Management of Acute Liver Failure

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Cutting Edge
Surgical Medical Group

Disclosures

- None

Learning Objectives

1. **Identify the key causes and risk factors of acute liver failure**: Understand the various etiologies, including viral infections, drug-induced liver injury, and metabolic disorders, that lead to acute liver failure.
2. **Explain the pathophysiology of acute liver failure**: Recognize the mechanisms underlying liver dysfunction and its impact on the kidneys, coagulation, and brain function.
3. **Describe the treatment strategies for acute liver failure**: Discuss the role of supportive care (fluid management, electrolytes), pharmacological treatments (e.g., N-acetylcysteine, antivirals), and the importance of liver transplantation.
4. **Assess the prognosis and outcomes of acute liver failure**: Understand the factors influencing survival rates, such as etiology, organ function, and the timing of liver transplantation, and be able to recognize when liver transplant is indicated.

Introduction

- Definition of Acute Liver Failure (ALF)
  - - Rapid deterioration of liver function
  - - Impaired synthetic function (e.g., coagulopathy, jaundice) in previously functional liver

Pathophysiology of Acute Liver Failure

- Liver function - Metabolic, detoxification, and synthetic functions
- Mechanisms of acute liver injury
  - 1. Hepatocyte necrosis
  - 2. Inflammatory response and immune activation
  - 3. Impaired microcirculation and ischemia
  - 4. Cascade of events leading to multiorgan failure - Renal failure, coagulation abnormalities, encephalopathy

Causes of Acute Liver Failure

- Infectious causes Viral hepatitis (e.g., Hepatitis A, B, and C)
- Herpes simplex virus (HSV)
- Drug-induced liver injury
  - 1. Acetaminophen toxicity
  - 2. Prescription and non-prescription medications
- C. Hepatic ischemia
  - 1. Shock, hypotension, and hypoperfusion

Causes of Acute Liver Failure

- D. Metabolic disorders
  - 1. Wilson's disease
  - 2. Fatty liver (e.g., NAFLD)
- E. Autoimmune liver disease
  - 1. Autoimmune hepatitis
- F. Toxins and substances
  - 1. Alcohol-related liver damage
  - 2. Herbal supplements and toxins
- G. Other causes
  - 1. Pregnancy-related (e.g., acute fatty liver of pregnancy

Clinical Presentation of Acute Liver Failure

- Early symptoms - Jaundice, fatigue, nausea, vomiting
- Complications
  - 1. Hepatic encephalopathy
  - 2. Coagulopathy and bleeding
  - 3. Renal failure (hepatorenal syndrome)
  - 4. Systemic inflammatory response syndrome (SIRS)
- C. Diagnosis
  - 1. Laboratory tests (liver function tests, coagulation studies)
  - 2. Imaging (e.g., ultrasound, CT/MRI)
  - 3. Clinical criteria and scoring systems (e.g., King's College Criteria)

Treatment of Acute Liver Failure

- *There is no rescue Liver Dialysis that will fix or temporize the condition such as in renal failure*
  - *Needs to Detoxify*
  - *Needs to synthesize*
  - *Needs to provide energy storage*

  - *Big ask of a machine in 2025……*

Treatment of Acute Liver Failure

- General supportive care
  - 1. Intensive monitoring
  - 2. Fluid and electrolyte management
    - Crystalloid
    - Albumin (colloids)
  - 3. Nutritional support
- Pharmacological interventions
  - 1. Antiviral therapy (for viral causes)
  - 2. N-acetylcysteine (NAC) for acetaminophen toxicity
  - 3. Corticosteroids for autoimmune hepatitis
- C. Specific treatments for complications
  - 1. Hepatic encephalopathy management (lactulose, rifaximin)
  - 2. Coagulopathy management (fresh frozen plasma, vitamin K)
  - 3. Renal failure management (dialysis)

