Acute Hepatic Failure (AHF) Management

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Liver offers almost no resistance to flow, withstanding significant increases in flow, without resulting in sure.

The normal portal venous system is a low-pressure system delivering blood to the liver, and draining into it.
NORMAL VASCULAR ANATOMY OF THE liver

The portal vein is the superior mesenteric vein (that collects blood from the spleen). Normally, blood from the portal system. After progressive ramifications, blood from the hepatic artery join at the hepatic sinusoids, a specialized vely interconnected. Hepatic sinusoidal blood drains into collecting veins that unite to form the hepatic veins into the liver, draining into the vena cava and the right heart.
ATHOPHYSIOLOGY OF HEPATIC ENCEPHALOPATHY

Hepatic Encephalopathy Pathogenesis

Toxins

GABA-BD receptors

NH₃ Shunting

Failure to metabolize NH₃

Bacterial action

Protein load

NH₃ Shunting

Failure to metabolize NH₃

Bacterial action

Protein load
AHF-Management

The essentials of management are:

1. Diagnosis of cause of liver injury and encephalopathy

2. Skilled intensive care to minimize aggravating factors and complications until liver function recovers or transplantation can be performed

3. Liver transplantation
AHF-Management

Get better liver

or

Get liver better
AHF-Management

- Managing patients with ALF requires a thorough understanding of the many complications that can be present, including:
  - Encephalopathy
  - Cerebral edema
  - Sepsis
  - Renal failure
  - Circulatory dysfunction
  - Coagulopathy, gastrointestinal bleeding
  - Metabolic derangements such as metabolic acidosis, hypoglycemia, and hypophosphatemia
AHF-Management (Team work)

Hepatologist

ICU doctor coordinator

Surgeon
AHF-Management (Intensive care)

- Support vital functions
- Avoid complications
- Identify patients with a bad prognosis
- Optimal conditions for liver regeneration
- Optimal conditions for transplantation
AHF-Management (Intensive care)

- Support
  - CNS
  - Respiration
  - Circulation
  - CRRT/MARS
  - Coagulation
  - Infection
  - Metabolism
AHF-Management

- **History taking** should include careful review of possible exposures to viral infection and drugs or other toxins.

- If severe encephalopathy is present, the history may be provided entirely by the family or may be unavailable. In this setting, limited information is available, particularly regarding possible toxin/drug ingestions.
AHF-Management

- **Physical examination** must include careful assessment and documentation of mental status and a search for stigmata of chronic liver disease. Jaundice is often but not always seen at presentation.

- Right upper quadrant tenderness is variably present. Inability to palpate the liver or even to percuss a significant area of dullness over the liver can be indicative of decreased liver volume due to massive **hepatocyte loss**.
AHF-Management

- An enlarged liver may be seen early in viral hepatitis or with malignant infiltration, congestive heart failure, or acute Budd-Chiari syndrome.

- History or signs of *cirrhosis should be absent* as such features suggest underlying chronic liver disease, which may have different management implications.
AHF-Management

Initial laboratory examination

- Prothrombin time/INR
- Chemistries: sodium, potassium, chloride, bicarbonate, calcium, magnesium, phosphate, glucose
- AST, ALT, alkaline phosphatase, GGT, total bilirubin, albumin, creatinine, blood urea nitrogen
- Arterial blood gas
- Arterial lactate
- Complete blood count
- Blood type and screen
- Acetaminophen level
- Toxicology screen
- Viral hepatitis serologies: anti-HAV IgM, HBSAg, anti-HBc IgM, anti-HEV S, anti-HCV
- Ceruloplasmin Level#
- Pregnancy test (females)
- Ammonia (arterial if possible)
- Autoimmune markers: ANA, ASMA, Immunoglobulin levels
- HIV status†
- Amylase and lipase
AHF-Management

- Therapy: General Considerations

- Determining Etiologies and Specific Therapies
Therapy: General Considerations

- Because there is no proven therapy for ALF in general, management consists of intensive care support once treatments for specific etiologies have been initiated.

