**Hepatorenal Syndrome**

**Key Points:**
1. Hepatorenal syndrome (HRS) is the finding of renal failure in the setting of acute or chronic advanced liver failure and is due to effective hypoperfusion to the kidneys.
2. HRS is a diagnosis of exclusion and other causes of renal failure need to be ruled out.
3. Laboratory data is similar to that of a prerenal state.
4. HRS carries a very poor prognosis. The ultimate therapy is liver transplant.

**What is it?** A phenomenon of functional renal failure in the setting of acute or chronic advanced liver failure, usually due to cirrhosis but can be seen in metastatic disease or severe alcoholic liver disease. A very poor prognostic sign.

**What is the mechanism for the renal failure?** Liver failure causes an increase in splanchnic vasodilatation which causes a fall in systemic vascular resistance and effective hypoperfusion of the kidneys. In response to this, the renin-angiotensin system is activated and sympathetic output is increased, leading to renal vasoconstriction.

**What biochemical factors are responsible?** Unclear, but some culprits include:
- Nitric oxide (endothelium-derived relaxing factor)
- Vasoconstrictor thromboxanes or vasodilator prostaglandins: suggested by increased urinary excretion of arachidonic acid metabolites
- Endotoxins not excreted by the liver, endothelins, false neurotransmitters
- Mechanically speaking, elevated liver sinusoidal pressures cause a reflex increase in renal sympathetic tone

**How do you define it?** Defined by International Ascites Club
- Serum creatinine <1.5mg/dL and creatinine clearance of 40mL/min without sustained improvement
- Proteinuria < 500mg/dL
- No ultrasound evidence of obstructive renal disease or parenchymal disease or other causes for renal failure (ie shock, infection, nephrotoxic drugs)

**Other criteria:**
- Urine volume <500mL/day
- Urine sodium <10mEq/day
- Urine osmolarity higher than plasma osmolarity
- Urine RBCs <50/HPF
- Serum sodium <130mEq/L

**What is in the differential?**
HRS is a diagnosis of exclusion once all other causes have been ruled out.
- ATN: while this is usually associated with FeNa >2% and casts in the sediment, FeNa may be low in hepatic failure due to renal hypoperfusion. Also you can see granular and epithelial casts in hyperbilirubinemia alone. Need to rule out toxin-induced ATN, sepsis, bleeding, contrast-induced causes.
- Prerrenal state: Multiple causes, several of which can overlap with hepatic failure. Should see improvement with fluid resuscitation in non HRS states.
- Glomerulonephritis and vasculitis can have RBCs in urine

**What are the types of HRS?**
- **Type I:** rapidly progressive. Serum creatinine doubles to >2.5mg/dL or creatinine clearance <20mL/min in <2weeks. Prognosis horrible—80% die in 2 weeks.
- **Type II:** slower deterioration. Serum creatinine >1.5mg/dL or creatinine clearance <40mL/min but decline is slow. Most patients will die within several weeks.
Are there any treatments?

The only truly effective treatment is liver transplant. Because this is functional renal failure and not intrinsic renal failure, kidneys usually recover after transplant and kidneys taken from cadavers and retransplanted in other patients function well. The following therapies are meant as a bridge to transplant. Of note, umbers in trials are very small.

- Albumin+midodrine(alpha-adrenergic)+octreotide: This has the most promise! Get benefit of systemic vasoconstriction and inhibition of vasodilator release. No serious side effects and some improvement in renal function.
- Ornipressin or terlipressin: synthetic forms of arginine vasopressin. Has vasoconstrictor effects. Improvement in renal function seen, but several patients had to stop ornipressin due to ischemic complications.
- N-acetylcysteine: may minimize splanchnic vasocilation and nitric oxide production by reducing oxygen radicals.
- TIPS(transjugular intrahepatic portosystemic shunt): short term benefit but encephalopathy is large risk.

Does dialysis help? Generally not helpful, especially since difficult to perform due to hemodynamic compromise. One recent study showed improved mortality at 7 and 30 days when a special dialysis system (MARS=molecular adsorbent recirculating system) was used that allowed for removal of albumin-bound substances.

References:
UpToDate 10.2 on hepatorenal syndrome.