Treatment of Acute Liver Failure

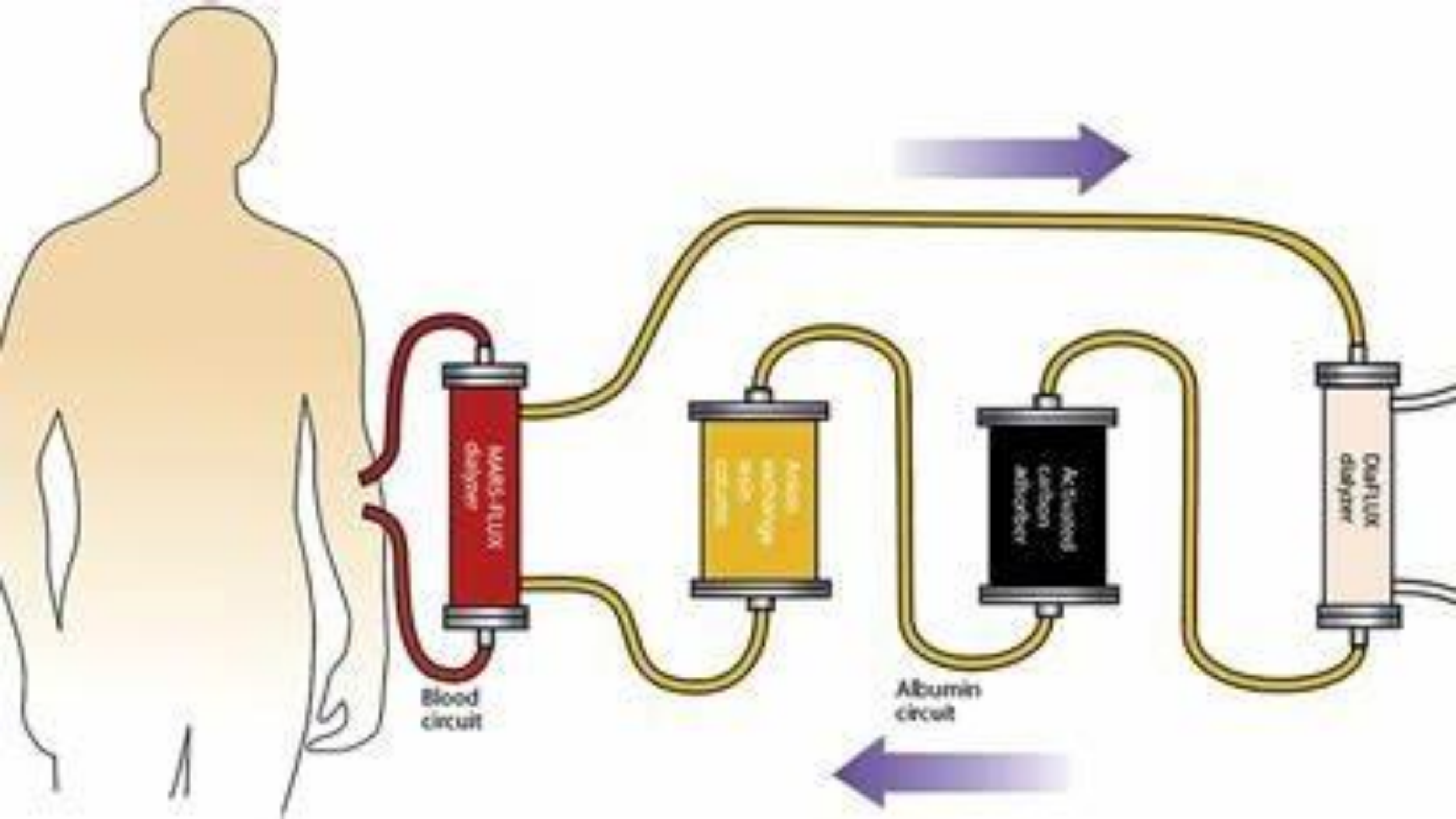
- Liver transplantation
  - 1. Indications for liver transplant
  - 2. Timing and patient selection
- E. Experimental therapies
  - 1. Extracorporeal liver support (e.g., MARS, Prometheus) → limited availability and significant cost
  - 2. Stem cell therapy and gene therapy research

