myocardial ischemia, including left ventricular hypertrophy and microvascular disease. In addition, hemodialysis, with its attendant episodes of hypotension and hypovolemia, may further aggravate coronary ischemia and repeatedly stun the myocardium. Interestingly, however, the largest increment in cardiovascular mortality rate in dialysis patients is not necessarily directly associated with documented acute myocardial infarction but, instead, presents with congestive heart failure and all of its manifestations and sudden death.

Cardiac troponin levels are frequently elevated in CKD without evidence of acute ischemia. The elevation complicates the diagnosis of acute myocardial infarction in this population. Serial measurements may be needed, and if the level is unchanged, it is possible that there is no acute myocardial ischemia. Therefore, the trend in levels over the hours after presentation may be more informative than a single, elevated level. Interestingly, consistently elevated levels are an independent prognostic factor for adverse cardiovascular events in this population.

**Heart Failure**   Abnormal cardiac function secondary to myocardial ischemia, left ventricular hypertrophy, and frank cardiomyopathy, in combination with the salt and water retention that can be seen with CKD, often results in heart failure or even pulmonary edema. Heart failure can be a consequence of diastolic or systolic dysfunction, or both. A form of "low-pressure" pulmonary edema can also occur in advanced CKD, manifesting as shortness of breath and a "bat wing" distribution of alveolar edema fluid on the chest x-ray. This finding can occur even in the absence of ECFV overload and is associated with normal or mildly elevated pulmonary capillary wedge pressure. This process has been ascribed to increased permeability of alveolar capillary membranes as a manifestation of the uremic state, and it responds to dialysis. Other CKD-related risk factors, including anemia and sleep apnea, may contribute to the risk of heart failure.

**Hypertension and Left Ventricular Hypertrophy**   Hypertension is one of the most common complications of CKD. It usually develops early during the course of CKD and is associated with adverse outcomes, including the development of ventricular hypertrophy and a more rapid loss of renal function. Many studies have shown a relationship between the level of blood pressure and the rate of progression of diabetic and nondiabetic kidney disease. Left ventricular hypertrophy and dilated cardiomyopathy are among the strongest risk factors for cardiovascular morbidity and mortality in patients with CKD and are thought to be related primarily, but not exclusively, to prolonged hypertension and ECFV overload. In addition, anemia and the placement of an arteriovenous fistula for hemodialysis can generate a high cardiac output state and consequent heart failure.

The absence of hypertension may signify poor left ventricular function. Indeed, in epidemiologic studies of dialysis patients, low blood pressure actually carries a worse prognosis than does high blood pressure. This mechanism, in part, accounts for the "reverse causation" seen in dialysis patients, wherein the presence of traditional risk factors, such as hypertension, hyperlipidemia, and obesity, appear to portend a better prognosis. Importantly, these observations derive from cross-sectional studies of late-stage CKD patients and should not be interpreted to discourage appropriate management of these risk factors in CKD patients, especially at early stages. In contrast to the general population, it is possible that in late-stage CKD, low blood pressure, reduced body mass index, and hypolipidemia indicate the presence of an advanced malnutrition-inflammation state, with poor prognosis.

The use of exogenous erythropoiesis-stimulating agents can increase blood pressure and the requirement for antihypertensive drugs. Chronic ECFV overload is also a contributor to hypertension, and improvement in blood pressure can often be seen with the use of dietary sodium restriction, diuretics, and fluid removal with dialysis. Nevertheless, because of activation of the RAS and other disturbances in the balance of vasoconstrictors and vasodilators, some patients remain hypertensive despite careful attention to ECFV status.

## TREATMENT   CARDIOVASCULAR ABNORMALITIES

### MANAGEMENT OF HYPERTENSION

The overarching goal of hypertension therapy in CKD is to prevent the extrarenal complications of high blood pressure, such as cardiovascular disease and stroke. Although a clear-cut generalizable benefit in slowing progression of CKD remains as yet unproven, the benefit for cardiac and neurologic health is compelling. In all patients with CKD, blood pressure should be controlled to levels recommended by national guideline panels. In CKD patients with diabetes or proteinuria >1 g per 24 h, blood pressure should be reduced to 130/80 mmHg, if achievable without prohibitive adverse effects. Salt restriction should be the first line of therapy. When volume management alone is not sufficient, the choice of antihypertensive agent is similar to that in the general population. ACE inhibitors and ARBs appear to slow the rate of decline of kidney function in a manner that extends beyond reduction of systemic arterial pressure and that involves correction of the intraglomerular hyperfiltration and hypertension involved in progression of CKD described above. Occasionally, introduction of ACE inhibitors and ARBs can actually precipitate an episode of acute kidney injury, especially when used in combination in patients with ischemic renovascular disease. The use of ACE inhibitors and ARBs may also be complicated by the development of hyperkalemia. Often the concomitant use of a kaliuretic diuretic, such as metolazone, can improve potassium excretion in addition to improving blood pressure control. Potassium-sparing diuretics should be used with caution or avoided altogether in most patients.

### MANAGEMENT OF CARDIOVASCULAR DISEASE

There are many strategies available to treat the traditional and nontraditional risk factors in CKD patients. Although these have proved effective in the general population, there is little evidence for their benefit in patients with advanced CKD, especially those on dialysis. Certainly hypertension, elevated serum levels of homocysteine, and dyslipidemia promote atherosclerotic disease and are treatable complications of CKD. Renal disease complicated by nephrotic syndrome is associated with a very atherogenic lipid profile and hypercoagulability, which increases the risk of occlusive vascular disease. Because diabetes mellitus and hypertension are the two most frequent causes of advanced CKD, it is not surprising that cardiovascular disease is the most frequent cause of death in dialysis patients. The role of "inflammation" may be quantitatively more important in patients with kidney disease, and the treatment of more traditional risk factors may result in only modest success. However, modulation of traditional risk factors may be the only weapon in the therapeutic armamentarium for these patients until the nature of inflammation in CKD and its treatment are better understood.

Lifestyle changes, including regular exercise, should be advocated. Hyperlipidemia in patients with CKD should be managed according to national guidelines. If dietary measures are not sufficient, preferred lipid-lowering medications, such as statins, should be used. Again, the use of these agents has not been of proven benefit for patients with advanced CKD.

**Pericardial Disease**   Chest pain with respiratory accentuation, accompanied by a friction rub, is diagnostic of pericarditis. Classic electrocardiographic abnormalities include PR-interval depression and diffuse ST-segment elevation. Pericarditis can be accompanied by pericardial effusion that is seen on echocardiography and can rarely lead to tamponade. However, the pericardial effusion can be asymptomatic, and pericarditis can be seen without significant effusion.

Pericarditis is observed in advanced uremia, and with the advent of timely initiation of dialysis, is not as common as it once was. It is now more often observed in underdialyzed, nonadherent patients than in those starting dialysis.