to judicious administration of intravenous fluids and diuretic withdrawal, making it easy to recognize. It is sometimes more difficult to distinguish CRS type 1 from ATN, because the processes often coexist.

Identification of AKI in the setting of heart failure is clinically relevant because reduced GFR is generally associated with a worse prognosis. Therapy is directed at improving cardiac function, especially in patients with low cardiac output, and relieving pulmonary and renal congestion. Loop diuretics are part of the central treatment strategy for relieving venous congestion; however, these agents can directly stimulate maladaptive neurohormonal responses, transiently worsening kidney function after their introduction. Patients with congestive heart failure often have some degree of diuretic resistance. Strategies to overcome this resistance include combination therapy with thiazide diuretics and sometimes device-driven ultrafiltration. With advanced AKI, RRT is required to treat uremia, metabolic complications, and volume overload. Therapies for end-stage cardiac failure include cardiac transplantation and placement of a left ventricular assist device for long-term destination therapy or as a bridge to transplantation.

Hepatorenal Syndrome

A strong physiologic interplay also occurs between liver disease and kidney impairment. Patients with advanced, decompensated cirrhosis or fulminant acute hepatic failure develop a unique form of prerenal AKI called hepatorenal syndrome (HRS). The International Ascites Club diagnostic criteria for HRS include (1) the presence of cirrhosis and ascites, (2) serum creatinine levels higher than 1.5 mg/dL, (3) no improvement in kidney function after at least 48 hours of diuretic withdrawal and volume expansion with albumin, (4) absence of shock, (5) no nephrotoxic drug exposure, and (6) absence of parenchymal kidney disease. There are two subtypes of HRS based on rapidity and severity of kidney impairment. Type 1 HRS is characterized by rapidly progressive renal failure, defined by doubling of the initial serum creatinine concentration (to >2.5 mg/dL in <2 weeks). Type 2 HRS is characterized by moderate kidney failure (serum creatinine increase from 1.5 to 2.5 mg/dL). The hallmark of HRS is profound renal vasoconstriction in the setting of systemic and splanchnic arterial vasodilatation. The hemodynamic changes that occur in HRS are summarized in E-Figure 31-3.

There is no test that is specific for the diagnosis of HRS, and diagnosis requires exclusion of other causes of AKI. The main differential diagnoses of type 1 HRS are prerenal AKI and ATN, which have an acute onset with progressive deterioration of kidney function. Recognition of prerenal AKI is typically easier, because it responds to intravenous fluids (albumin and saline), whereas HRS type 1 and ATN are more difficult to differentiate. Distinguishing ATN from HRS is crucial, because therapies for these two forms of AKI are very different, as are their prognoses and outcomes. For HRS, midodrine and octreotide, vasopressin (or its analogue terlipressin outside of the United States), or norepinephrine is used, whereas ATN requires primarily supportive therapy with initiation of RRT if necessary. Liver (or combined liver-kidney) transplantation is the definitive therapy for HRS.

Intrinsic AKI

Intrinsic AKI reflects kidney injury that arises from a process that damages one of the compartments of the renal parenchyma. To simplify the approach, kidney disease is organized into anatomic sites of injury in the vasculature, glomerulus, tubules, and interstitium.

Vascular Disease

Intrinsic AKI may result from vascular disease in large or medium-sized arteries, small arteries, and arterioles within the renal parenchyma and veins draining the kidneys. Bilateral renal artery thrombosis superimposed on underlying high-grade stenoses, significant cardiac or aortic thromboembolism occluding the renal arteries, or dissection of the renal arteries may cause AKI. With acute presentations, the clinical features often include flank or abdominal pain, fever, hematuria, and oligo-anuria or anuria. Therapy with thrombolytics may reverse acute thrombosis and thromboembolism and restore renal blood flow with early diagnosis. Percutaneous angioplasty with stent placement can noninvasively correct significant underlying renal artery stenosis. Renal artery dissection often requires surgical repair, but at times stent placement may suffice. Vasculitis of large renal vessels (e.g., Takayasu's arteritis, giant cell arteritis) is an extremely rare cause of AKI.

Induction of AKI by renal atheroemboli occurs less commonly than before, perhaps because of improved techniques and use of softer wires during vascular procedures. Cholesterol crystal embolization is caused most often by invasive vascular procedures in patients with atherosclerotic disease that disrupt the fibrous cap on the ulcerated plaque. However, thrombolytic therapy and therapeutic anticoagulation can also precipitate embolization in patients who have a significant burden of renal artery or aortic plaque. When it occurs, atheromatous material may lodge in interlobar, arcuate, or interlobular arteries in the kidneys. In addition to AKI, clinical manifestations include abrupt onset of severe hypertension, livedo reticularis, digital or limb ischemia, abdominal pain from pancreatitis or bowel ischemia, gastrointestinal bleeding, muscle pain, central nervous system symptoms such as focal neurologic deficits, confusion, amaurosis fugax, and retinal ischemic symptoms. Peripheral eosinophilia, hypocomplementemia, elevated sedimentation rate, and eosinophiluria variably accompany the syndrome. Treatment is primarily preventive by avoiding the factors known to precipitate atheroembolization. BP control, treatment with statins, amputation of necrotic limbs, aggressive nutrition, avoidance of anticoagulation (to reduce the risk for further embolization), and RRT for severe AKI may improve the dismal prognosis associated with this syndrome. Steroids and iloprost are sometimes used, but their therapeutic role is uncertain.

AKI from vasculitis involving the medium and small vessels has been described with classic polyarteritis nodosa. It is either idiopathic or secondary to hepatitis B antigenemia and manifests with severe hypertension and AKI. Renal arteriography demonstrating beading in the arterial tree of the kidney (and other organs) is diagnostic. Scleroderma is a disorder characterized by arterial and arteriolar narrowing due to deposition of mucinous material. Scleroderma renal crisis manifests as AKI and