- While some patients with evidence of acute liver injury but without significant coagulopathy or encephalopathy may be monitored on a medicine ward, any patient with altered mental status warrants admission to an ICU as the condition may deteriorate quickly.
Therapy: General Considerations

- Managing patients with ALF requires a thorough understanding of the many complications that can be present, including:
  - Encephalopathy
  - Cerebral edema
  - Sepsis
  - Renal failure
  - Circulatory dysfunction
  - Coagulopathy, gastrointestinal bleeding
  - Metabolic derangements such as metabolic acidosis, hypoglycemia, and hypophosphatemia
Hepatic Encephalopathy

- Hepatic encephalopathy is a major complication of ALF, although the precise mechanism remains unclear.

- The most widely accepted theory is related to increased production of ammonia from nitrogenous substances within the gut lumen.

- Thus, treatment has been directed toward reducing the production and absorption of nitrogenous products with modalities such as lactulose.
Hepatic Encephalopathy Pathogenesis

Hepatic Encephalopathy occurs when ammonia bypasses the liver, either through porto-systemic shunt and ultimately reaches the brain.

- Failure to metabolize NH₃
- NH₃ Shunting
- GABA-BD receptors
- Toxins
- Bacterial action
- Protein load
Cerebral Edema

- Cerebral edema and intracranial hypertension (ICH) have long been recognized as the most serious complications of ALF.

- **Uncal herniation** may result and is uniformly fatal. Cerebral edema may also contribute to ischemic and hypoxic brain injury, which may result in long-term neurological deficits in survivors.

The pathogenic mechanisms leading to the development of cerebral edema and ICH in ALF are not entirely understood.

It is likely that multiple factors are involved, including osmotic disturbances in the brain and heightened cerebral blood flow due to loss of cerebrovascular autoregulation.

Inflammation and/or infection, as well as factors yet unidentified may also contribute to the phenomenon.

Pathogenesis of hepatic encephalopathy in acute liver failure. Semin Liver Disease 2003;23:259
Cerebral Edema

- The occurrence of cerebral edema and ICH in ALF is related to severity of encephalopathy.

- Cerebral edema is seldom observed in patients with grade I-II encephalopathy.

- The risk of edema increases to 25% to 35% with progression to grade III, and 65% to 75% or more in patients reaching grade IV coma.
Cerebral Edema

- The clinical signs of elevated ICP including hypertension, bradycardia and irregular respirations (Cushing’s triad) are not uniformly present; these and other neurological changes such as pupillary dilatation or signs of decerebration are typically evident only late in the course.

- CT of the brain does not reliably demonstrate evidence of edema especially at early stages.
Intracranial Pressure Monitoring

- The use of ICP monitoring devices in ALF is a subject of ongoing debate.
- A primary purpose of ICP monitoring is to detect elevations in ICP and reductions in cerebral perfusion pressure (CPP; calculated as mean arterial pressure minus ICP) so that interventions can be made to prevent herniation while preserving brain perfusion.
Intracranial Pressure Monitoring

- There are documented studies and reports of experience which indicate ICP monitoring devices can safely provide helpful information.

- Recent data did not show improved outcomes when ICP monitoring devices were used.

Outcome of intracranial pressure monitoring in acute liver failure (ALF) HEPATOLOGY 2004; 40(Suppl 1):212A.
Intracranial Pressure Monitoring

- Four types of catheters have been used to measure ICP:
  - Epidural
  - Subdural
  - Parenchymal
  - Intraventricular

- The advantage of the Epidural Catheters compared to the others is that they are less invasive

- The major complications from intracranial pressure monitoring are infection and bleeding
Intracranial Pressure Monitoring

- Control of ICP
  - ICP monitoring
    - PK(INR) <1.4
    - TPK >50 x 10^9 /l
    - RLS ≥4 or sedated patient on ventilator
  - ICP <20 mmHg
  - CPP >50-60 mmHg

- EEG monitoring
  - Sedated patient on ventilator
Intracranial Pressure Monitoring

- We suggest that an Epidural ICP Monitor should be placed in patients with:
  - Grade IV encephalopathy
  - Patients in whom grade III encephalopathy is rapidly progressing.

- If an ICP monitor is placed, key parameters to follow are both ICP and CPP.

