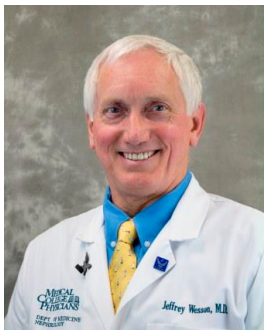
SPECIAL PHYSICAL CHEMISTRY SEMINAR

Monday
June 27, 2016

3:00 pm

Room 8335
Chemistry

The inhibitor/promoter paradox in kidney stone disease: Contributions of proteins and other macromolecules to calcium oxalate stone formation.



Professor Jeffrey A. Wesson

Department of Medicine/Nephrology
Department of Veterans Affairs Medical Center
and Medical College - Milwaukee

Host: Hyuk Yu

All kidney stones form as aggregates of crystals with a bio-organic material layer that is primarily protein coating each crystal surface. Crystal formation and its connection to supersaturation have been extensively studied for all stone types, and supersaturation reduction forms the basis of all current stone prevention therapies. Unfortunately, supersaturation data are poorly correlated with stone risk in calcium oxalate stone formers (the most common type), so considerable attention has been given to the organic matrix over the past several decades, though the role of proteins in stone formation remains poorly understood. Most proteins thought to be important to stone formation contain a large number of acidic amino acids (aspartic acid or glutamic acid) or posttranslational sites (phosphorylation or glycosylation). Most of these proteins studied individually *in vitro* inhibit the various crystallization processes (nucleation, growth, aggregation and cell attachment) that must comprise the stone forming process. On the other hand, many proteins, including osteopontin, are consistently identified in stone matrix and are correlated with increased risk for stone formation in some animal models. In this presentation, a series of experiments that probe the nature of protein or polymer interactions with pre-existing or growing calcium oxalate crystal surfaces at a near molecular level will be summarized. By correlating these data with studies of bulk crystallization effects on growth and aggregation rates, the effects polymer structure on crystal surface interactions can be isolated. These experiments suggest that similar crystal surface interactions are likely common to both inhibitors and promoters of stone formation, dominated by the presence of anionic side chains on the macromolecules and sensitive to very local interactions. Conversely, differentiation between inhibition and promotion of stone forming processes appears to be dependent on polymer-polymer (protein-protein) interactions (i.e., solution phase behavior). These observations have helped us understand the pattern of protein inclusion in stone matrix.