INTRODUCTION

The management of nephrolithiasis forms an important part of urologic practice. The recurrence rate after forming an initial stone is reported to be as high as 50% at 5 yr and 80–90% at 10 yr, highlighting the importance of medical prophylactic therapy. A better understanding of pathophysiology and formulation of diagnostic criteria for different

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etioologies of nephrolithiasis have made feasible the adoption of selective treatment programs. The objectives of medical stone management should be:

1. Correct the underlying physicochemical and physiologic derangements
2. Prevent new stone formation
3. Avoid nonrenal complications of the disease process
4. Be free of serious side-effects

The background for the selection of certain medical treatment programs is the assumption that specific physicochemical and physiological abnormalities identified with a given disorder are etiologically important in the formation of renal stones, and that the correction of these disturbances would prevent stone formation. Moreover, it is assumed that such a selective treatment program would be more effective and safe than a “random” treatment approach.

These hypotheses appear reasonable and logical. For many pharmacologic treatment programs recommended for the prevention of recurrent nephrolithiasis, sufficient information is now available to characterize their physicochemical and physiological actions.

**PATHOPHYSIOLOGY OF HYPERCALCIURIA**

Hypercalciuria is defined as the excretion of urinary calcium exceeding 200 mg/24 h (or an excess of 4 mg of calcium/kg/24 h). The association of hypercalciuria with recurrent calcium nephrolithiasis has long been recognized, although the exact nature of this relationship continues to be investigated. Nephrolithiasis resulting from hypercalciuria is heterogeneous in origin, and comprises several entities.

**Absorptive Hypercalciuria**

The primary abnormality in absorptive hypercalciuria is increased intestinal absorption of calcium (1). The exact cause for the hyperabsorption of calcium is not fully understood. A subsequent increase in serum calcium concentration enhances the renal filtered load and suppresses parathyroid function (Fig. 1). The combination of an increase in the filtered load and a decrease in renal tubular reabsorption of calcium, caused by parathyroid suppression, results in development of hypercalciuria and potential stone formation. The excessive renal loss of calcium compensates for the intestinal hyperabsorption, thereby maintaining serum calcium in the normal range.

Absorptive hypercalciuria type I (AH-I) is the most severe form of absorptive hypercalciuria, characterized by a urine calcium level >200mg/d, with high or low dietary calcium intake. In AH-I, patients have normal serum levels of calcium and phosphorus and a normal or low serum PTH level. Fasting urinary calcium is normal, whereas an oral calcium load results in exacerbated hypercalciuria. Absorptive hypercalciuria Type II (AH-II) is a mild to moderate form of this disorder in which hypercalciuria only occurs with high calcium intake. These patients have normal urinary calcium excretion either while fasting or on a restricted calcium diet.

**Renal Hypercalciuria**

The underlying abnormality in renal hypercalciuria (or “renal leak” hypercalciuria) is thought to be impairment of renal tubular reabsorption of calcium (1). The consequent reduction in serum calcium concentration stimulates parathyroid function (Fig. 2). Parathyroid hormone (PTH) excess results in mobilization of calcium from bone and enhanced intestinal absorption of calcium, with ensuing stimulation of renal synthesis