- ICP should be maintained below 20-25 mm Hg if possible, with CPP maintained above 50-60 mm Hg.
Management of Elevated Intracranial Pressure (ICP)

- **Encephalopathy Grades I-II.** Depending on the overall clinical picture, patients with only grade I encephalopathy may sometimes be safely managed on a medicine ward with skilled nursing in a quiet environment to minimize agitation, although management in an ICU is preferable.
Management of Elevated Intracranial Pressure (ICP)

- Head imaging with computerized tomography (CT) is used to exclude other causes of decline in mental status such as intracranial hemorrhage.

- Sedation is to be avoided if possible; unmanageable agitation may be treated with short-acting benzodiazepines in small doses.
Management of Elevated Intracranial Pressure (ICP)

- **Lactulose** There is increasing evidence that ammonia may play a pathogenic role in the development of cerebral edema/ICH; ammonia infusion has been shown to cause brain edema in animal models.

- Some human studies have supported these findings, with an arterial ammonia level 200 ug/dL being strongly associated with cerebral herniation.

Management of Elevated Intracranial Pressure (ICP)

- A preliminary report from the United States Acute Liver Failure Study Group (US ALFSG), found that lactulose therapy was associated with a small increase in survival time, but with no difference in severity of encephalopathy or in overall outcome.

- One concern regarding the use of lactulose in this setting is the potential for gaseous abdominal distension that could present technical difficulties in a subsequent transplantation procedure.

Lactulose therapy in acute liver failure. J Hepatol 2002;36:33A
Management of Elevated Intracranial Pressure (ICP)

- **Encephalopathy Grades III-IV.** As patients progress to grade III or IV encephalopathy it is advisable to intubate the trachea for airway protection.

- Choice of sedation in this instance will vary according to clinician preference: **propofol** is often used because it may reduce cerebral blood flow; however, its effectiveness in this regard has not been shown in controlled studies.

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Management of Elevated Intracranial Pressure (ICP)

- Efforts should be made to **avoid patient stimulation**.

- Maneuvers that cause straining or Valsalva-like movements in particular may increase ICP; it may be advisable to use endotracheal lidocaine prior to endotracheal suctioning.

- Placement of a nasogastric tube can cause gagging and thus their use should be minimized. Similarly, endotracheal suction should be minimized.
Management of Elevated Intracranial Pressure (ICP)

- **Seizures.** Seizures, which may be seen as a manifestation of the process that leads to hepatic coma and ICH, should be controlled with phenytoin.

- Use of any sedative is discouraged in light of its effects on the evaluation of mental status. Only minimal doses of benzodiazepines should be used given their delayed clearance by the failing liver.

- Seizure activity may acutely elevate ICP and may also cause cerebral hypoxia and thus contribute to cerebral edema.

_Intracranial pressure during epileptic seizures. Electroencephalogr Clin Neurophysiol 1984; 57:497._
Specific Treatment of Elevated Intracranial Pressure

**Indomethacin** (25 mg IV over 1 minute) has been used in patients with elevated intracranial pressure refractory to other therapeutic modalities. It exerts its effects by causing cerebral vasoconstriction, and can acutely decrease ICP.

Although the authors' experience with this treatment modality is limited, we would not hesitate to use it in the appropriate clinical scenario.

The effect of indomethacin on interacranial pressure in patients with fulminant hepatic failure.

*J cereb Blood flow metab* 2004; 24: 798
Specific Treatment of Elevated Intracranial Pressure

- **Mannitol.** (in a bolus dose of 0.5-1g/kg) is therefore recommended to treat ICH in ALF.

- **Hyperventilation.** Hyperventilation to reduce PaCO₂ to 25-30 mm Hg is known to quickly lower ICP via vasoconstriction causing decreased cerebral blood flow (CBF), but this effect is short-lived.

- **Hypertonic Sodium Chloride**
Specific Treatment of Elevated Intracranial Pressure

- **Barbiturate**

- **Corticosteroids.** Corticosteroids, which are often used in the prevention and management of ICH caused by brain tumors and some infections of the central nervous system, have been shown in a controlled trial to confer **no benefit** in patients with ALF with respect to controlling cerebral edema or improving survival.