Evidence and Clinical Studies

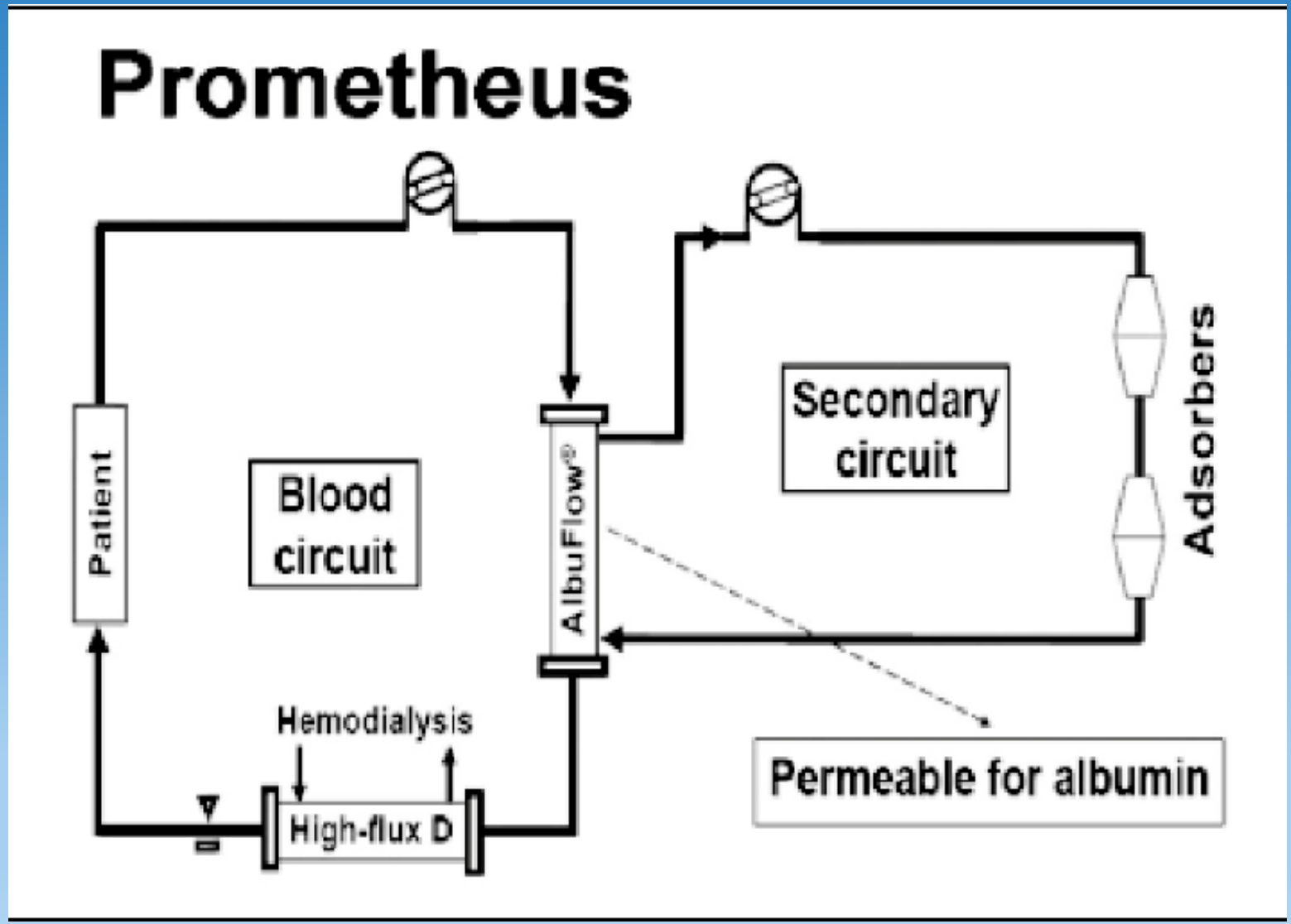
- **MARS (Molecular Adsorbent Recirculating System) and Prometheus** have been studied in both **acute liver failure** and **chronic liver disease**.
  - **MARS** has shown positive effects in **reducing bilirubin levels**, **improving hemodynamics**, and **decreasing mortality rates** when used in patients with **acute liver failure** or **hepatic encephalopathy** (including those waiting for liver transplantation). However, its impact on long-term survival and liver recovery remains mixed in some studies.
  - **Prometheus** has demonstrated improvements in **renal function** and **hepatic encephalopathy** in patients with **acute-on-chronic liver failure** and **acute liver failure**. However, its survival benefits when compared to standard supportive therapy alone are still a subject of debate.

