	67	56	45/44	76
Jaundice (Days) (median)	0	10	10	3/7	7
Coma ≥3 (%)	51	38	48	55/52	42
ALT (median)	4149	571	851	2404/1601	677
Bili (median)	4.5	21.6	23.0	11.9/20.8	15.2
Tx (%)	9	40	42	29/47	35
Spontaneous Survival (%)	64	26	27	58/24	30
Overall Survival (%)	71	63	65	84/64	60

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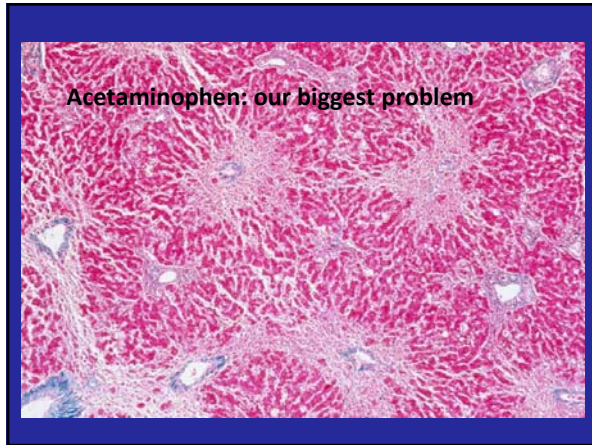
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**'Suicidal' vs. 'Accidental' APAP cases**

	N=606 (56=unk)	Intentional (n=251)	Unintentional (n=296)	p-value
Female (%)		77	71	NS
Age		35	39	< 0.001
ACM dose(g)		38/38	47/7.5	NS
Coma (% ≥3)		39	55	< 0.026
ALT (IU/L)		6053	4207	< 0.0001
Alcohol use/abuse (%)		50/18	50/17	NS
Antidepress't		39	34	NS
History of depression		45	24	< 0.001
Narcotic cpd (%)		18	63	< 0.001
Multiple preps		5	38	< 0.001
Spont surv (%)		70	65	NS

Larson AM, et al. Hepatology 2005;42:1367-72

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### Prognosis in Acute Liver Failure

Etiology the important outcome determinant

<b>Good prognosis:</b>	<b>Bad prognosis:</b>
<ul style="list-style-type: none"><li>• Acetaminophen</li><li>• Hepatitis A</li><li>• Shock</li></ul>	<ul style="list-style-type: none"><li>• Drugs</li><li>• Indeterminate</li><li>• Hepatitis B</li><li>• Wilson Disease</li></ul>

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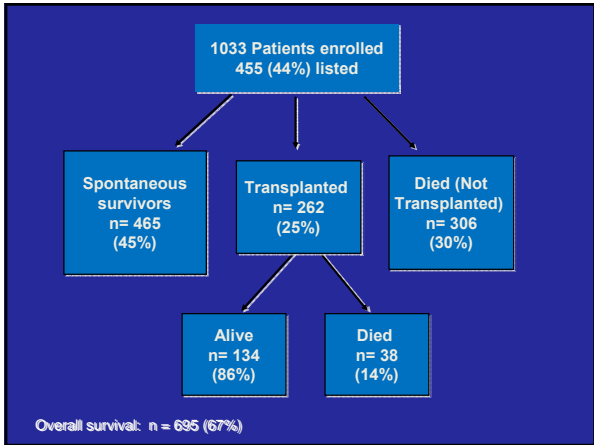
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### Prognosis Models

- Kings college criteria  
APAP-arterial ph <7.3, PT > 100 s (INR >6.5), Cr > 3.4 mg/dl, grade > 3 encephalopathy  
NonAPAP- PT > 100 s (INR >6.5), Drug, Jaundice > 7 days, Bilirubin >17.4 mg/dl
- MELD-> 30, > 33
- APACHE II score- > 15
- Phosphate level (APAP) > 1.2 mm/L day 2
- Lactate APAP- on admission, > 3.5 mm/L

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## Initial Evaluation

- History (ask family, others)
- PE – pupil, neurological, encephalopathy grade
- Bili, INR, Cr, Ph, lactate, phosphate (prognosis)
- AST, ALT (not prognostic)
- Serology, APAP, ceruloplasmin
- U/S liver (texture, flows)
- CT head (grade > 3)
- Labs every 8-12 hrs

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## Initial Treatment

- APAP-oral acetylcysteine 140 mg/kg loading dose, 70 mg/kg every 4 hrs, 72 hrs.  
IV- 150 mg/kg loading dose, 12.5 mg/kg for 4 hrs, then 6.25 mg/kg 72-96 hrs.
- Herpes virus-acyclovir 10 mg/kg q 8 hrs
- Autoimmune-No good data with steroids

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## A multi-center, randomized, double blind study of IV NAC vs. placebo for non-acetaminophen acute liver failure

Group	Outcome	Coma at Randomization		Total
		1-2	3-4	
Placebo	Spontaneous Survival	17/56 (30%)	8/36 (22%)	25/92 (27%)
NAC	Spontaneous Survival	30/58 (52%)	2/23 (9%)	32/81 (40%)

Overall spontaneous survival by treatment group:  $p = 0.043$   
 $\chi^2$  for coma grade I-II:  $p = 0.010$ ; III-IV  $p = 0.912$   
 NAC Odds Ratio = 11.3 vs. PLB Odds Ratio = 1.5  
 Breslow-Day  $\chi^2 (1) = 5.11, p = 0.02$

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# Acute Liver Failure: What's the Casue and How Do I Keep Them Alive?