- **Hypothermia.** Moderate hypothermia (32-34°C) may prevent or control

Cerebral Edema - Recommendations

- In early stages of encephalopathy, sedation should be avoided if possible.

- Lactulose may be used, but concern has been raised about increasing bowel distention during the subsequent transplant procedure.

- In patients progressing to grade III or IV encephalopathy, the head should be elevated to 30 degrees, and endotracheal intubation should be performed.
Cerebral Edema - Recommendations

- Although there is no consensus among the centers and experts, intracranial pressure monitoring is mainly considered for patients who are listed for transplantation.

- In the absence of ICP monitoring, frequent evaluation for signs of intracranial hypertension are needed to identify early evidence of uncal herniation.
Cerebral Edema - Recommendations

- In the event of intracranial hypertension, **mannitol** should be given and **hyperventilation** may be considered in order to temporarily reduce the ICP, but prophylactic use of these interventions is not helpful and therefore not recommended.

- Corticosteroids should not be used to control elevated ICP in patients with acute liver failure.
Infection

- All patients with ALF are at risk for acquisition of bacterial or fungal infection or sepsis, which may preclude transplantation or complicate the post-operative course. Prophylactic antimicrobial therapy reduces the incidence of infection in certain groups of patients with ALF, but **no actual survival benefit has been shown**, making it difficult to recommend antibiotic prophylaxis uniformly.

Infection and the progression of encephalopathy in acute liver failure. Gastroenterology 2003;125:755-764
Infection

- Recent studies have suggested an association between infection and/or the systemic inflammatory response syndrome (SIRS) and progression to deeper stages of encephalopathy.
- The most common sites of infection are the respiratory and urinary tracts and blood.
- There are no controlled trials available to confirm whether the use of prophylactic antimicrobials decreases the likelihood of progression of encephalopathy and/or development of cerebral edema in ALF.

The role of prophylactic antibiotics is controversial. Empiric broad spectrum antibiotics should be considered in the following patients:

- Presence of or the rapid progression to advanced stages of encephalopathy
- Refractory hypotension
- Presence of systemic inflammatory response syndrome

Infection-Recommendations

- Periodic surveillance cultures should be performed to detect bacterial and fungal infections as early as possible and prompt treatment should be initiated accordingly.

- Prophylactic antibiotics and anti-fungals may be considered but have not been shown to improve overall outcomes.
Coagulopathy

- In the absence of bleeding it is not necessary to correct clotting abnormalities with fresh frozen plasma (FFP).
- An exception is when an **invasive procedure** is planned and perhaps in the setting of profound coagulopathy (e.g., INR 7).
- **Vitamin K** is routinely given in a dose of 5-10 mg subcutaneously, regardless of whether poor nutritional status appears to be contributing to the coagulopathy.
- In the absence of bleeding, it is safe to use a threshold **platelet count of 10,000/mm³**.
Gastrointestinal Bleeding

- Gastrointestinal (GI) bleeding is a recognized complication of ALF.

- A large prospective multi-center cohort study found that mechanical ventilation for more than 48 hours and coagulopathy were the only significant risk factors for bleeding in critically ill patients of all types.

Gastrointestinal Bleeding

- **Histamine-2 receptor (H2) blocking** agents such as ranitidine have long been used in the prophylaxis of GI bleeding in critically ill patients; their efficacy has been supported in several trials.

- **Sucralfate** has also been found to be effective in many studies, and there have been smaller randomized trials and a meta-analysis which suggested that sucralfate may be as effective in preventing gastrointestinal bleeding and might be associated with lower risk of nosocomial pneumonia than H2 blockers which lower gastric pH.

Gastrointestinal Bleeding

- More recently, however, a much larger (1,200 patients), well-designed trial comparing ranitidine to sucralfate in mechanically-ventilated patients found that Ranitidine but not sucralfate decreased the risk of clinically significant bleeding; the incidence of pneumonia was similar for the two groups.

- Patients with ALF in the ICU should receive prophylaxis with H2 blocking agents or PPIs (or sucralfate as a second-line agent) for acid-related gastrointestinal bleeding associated with stress.
Hemodynamics/Renal Failure

- Careful attention must be paid to fluid resuscitation and maintenance of adequate intravascular volume in patients with acute liver failure.