Evidence and Clinical Studies

- **Mortality Rates**:
  - Studies have indicated that patients who receive **extracorporeal liver support** (MARS, Prometheus) may have **lower short-term mortality rates** compared to those receiving only supportive care. However, **long-term survival** rates still depend heavily on **liver transplantation** as the definitive treatment.
  - **MARS** has been shown to significantly reduce **mortality** in patients with **hepatorenal syndrome**, **acute liver failure**, or **chronic liver failure**, but there is no clear evidence showing **long-term survival benefit** unless liver transplantation is performed.


Blood circuit
Albumin circuit

Prometheus



Key Takeaways on Mortality Reduction

- **MARS**: Studies have consistently reported a **30-50% reduction in mortality** for patients treated with MARS, particularly in the **acute liver failure** and **hepatorenal syndrome** populations.
- **Prometheus**: Mortality reduction is estimated at **20-30%**, with better results seen in patients with **acute-on-chronic liver failure** or **hepatic encephalopathy**.

Which Hospitals are doing Liver Dialysis

Medical Center	Treatment System	Estimated Cost per Session (USD)	Total Estimated Cost (USD)
Mayo Clinic (Rochester, MN, USA)	MARS, Prometheus	**$10,000 - $20,000**	**$20,000 - $60,000** for 2-3 sessions
Cleveland Clinic (Cleveland, OH, USA)	MARS, Prometheus	**$10,000 - $20,000**	**$20,000 - $60,000**
Johns Hopkins Hospital (Baltimore, MD, USA)	MARS, Prometheus	**$10,000 - $20,000**	**$20,000 - $60,000**
Mount Sinai Hospital (New York, NY, USA)	MARS, Prometheus	**$10,000 - $20,000**	**$20,000 - $60,000**
UCSF Medical Center (San Francisco, CA, USA)	MARS, Prometheus	**$10,000 - $20,000**	**$20,000 - $60,000**
King's College Hospital (London, UK)	MARS, Prometheus	**$10,000 - $20,000**	**$20,000 - $60,000**
University Hospital Zurich (Zurich, Switzerland)	MARS, Prometheus	**$10,000 - $20,000**	**$20,000 - $60,000**

Outcomes and Prognosis

- Prognostic factors
  - 1. Etiology of ALF
  - 2. Age, comorbidities, and severity of liver damage
- B. Mortality rates
  - 1. Overall mortality (estimated 20-40% depending on etiology and timing)
  - 2. Mortality based on transplant availability and timing
- C. Long-term outcomes for survivors
  - 1. Recovery of liver function
  - 2. Risk of chronic liver disease
  - 3. Post-transplant care and survival rates

Summary

- Importance of early recognition and management
- Comprehensive approach to treatment

Need for further research in improving outcomes

Type 1 Hepatorenal Syndrome

1. Type 1 Hepatorenal Syndrome (HRS-1)

- **Definition:** Type 1 HRS is characterized by **rapid progression** of renal failure and a **poor prognosis**. It is often seen in patients with **acute liver failure** or **acute-on-chronic liver failure**, usually triggered by a precipitating event such as infection (e.g., spontaneous bacterial peritonitis, SBP), gastrointestinal bleeding, or the use of nephrotoxic drugs.
- **Pathophysiology:**
  - In **Type 1 HRS**, there is an **extreme and rapid decrease in renal function**, with a **doubling of serum creatinine** or a decline in **creatinine clearance to less than 20 mL/min** over a short period (typically less than 2 weeks).
  - This results from **marked renal vasoconstriction**, often in the setting of **severe circulatory dysfunction**, **hypovolemia**, or **hepatic vasodilation**. The kidneys are poorly perfused, and renal blood flow is significantly reduced.

