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Parfitt A M. Soft tissue calcification in uremia.
Arch. Intern. Med. **124**:544-56, 1969.
[Depts. Med., Cedars-Sinai Med. Ctr., Los Angeles, CA, and Univ. Queensland, Brisbane, Australia]

In chronic renal failure, calcium salts can be deposited in the tunica media of large and small arteries, in the cornea and conjunctiva, as nodular or tumoral masses around joints, in the skin and subcutaneous tissues, and in viscera such as lungs, kidney, stomach, and heart, with a wide spectrum of clinical effects. Pathogenesis depends on chronic hyperphosphatemia and on alterations in connective tissue proteins from a variety of causes to form a calcifiable matrix that binds calcium and phosphate ions. [The *SCI*® indicates that this paper has been cited in over 170 publications since 1969.]

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"In August 1968, I began a sabbatical leave in Los Angeles at the invitation of Charles R. (Chuck) Kleeman, who was busy organizing the third National Institutes of Health supported conference on chronic renal failure and dialysis, to be held in November at the Miramar Hotel, Santa Barbara. He had asked me to cover the subject of soft tissue calcification and I had reluctantly agreed, in the spirit that in the country of the blind the one-eyed man was king! My presentation was based on extensive clinical experience, both of renal osteodystrophy and its geographic variation in three continents, and of mineral metabolism generally, which I now had the opportunity to reflect upon and to codify. I also made a detailed but selective analysis of the experimental literature from a clinical perspective, a task made easier by the superb medical library at the University of California in Los Angeles.

"After the conference, Chuck was disappointed that I did not begin some experimental work on the subject, but my research interests were shifting away from the kidney and systemic mineral metabolism toward the bone. Completion of the manuscript was interrupted by my falling ill with hepatitis, but with my wife, Elaine, as courier, and my first systematic use of *Current Contents*®, I was able to get all the material needed and to keep abreast of recent developments. The conference proceedings were published in four consecutive issues of *Archives of Internal Medicine*, later collected into a single symposium volume entitled *Divalent Ion Metabolism and Osteodystrophy in Chronic Renal Failure*[1] with Chuck as guest editor. For several years this was an indispensable reference source, marred only by some excessively pedantic subediting.

"I believe the paper has been frequently cited for three main reasons. First, it was the earliest review of the subject during the modern era of treatment for chronic renal failure; hemodialysis and renal transplantation had only recently been widely applied, with a manifold increase in the number of patients at risk. Second, I was able to put what had been an area of great confusion into some sort of order. The clinical classification I proposed is still in use, with minor modifications,[2] and each clinical type was compared with a counterpart occurring in the absence of uremia. I clarified the relationships between several different syndromes of articular and periarticular calcification, so that the article was useful to rheumatologists and orthopedists as well as to nephrologists. Concerning pathogenesis, I emphasized the interplay of both local factors leading to so-called dystrophic calcification, and systemic factors leading to so-called metastatic calcification. Third, substantial improvement in the control of hyperphosphatemia and secondary hyperparathyroidism in renal patients has greatly reduced the incidence of all forms of soft tissue calcification, so that the subject has since received comparatively little investigative attention. The most important subsequent advances[2,3] have been the identification of different calcium salts, such as oxalate[3] and a magnesium-containing compound resembling Whitlockite,[4] the increasing recognition of cardiopulmonary complications of calcium deposition[3,5] and their detection with variable success by scintigraphy,[6] and the likely role of abnormal pyrophosphate metabolism in pathogenesis."[7]

1. **Kleeman C R,** ed. *Divalent ion metabolism and osteodystrophy in chronic renal failure*. Chicago: American Medical Association, 1969. 54 p.
2. **Coburn J W & Slatopolsky E.** Vitamin D, parathyroid hormone and renal osteodystrophy. (Brenner B M & Rector F C, eds.) *The kidney*. Philadelphia: Saunders, 1981. Vol. II. p. 2213-305.
3. **Parfitt A M.** Soft tissue calcification in uremia. *Dialysis Transplant.* 5:17-24, 1976.
4. **LeGeros R Z, Contiguglia S R & Alfrey A C.** Pathological calcifications associated with uremia. Two types of calcium phosphate deposits. *Calcified Tissue Res.* 13:173-85, 1973.
5. **Conger J D, Hammond W S, Alfrey A C, Contiguglia S R, Stanford R E & Huffer W E.** Pulmonary calcification in chronic dialysis patients. *Ann. Intern. Med.* 83:330-6, 1975. (Cited 70 times.)
6. **De Graaf P, Schicht I M, Pauwels E K J, Souverijn J H M & de Graeff J.** Bone scintigraphy in uremic pulmonary calcification. *J. Nucl. Med.* 20:201-6, 1979.
7. **Alfrey A C, Solomons C C, Ciricillo J & Miller N L.** Extraosseous calcification. Evidence for abnormal pyrophosphate metabolism in uremia. *J. Clin. Invest.* 57:692-9, 1976.