- If dialysis support is needed for acute renal failure, it is recommended that a continuous mode rather than an intermittent mode be used.

- Pulmonary artery catheterization should be considered in a hemodynamically unstable patient to ensure that appropriate volume replacement has occurred.

- Systemic vasopressor support with agents such as epinephrine, norepinephrine, or dopamine but not vasopressin should be used if fluid replacement fails to maintain MAP of 50-60 mm Hg.
Hemodynamics/Renal Failure

- **NAC** may improve systemic circulation parameters in patients with ALF, but this was not observed in all studies.
- NAC has been shown to improve liver blood flow and function in patients with septic shock. Use of NAC in all forms of ALF cannot be justified based on current evidence.
- **prostacyclin** and other prostaglandins have appeared promising in some reports.

Metabolic Concerns

- Metabolic homeostasis must be carefully maintained in patients with acute liver failure. Overall nutritional status as well as glucose, phosphate, potassium and magnesium levels should be monitored frequently, with expeditious correction of derangements.
Pulmonary complications

- **Pulmonary edema and pulmonary infections** are encountered in approximately 30 percent of patients with ALF.

- Mechanical ventilation may be required to ensure adequate oxygenation. However, extreme caution must be used with positive end-expiratory pressure in patients with ALF since PEEP can worsen cerebral edema.
Malnutrition

- Nutrition is a vital component in the treatment of ALF. In patients with grade I or II encephalopathy, oral or enteral feeding with a low protein diet is usually sufficient to meet metabolic requirements.

- Placement of a nasogastric tube can increase intracranial pressure (because of gagging) and thus should generally be performed only in patients who are intubated and sedated.

Malnutrition

- In patients with advanced encephalopathy, parenteral nutrition should be considered early to prevent catabolism of body stores of proteins.

- Branched chain amino acids have been advocated as a source of protein.
Determining Etiologies and Specific Therapies
Acetaminophen Hepatotoxicity

- Acetaminophen is a doserelated toxin; most ingestions leading to ALF exceed 10 gm/day. However, severe liver injury can occur rarely when doses as low as 3-4 gm/day are taken.
- **Acetaminophen levels** should be drawn in all patients presenting with ALF. Low or absent acetaminophen levels do not rule out acetaminophen poisoning since the time of ingestion may be remote or unknown, especially when overdose may have been unintentional and/or occurred over several days.
Acetaminophen Hepatotoxicity

- **Activated charcoal** may be useful for gastrointestinal decontamination. While it is most effective if given within one hour of ingestion, it may be of benefit as long as 3 to 4 hours after ingestion.

- Administration of activated charcoal (standard dose 1g/kg orally, in a slurry) just prior to administration of N-acetylcysteine does not reduce the effect of N-acetylcysteine.

Acetaminophen Hepatotoxicity

- Administration of NAC is recommended in any case of ALF in which acetaminophen overdose is a suspected or possible cause.
- NAC should be given as early as possible, but may still be of value 48 hours or more after ingestion.
- NAC may be given orally (140 mg/kg by mouth or nasogastric tube diluted to 5% solution, followed by 70 mg/kg by mouth q 4 h 17 doses) and has few side effects (occasional nausea, vomiting, rare urticaria or bronchospasm).
Acetaminophen Hepatotoxicity

- In patients with ALF oral administration may often be precluded (for instance, by active gastrointestinal bleeding or worsening mental status), and NAC may be administered intravenously (loading dose is 150 mg/kg in 5% dextrose over 15 minutes; maintenance dose is 50 mg/kg given over 4 hours followed by 100 mg/kg administered over 16 hours).
- Allergic reactions may be successfully treated with discontinuation, antihistamines and epinephrine for bronchospasm
Mushroom Poisoning

- Mushroom Poisoning (usually *Amanita phalloides*) may cause ALF, and the initial history should always include inquiry concerning recent mushroom ingestion. Patients with a history of severe gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal cramping), which occur within hours to a day of ingestion
Mushroom Poisoning

- If these effects are present, it may be early enough to treat patients with gastric lavage and activated charcoal via naso-gastric tube. Fluid resuscitation is also important.
- **Penicillin G and silibinin** (silymarin or milk thistle) are the accepted antidotes despite no controlled trials proving their efficacy. Average doses of 30-40 mg/kg/day (either intravenously or orally) for an average duration of 3 to 4 days.