Type 2 Hepatorenal Syndrome

2. Type 2 Hepatorenal Syndrome (HRS-2)

- **Definition:** Type 2 HRS is a **slowly progressive** form of renal failure, commonly seen in patients with **cirrhosis and ascites**. Unlike Type 1 HRS, which progresses rapidly, Type 2 HRS has a **chronic, insidious course**.
- **Pathophysiology:**
  - Type 2 HRS is associated with **moderate renal dysfunction** and **gradual deterioration** of kidney function. The decline in renal function is usually slower compared to Type 1, and the progression is often linked to **persistent ascites** despite diuretic therapy.
  - The condition is primarily due to **renal vasoconstriction** and **splanchnic vasodilation**, leading to a reduced effective circulating volume and subsequent renal hypoperfusion.

Hepatorenal Syndrome

III. Summary of Treatment and Mortality Rates

Feature	Type 1 HRS	Type 2 HRS
Progression	Rapid (within weeks)	Slow (over months)
Renal Function	Acute renal failure (rapid worsening of creatinine)	Chronic renal failure (gradual worsening of creatinine)
Primary Cause	Acute-on-chronic liver failure, infections, GI bleeding	Cirrhosis with refractory ascites
Treatment	Vasoconstrictors (terlipressin), albumin, dialysis, liver transplantation	Vasoconstrictors (terlipressin), albumin, liver transplantation, TIPS, dialysis
Mortality	High (50-60% within 1 month without liver transplant)	Moderate (20-40% 1-year survival without liver transplant)

1. **Overall 5-Year Survival Rate:**

   The 5-year survival rate for **liver transplant recipients** is approximately **70-80%**. This means that around **70-80%** of patients will survive 5 years post-transplant, depending on various factors.

Summary of 5-Year Survival Rates:

- **Overall adult liver transplant survival rate:** 70-80%.
- **Pediatric liver transplant survival rate:** ~90%.
- **Factors influencing survival:** Age, liver disease etiology, comorbidities, donor quality, post-transplant complications.

Liver Transplant Survival

Liver Trauma

- **Epidemiology & Significance**
- Liver = **most commonly injured solid organ** in abdominal trauma
- Occurs in:
  - Blunt trauma (~80–90%)
  - Penetrating trauma
- High vascularity → **major hemorrhage risk**
- Mortality associated with:
  - Hemorrhagic shock
  - Associated injuries
- Right lobe more frequently involved

Liver Trauma

- **Mechanism of Injury**
- **Blunt**
- MVCs (most common)
- Falls
- Crush injuries
- **Penetrating**
- Gunshot wounds (GSW)
- Stab wounds
- **Pathophysiology**
- Shearing forces → parenchymal disruption
- Venous bleeding > arterial (most cases)
- Risk of delayed hemorrhage & bile leak

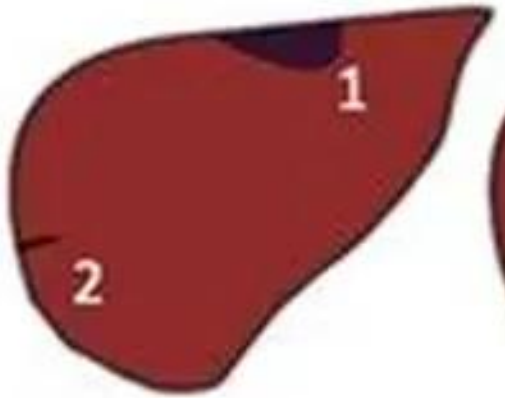
Liver Trauma

- **AAST Liver Injury Scale**
- **Grade I–VI**
- **I:** Subcapsular hematoma <10%, capsular tear <1 cm
- **II:** Hematoma 10–50%, laceration 1–3 cm
- **III:** Hematoma >50% or expanding, lac >3 cm
- **IV:** Parenchymal disruption 25–75% of lobe
- **V:** >75% disruption or major venous injury
- **VI:** Hepatic avulsion (rare, fatal)

