Vascular Calcification in Chronic Renal Failure

William G. Goodman, M.D.

Division of Nephrology, UCLA School of Medicine, USA

Vascular calcification is an important and potentially serious complication of chronic renal failure. Calcification occurs predominantly in the medial wall of arteries, a process known a Monckerberg's sclerosis. This type of vascular calcification also occurs in diabetes mellitus, but disturbances in calcium and phosphorus metabolism have traditionally been considered to play a pathogenic role in renal failure by promoting the passive deposition of mineral, predominantly calcium and phosphorus, in blood vessels and other soft-tissues. Accordingly, hyperphosphatemia, hypercalcemia, elevated values of the calcium-phosphorus ion product in serum, and treatment with vitamin D sterols have each been implicated as contributors to the development of vascular calcification in end-stage renal disease (ESRD).

Recent evidence further implicates certain abnormalities in mineral metabolism and/or the therapeutic interventions designed to manage them as risk factors not only for vascular calcification but also for cardiovascular morbidity and mortality in the ESRD population. Hyperphosphatemia *per se* has been shown to independently increase the risk for all-cause mortality, mostly from cardiovascular causes, in patients undergoing hemodialysis. Several groups of investigators have reported that the use of large oral doses of calcium as a phosphate-binding agent is associated with evidence of arterial calcification as documented by non-invasive methods. Such findings raise concerns about the long-term safety and efficacy of calcium-containing compounds for managing phosphate retention in patients who have little or no residual renal function to excrete excess amounts of calcium that may be absorbed from the gastrointestinal tract. Indeed, current paradigms for the management of secondary hyperparathyroidism and renal bone disease are being re-evaluated in the context of these developments and revised treatment regimens have been suggested to limit therapeutic risks.

It is now generally appreciated that arterial calcification is an integral component of the atherosclerotic process. Indeed, 80 to 90% of atherosclerotic plaques contain calcium. Evidence has accumulated in recent years to suggest that various genes and proteins that normally modulate bone and mineral metabolism are involved in atherosclerotic arterial calcification, and similar observations apply to medial wall calcification. Thus, uremic vascular calcification may not simply reflect passive mineral accumulation, or dystrophic calcification, in the arterial wall. Rather, alterations in the expression of selected genes and proteins that either promote or inhibit the calcification process in blood vessels and other soft-tissue may play a key pathogenic role in the vascular calcification of chronic renal failure.