Drug Induced Hepatotoxicity

- Drugs other than acetaminophen rarely cause dose-related toxicity. Most examples of idiosyncratic drug hepatotoxicity occur within the first 6 months after drug initiation.

- There are no specific antidotes for idiosyncratic drug reactions; corticosteroids are not indicated unless a drug hypersensitivity reaction is suspected.
Some Drugs Which May Cause Idiosyncratic Liver Injury Leading to ALF

- Isoniazid
- Isoflurane
- Sulfonamides
- Lisinopril
- Phenytoin
- Nicotinic acid
- Statins
- Imipramine
- Propylthiouracil
- Gemtuzumab
- Halothane
- Amphetamines/Ecstasy
- Disulfiram
- Labetalol
- Valproic acid
- Etoposide
- Amiodarone
- Flutamide
- Dapsone
- Tolcapone
- Herbals*
- Quetiapine
- Didanosine
- Nefazodone
- Efavirenz
- Allopurinol
- Metformin
- Methyldopa
- Ofloxacin
- Ketoconazole
- PZA
- Troglitazone
- Diclofenac
Viral Hepatitis (HBV)

- As a general rule, we treat patients with a severe (such as those who develop a **coagulopathy** \( \text{INR} > 1.5 \)) or a protracted course (such as persistent symptoms or marked jaundice \( \text{bilirubin} > 10 \text{ mg/dl} \) for more than four weeks after presentation).

- We also suggest treating patients with fulminant hepatitis B to reduce the likelihood of reinfection post-liver transplant, those who are immunocompromised, have concomitant infection with hepatitis C or D virus, have preexisting liver disease, or are elderly.
Viral Hepatitis (HBV)

- **Interferon** should be avoided because of the increased risk of hepatic necroinflammation. Telbivudine, Lamivudine, Adefovire, entecavie, or Tenofovir are acceptable options given as monotherapy as the duration of treatment should be short.

- Treatment can be stopped after confirmation (two consecutive tests four weeks apart) that the patient has cleared HBsAg.
Viral Hepatitis

- HBV – HAV- HEV
- **Herpes virus infection** rarely causes ALF. Immunosuppressed patients or pregnant women (usually in the third trimester) are at increased risk. Skin lesions are present in only about 50% of cases. **Liver biopsy** is helpful in making the diagnosis.
- Treatment should be initiated with acyclovir for suspected or documented cases. Other viruses such as varicella zoster have occasionally been implicated in causing hepatic failure.

Wilson disease

- Wilson disease is an uncommon cause of ALF (2%-3% of cases in the US ALFSG). Early identification is critical because the fulminant presentation of Wilson disease is considered to be uniformly fatal without transplantation.

- The disease typically occurs in young patients, accompanied by the abrupt onset of hemolytic anemia with serum bilirubin levels 20 mg/dL.
Wilson disease

- High serum and urinary copper levels as well as hepatic copper measurement may confirm the diagnosis. Very low serum alkaline phosphatase or uric acid levels are hints to suggest Wilson disease in the absence of other indicators.
- Treatment to acutely lower serum copper and to limit further hemolysis should include albumin dialysis, continuous hemofiltration, plasmapheresis or plasma exchange.
- Initiation of treatment with penicillamine is not recommended in ALF as there is a risk of hypersensitivity to this agent.
Wilson disease

- Although such copper lowering measures should be considered, recovery is infrequent without transplantation.
- Wilson disease is one of the special circumstances in which patients may already have evidence of cirrhosis and still be considered to have a diagnosis of ALF when rapid deterioration occurs.

Autoimmune hepatitis

- With autoimmune hepatitis as with Wilson disease, patients may have **unrecognized preexisting chronic disease** and yet still be considered as having ALF. Such patients represent the most severe form of the disease, and would generally fall into the category of patients recommended for corticosteroid therapy.