Leeds Radiology

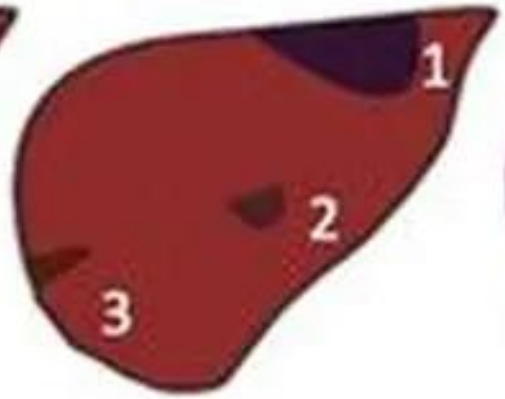
AAST Liver Injury Scale

Grade I



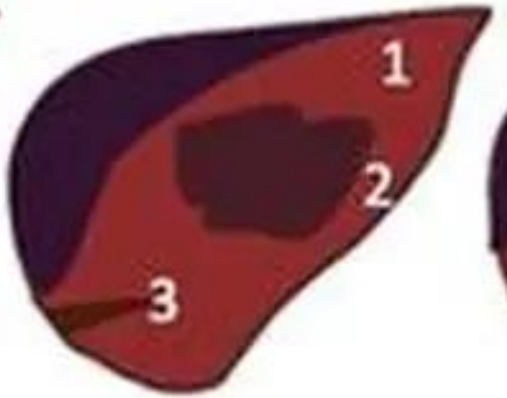
1. Subcapsular hematoma <10% surface area
2. Parenchymal laceration <1 cm in depth

Grade II



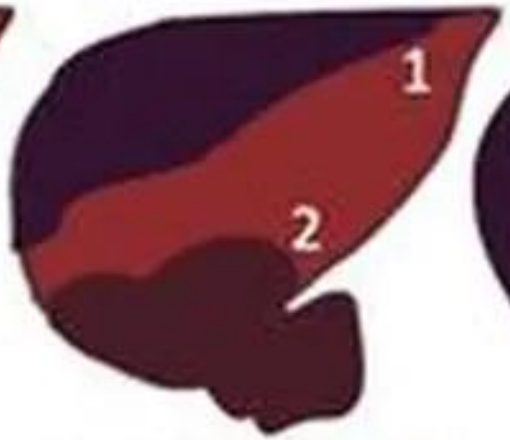
1. Subcapsular hematoma 10–50% surface area
2. Intraparenchymal hematoma <10 cm in diameter
3. Laceration 1–3 cm in depth and ≤ 10 cm length

Grade III



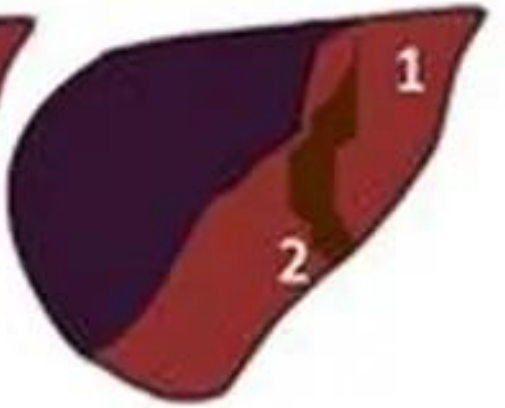
1. Subcapsular hematoma >50% surface area; ruptured subcapsular or parenchymal hematoma
2. Intraparenchymal hematoma >10 cm
3. Laceration >3 cm depth
4. Any injury in the presence of a liver vascular injury or active bleeding contained within liver parenchyma

Grade IV



1. Parenchymal disruption involving 25–75% of a hepatic lobe
2. Active bleeding extending into the peritoneum

Grade V



1. Parenchymal disruption >75% of hepatic lobe
2. Juxtahepatic venous injury to include retrohepatic vena cava and central major hepatic veins

- **The AAST guidelines recommend dual arterial/portal venous phase imaging for evaluation of a vascular injury of liver, spleen, or kidney**
- **Advance one grade for multiple hepatic injuries up to grade 3**