## Neurological

- Hepatic encephalopathy-no benefit of RX
- Grade 3-4 encephalopathy  
Intracranial pressure monitor (epidural)
- Head of bed 30 degree angle  
goals ICP >20-25 mm Hg, CPP 50-80 mm Hg
- Mannitol (0.5 gm/kg), osm >320 meq/L
- ? Hypertonic saline (145-155 Na mEq/L)
- Pentobarbitol (3-5 mg/kg bolus, 1-3 mg/kg)
- Indomethacine 25 mg
- IC HTN 20% of deaths in ALF

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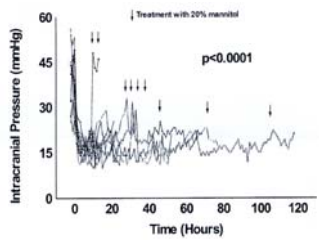
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## Hypothermia and ALF



Jalan R, et al. Gastroenterology 2004;127:1338-1346

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## Systems Management

### Pulmonary

- Intubate for grade 3-4 encephalopathy  
(rapid intubation technique/cis-atracurium)
- Tidal volumes (6 ml/kg) Limit PEEP
- PCO2  $\approx$  30-35 mm Hg
- Sedation-propofol (5mg/kg/hr)

### Infection

- Most common lungs/urinary G+C, GNR, fungal
- Unknown better for prophylaxis vs. surveillance

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# Acute Liver Failure: What's the Casue and How Do I Keep Them Alive?

## Systems Management

### Cardiovascular

- Monitor CVP, MAP > 65 mm Hg
- NS, followed by 0.45% NS w 75 mmol/l NaHCO<sub>2</sub>
- Norepinephrine
- ? Hydrocortisone (200-300 mg/day)

### Renal

- ATN vs HRS (measure urine Na) ≈50% of patients
- Continuous renal replacement better than intermittent hemodialysis.
- Avoid heparin

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## Systems Management

### Coagulation/bleeding

- No routine use of FFP (use INR for prognosis)
- If invasive procedures use 2-4 U FFP goal of INR < 1.8, vit K 10 mg IV X 3 days, Plt > 50 k.
- Recombinant factor VIIa (40 ug/kg) \$\$\$\$  
do procedure within 60 minutes

### Nutrition

- Enteral feeds if possible
- Parenteral (35-40 kcal/kg/d)
- Glucose control (no data ALF)

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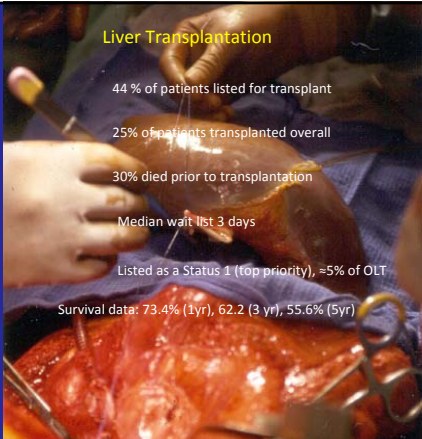
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**Liver Transplantation**

- 44% of patients listed for transplant
- 25% of patients transplanted overall
- 30% died prior to transplantation
- Median wait list 3 days
- Listed as a Status 1 (top priority), ≈5% of OLT
- Survival data: 73.4% (1yr), 62.2 (3 yr), 55.6% (5yr)

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# Acute Liver Failure: What's the Casue and How Do I Keep Them Alive?

## Acute Liver Failure Summary

- Rare disease (< 2000 case/yr, 5% of OLT/yr)
- Good prognosis: APAP, Hep A
- Poor prognosis: Drug, indeterminate
- Use Prognosis models
- Transfer early to transplant centers (INR > 2, Encephalopathy grade 2)
- Transplantation survival comparable to chronic liver disease

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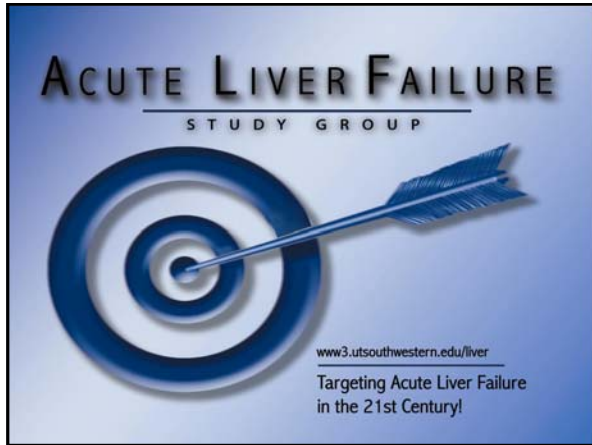
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