- Autoantibodies may be absent making a definitive diagnosis difficult. **Liver biopsy** may be helpful if findings include presence of severe hepatic necrosis accompanied by interface hepatitis, plasma cell infiltration and hepatocyte rosettes.
Acute Fatty Liver of Pregnancy/HELLP Syndrome

- The triad of jaundice, coagulopathy, and low platelets may occasionally be associated with hypoglycemia.
- Features of pre-eclampsia such as hypertension and proteinuria are common. Steatosis documented by imaging studies supports the diagnosis. The Oil-red O staining technique best demonstrates hepatic steatosis on biopsy.
- Intrahepatic hemorrhage and/or hepatic rupture constitute rare emergent situations requiring rapid resuscitation and intervention.
Acute Fatty Liver of Pregnancy/HELLP Syndrome

- Early recognition of these syndromes and prompt delivery are critical in achieving good outcomes.
- **Recovery is typically rapid after delivery**, and supportive care is the only other treatment required. Postpartum transplantation has occasionally been necessary.

Fulminant hepatic failure caused by acute fatty liver of pregnancy treated by orthotopic liver transplantation.

*HEPATOLOGY 1990;11:59-64.*
Acute Ischemic Injury

- A syndrome often referred to as “shock liver” occurs after cardiac arrest, a period of significant hypovolemia/hypotension, or in the setting of severe congestive heart failure. Documented hypotension is not always found.
- Drug-induced hypotension or hypoperfusion may be observed with long-acting niacin, or with cocaine, or methamphetamine.
Budd-Chiari Syndrome

- The Budd-Chiari syndrome (acute hepatic vein thrombosis) can also present as ALF. Abdominal pain, ascites and striking hepatomegaly are often present. The diagnosis should be confirmed with hepatic imaging studies (computed tomography, doppler ultrasonography, venography, magnetic resonance venography). In the presence of significant liver failure, transplantation may be required as opposed to venous decompression.

- As malignancy-associated hypercoagulability is one of the causes of Budd-Chiari syndrome, it is important to rule out underlying cancer prior to transplantation of these patients.
Malignant infiltration of the liver may cause ALF. Massive hepatic enlargement may be seen. Diagnosis should be made by imaging and biopsy, and treatment appropriate for the underlying malignant condition is indicated. **Transplantation is not an option** for such patients. Acute severe hepatic infiltration occurs with:

- Breast cancer
- Small cell lung cancers
- Lymphoma
- Melanoma
Indeterminate Etiology

- When the etiology of ALF cannot be determined after routine evaluation, **biopsy using a transjugular approach** may be helpful in diagnosing malignant infiltration, autoimmune hepatitis, certain viral infections and Wilson disease.

- Lack of a clear diagnosis suggests that the history may have been inadequate regarding toxin or drug exposures.
Artificial hepatic assist devices

- Extracorporeal assist devices currently under development use hepatocytes from human or nonhuman cell lines to provide synthetic capability
Albumin dialysis

- Albumin synthesis was inhibited in ALF.
- Some components is elevated in patient of ALF.
  - Bilirubin, aromatic amino acids, endogenous benzodiazepines, mercaptans, nitric oxide, prostacyclins, and tryptophan.
- Elevated toxic substance may be correlated with clinical status.
The Molecular Absorbent and Recirculating System (MARS)
Figure 1. The MARS® albumin treatment method, (Printed with permission, Teraklin AG, 2005)
MARS

- Ameliorate hepatic encephalopathy and decrease the elevations of intracranial pressure (ICP).
- Decrease in cerebral oxygen extraction concurrent with a clinical improvement in neurologic status.
- The effect is independent of plasma ammonia levels or hemodynamic status.
MARS

- Large increases in factor VII levels, albumin levels, and the ratio of branched-chain amino acids to aromatic amino acids (phase I trial).

- A notable decrease in patient mortality seen with MARS treatment (30-day mortality: 8.3% and 50% with MARS or medical treatment alone; p=0.0027) (a prospective RCT, 2002).

- MARS treatment did result in a marked increase in mean survival time in patients of **hepatorenal syndrome**. (25.2 ± 34.6 days in the MARS versus 4.6 ± 1.8 days in the hemodiafiltration alone group, 2000).