Liver Trauma

- **Hemodynamically Stable Patients**
- **CT Abdomen with IV contrast = gold standard**
  - Identifies:
    - Active extravasation (“blush”)
    - Grade of injury
    - Associated injuries
- **Unstable Patients**
- FAST → OR if positive and unstable

Liver Trauma

- **Nonoperative Management (NOM)**
- **Standard of care in stable patients (~80–90%)**
- **Criteria**
- Hemodynamically stable
- No peritonitis
- No other operative indications
- **Components**
- ICU or monitored setting
- Serial exams & hemoglobin
- Limited activity
- **Adjunct**
- **Angioembolization** for contrast blush

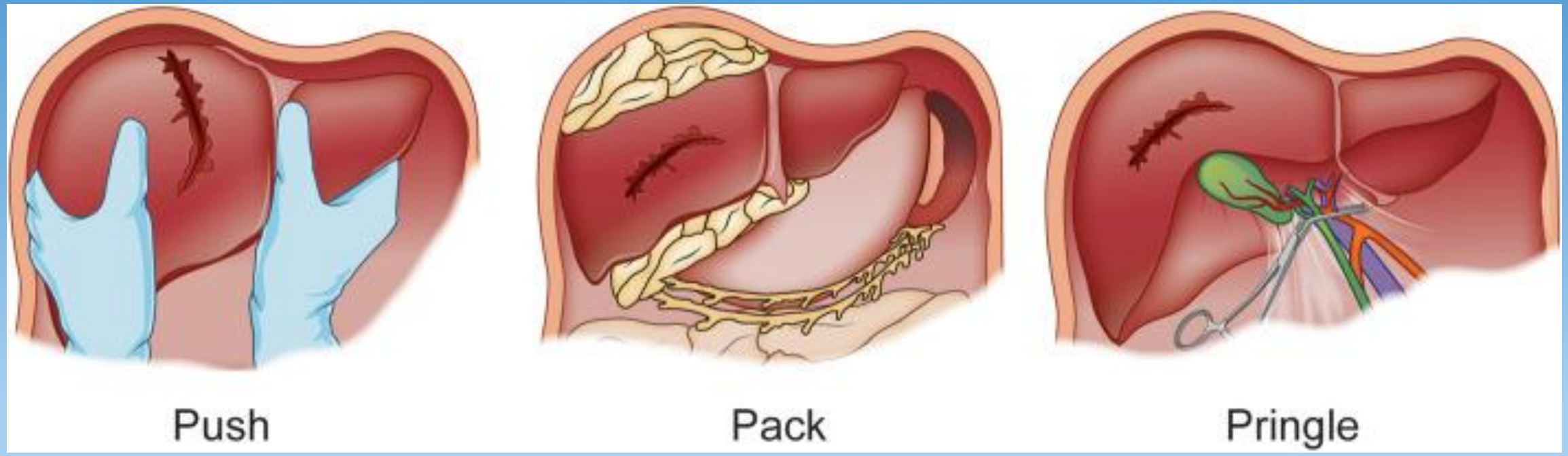
Liver Trauma

- **Indications for Operative Management**
- Hemodynamic instability despite resuscitation
- Peritonitis
- Ongoing transfusion requirement
- Failure of NOM

Liver Trauma

- **Operative Techniques**
- **Damage Control Surgery**
  - Perihepatic packing
  - Temporary abdominal closure
- **Definitive Management**
  - Hepatorrhaphy
  - Resectional debridement
  - Pringle maneuver (portal triad occlusion)
- **Severe injuries**
  - Consider REBOA (adjunct in select cases)

Liver Trauma



Liver Trauma

- **Complications**
- Early:
  - Hemorrhage
  - Coagulopathy
- Late:
  - Bile leak / biloma
  - Hepatic abscess
  - Pseudoaneurysm
  - Delayed hemorrhage

Liver Trauma

- **Key Takeaways**
- Hemodynamics > grade in decision-making
- NOM is **safe and standard** in stable patients
- Angioembolization plays a major role
- Operative management = **damage control first**
- Vigilance for delayed complications is critical

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