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## Renal calculi: The current concept

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### Abstract

Nephrolithiasis is a long-standing medical condition, although the precise processes behind the production and progression of kidney stones remain mainly elusive. In recent years, advancements in technology have led to the development and implementation of several theories and tactics for surgically managing kidney stones. Authors and other research groups have observed that there are five distinct mechanisms responsible for the production of kidney stones. Urinary super saturation and crystallization are the main factors that cause crystals to form within the kidneys. Randall's plaques are acknowledged as the source of calcium oxalate stone development. Sex hormones are likely to have a crucial role in the development of nephrolithiasis and could therefore be potential targets for novel medications aimed at inhibiting the formation of kidney stones. The microbiome, which consists of bacteria that produce urease, nano-bacteria, and intestinal microbiota, is expected to significantly impact urological health in both beneficial and detrimental ways due to its metabolic output and other contributions. Finally, the immunological response, specifically the development of macrophages, plays a vital role in the creation of calcium oxalate crystals in the kidneys. The current understanding of each of these five components of kidney stone production is examined in this study. This knowledge can be utilized to investigate new study prospects and enhance the comprehension of the onset and progression of kidney stones for urologists, nephrologists, and primary care practitioners.

**Keywords:** Nephrolithiasis, kidney stones, urinary super saturation, crystallization, Randall's plaques, calcium oxalate stones

### Introduction

Kidney stone disease, commonly referred to as nephrolithiasis or urolithiasis, is a long-standing medical condition with a rich historical background. Approximately 1-15% of persons experience kidney stone formation at some point in their lives, and there is a global trend of growing prevalence and incidence of kidney stones. A recent study determined that the incidence of kidney stones among Chinese people was 5.8%, with a higher rate of 6.5% in males and a lower rate of 5.1% in women. This means that approximately 1 in 17 adults in China are currently affected by kidney stones. Untreated kidney stones can lead to the obstruction of the ureter, haematuria, recurrent urinary tract infections, emesis or dysuria, ultimately resulting in irreversible renal impairment <sup>[1]</sup>.

Urolithiasis has become more common globally in recent decades. Urolithiasis is a condition that frequently occurs repeatedly during a person's life, with a recurrence rate of 50% within 5-10 years and 75% within 20 years. Several studies have suggested that there would likely be a rise in the occurrence of kidney stones due to several environmental factors, such as alterations in lifestyle and food patterns, together with the effects of global warming. However, the specific reasons that are responsible for the increasing prevalence and recurrence of urolithiasis have not yet been determined. The high prevalence of kidney stone disease in working-age adults has a significant impact on both individuals and society <sup>[1, 2]</sup>.

This has led to it being a public health concern, especially in countries with a hot and dry climate. The mineralogical composition of kidney stones can be categorised into five primary types: calcium oxalate (caOx; 65.9%), carabapatite (15.6%), urate (12.4%), struvite (magnesium ammonium phosphate, 2.7%), and brushite (1.7%). Kidney stones can be classified into two main types: calcareous stones, which contain calcium, and non-calcareous stones. The predominant forms of kidney stones in humans are caOx and calcium phosphate (caP), either individually or in combination <sup>[2]</sup>. These stones are characterised by their calcareous nature and ability to be detected on radiographs.

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Kidney stones develop on a base of calcium phosphate called Randall's plaques (RPs), which originate at the basement membranes of the thin limbs of the loop of Henle on the surface of the renal papilla. Calcium oxalate (caOx) and urate stones are more common in males, while females have a larger prevalence of carbapatite and struvite stones compared to males. Nevertheless, our comprehension of the precise involvement of sex differences in the pathophysiological pathways of urinary stone disease remains incomplete<sup>[3,4]</sup>.

Kidney stone production is an intricate and multi-step process that involves urine super-saturation, crystal nucleation, growth, and aggregation, regardless of the type. Kidney stone production is linked to systemic problems such as diabetes, obesity, cardiovascular diseases, hypertension, and metabolic syndrome. On the other hand, individuals with nephrolithiasis, sometimes referred to as kidney stone formers (KSF), face a heightened likelihood of developing hypertension, chronic kidney disease (cKd), and eventually progressing to end-stage renal disease (ESRD). Various promoting factors and inhibitors have been documented to have crucial roles in the production of kidney stones. Hyperoxaluria, hyperuricosuria, and phosphaturia are often observed contributing variables associated with the development of kidney stones<sup>[4]</sup>.

*In vitro* studies have demonstrated that inter- $\alpha$ -inhibitor (I $\alpha$ I), a member of the protease inhibitor family, effectively inhibits the crystallisation of calcium oxalate (caOx). Despite the accumulation of information regarding human stone development, the mechanisms behind the formation and growth of kidney stones are still not fully understood. This study aims to enhance the comprehension of kidney stone development among urologists, nephrologists, and primary care providers by providing an updated analysis of the underlying mechanisms<sup>[3,5]</sup>.

The prevalence of uric acid nephrolithiasis seems to be increasing. The correlation between uric acid stones and low urine pH has been well-established for a long time. However, current research has revealed further connections with other metabolic states and underlying pathophysiological mechanisms. Low urine pH is connected with certain illnesses such as diabetes, metabolic syndrome disease, excessive food intake, and increased endogenous uric acid production and/or impairment in ammoniogenesis. Furthermore, the occurrence of global warming may lead to a rise in regions with heightened climate vulnerability for the production of uric acid stones. The management of uric acid stones involves three therapeutic steps: determining urine pH profiles, evaluating urinary volume status, and identifying conditions that cause excessive uric acid generation. The acid urine pH is the primary component that contributes to the production of uric acid stones, as it is necessary for uric acid to precipitate<sup>[6]</sup>.

## Conclusion

This review provides a comprehensive overview of the latest understanding of the mechanisms involved in the formation of kidney stones. It explores the impact of metabolic risk factors, receptors, promoters, and inhibitors on kidney stone disease. Additionally, it examines the roles of immune response, microbiome, and sex hormones in the formation and development of kidney stones. The aetiology of kidney stone illness cannot be fully elucidated by crystallization mechanisms alone. Nevertheless, several aspects of kidney stone production are still inadequately comprehended due to existing research constraints, and have not been addressed in this discussion. Additional in-depth research is necessary to gain a better

understanding of the relationship between the microbiome, immune response, and the production of kidney stones. This will enable the development of new preventive and treatment methods.

## Conflict of Interest

Not available

## Financial Support

Not available

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