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Nephrolithiasis: Introduction

Nephrolithiasis is one of the most common urologic diseases. In industrialized countries up to 12% of men and 7% of women will form a kidney stone in their lifetime, and the prevalence appears to be increasing. Surgical management of nephrolithiasis was transformed in the 1980s and 1990s by the introduction of lithotripsy and minimally invasive surgery, making open surgery for stone disease a relic of the past. Equally important progress has been made in our understanding of the pathophysiology of kidney stone disease: from the initial formation of crystals in the renal papillae to greater understanding of calcium, oxalate, and uric acid metabolism, and even into the genetic underpinnings of kidney stone disease. This issue of *Seminars in Nephrology* provides the reader with an up-to-date review of the most important research in the field over the past decade as well as critical information from the field of urology that needs to be brought to the attention of the nephrologic community.

The issue begins with an overview of the medical evaluation of patients with nephrolithiasis. The article stresses the importance of identifying environmental and dietary factors that contribute to stone risk that can be modified by the patient, and provides guidelines for the laboratory evaluation of stone patients. Some aspects of nephrolithiasis are often thought of as the purview of the urologist, but the nephrologist and other medical practitioners need a better knowledge of the care of acute renal colic and the potential risks associated with urologic intervention to remove stones. Sterrett and Nakada present an important update on medical expulsive therapy to aid in spontaneous passage of ureteral stones. A number of drugs have been shown to relax smooth muscle in the ureter and are now being used to facilitate stone passage in patients presenting with acute renal colic. They present the underlying physiologic mechanisms by which these drugs work and the current state of clinical trials showing the effectiveness of such therapy in reducing the need for surgery and alleviating pain. Extracorporeal shock wave lithotripsy was introduced in the mid-1980s and revolutionized the care of patients with kidney stones. However, renal and systemic effects have not been appreciated by the nephrology community. McAteer and Evan provide an in-depth overview of the acute and chronic adverse effects of lithotripsy therapy from animal models and human studies. Clinicians need to be aware of these potential adverse effects, especially in patients with recurrent stone disease who may undergo multiple bilateral lithotripsy procedures in their lifetime.

The events that lead to stone formation have long been an interest in the stone research community. Recent advances in endoscopic and ureteroscopic surgery now allow direct visualization of stones in the renal pelvis and even allow biopsy of small stones and the underlying plaque to which they adhere. Evan et al provide a summary of their paradigm-shifting work, showing the formation of apatite plaque in the renal papilla and how calcium oxalate stones form on the plaque. The combination of digital endoscopic surgery, histology, mineral analysis, and clinical laboratory evaluation of the patients provides new insights that the field of stone research has long awaited.

Idiopathic hypercalciuria is the most common metabolic abnormality found in patients with calcium nephrolithiasis. Worcester and Coe provide an overview of the pathophysiology of idiopathic hypercalciuria, focusing on the multiple organ systems involved in the hypercalciuria phenotype and highlighting their recent work on changes in renal reabsorption

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in response to feeding. Zerwekh reviews an under-recognized phenomenon: bone disease in hypercalciuric stone formers. The article summarizes the clinical data showing reduced bone mineral density and increased fracture risk in these patients and reviews the potential pathophysiologic mechanisms responsible for the bone loss.

The vast majority of kidney stones in industrialized countries are calcium oxalate. The importance of urine oxalate excretion in the formation of kidney stones cannot be questioned, but historically little effort was focused on oxalate because of limited therapeutic options beyond restricting diet oxalate. However, recent advances in our understanding of intestinal oxalate handling has led to new interest in using the gut to dispose of the daily oxalate load. Hatch and Freel provide a summary of intestinal oxalate handling, focusing on the gut as an oxalate excretion pathway. The role of intestinal bacteria in normal oxalate metabolism and probiotics as a potential therapy to reduce urine oxalate also is explored. Another example of the role of the gut in oxalate metabolism is the subject of the article by Lieske et al. It has been well documented that extensive small-bowel resection or diversion, as in the case of jejunoileal bypass for obesity, can lead to malabsorption with paradoxic hyperabsorption of oxalate from the diet. Gastric bypass and other procedures quickly replaced the jejunoileal bypass once it was banned. Lieske et al present data showing the strong association of hyperoxaluria with contemporary bariatric surgery and review the possible mechanisms that might lead to hyperoxaluria.

Primary hyperoxaluria and cystinuria are inherited diseases that cause kidney stones. The stone disease often presents in childhood and can be a severe and recurrent form of stone disease. Loss of kidney function can complicate either of these disorders, although it is more common in primary hyperoxaluria. Bobrowski and Langman review the gene defects, clinical presentation, medical management, and the role of transplantation in primary hyperoxaluria. Mattoo and Goldfarb provide a thorough discussion of the recent advances in our knowledge of the genetic abnormalities in cystinuria. They also provide a review of the clinical evaluation of the cystinuric patient and a comprehensive guide to management of patients with cystinuria.

Metabolic syndrome has received considerable attention over the past decade, particularly the cardiovascular risks. Maalouf and Sakhaee focus on their recent research into the association of metabolic syndrome and uric acid stone formation. The authors review the pathophysiology of overly acidic urine in these uric acid stone formers and link it to a deficit in ammonia production, perhaps mediated by changes in insulin signaling in the kidney.

Nephrolithiasis is a multidisciplinary disease, the urologists handle all surgical aspects of the disease but the medical management may be done by urology, primary care, endocrinology, or nephrology. Nephrolithiasis is not a significant component of many nephrology practices, even though the nephrologist is uniquely qualified to manage the subtleties of this disorder. Our goal with this issue is to provide an update that will allow nephrologists to practice at the standard of care and hopefully stimulate greater interest in the medical care and research of nephrolithiasis within the nephrology community. Finally, I would like to thank the contributing authors of this issue of *Seminars in Nephrology* for their efforts in creating an outstanding overview of nephrolithiasis. Their knowledge, clinical expertise, and diligence made this issue possible.

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