STONE INCIDENCE AND PREVENTION

HANS-GÖRAN TISELIUS

Department of Urology, Huddinge University Hospital and Karolinska Institute, Stockholm, Sweden

ABSTRACT

The recurrent nature of stone disease makes it important not only to remove stones from the urinary tract and to assist in the spontaneous passage of stones, but also to offer these patients an appropriate metabolic care.

The average lifetime risk of stone formation has been reported to be in the range of 5-10% with a considerable geographical variation. The annual incidence varies between 0.1 and 0.4% and it is roughly estimated that in Europe stones form in 2000 persons of a population of one million. Of these patients 500 (25%) will require active stone removal. It has been shown in some series that as many as 75% of the patients suffers the risk of repeated stone formation during a follow-up period of 20 years.

In almost all reports on stone composition there is a striking predominance of calcium oxalate stones with or without calcium phosphate (70-80%). The remaining 20-30% of the stones are composed of magnesium ammonium phosphate (struvite), carbonate apatite, uric acid, ammonium urate and cystine. Stones composed of struvite and carbonate apatite are usually referred to as infection stones and also ammonium urate stones are in most cases associated with urinary tract infection. Cystine stones are found in 1-2% of the patients, whereas uric acid stones are subject to the most pronounced geographical variation. Recurrent stone formation is a common problem with all these types of stones and recurrence prevention thus is an important part of the medical care of patients with stone disease.

The intention of this paper is to discuss some metabolic risk factors and preventive treatment of stone disease and also to describe a few simple principles that can be followed in the clinical routine.

Key words: kidney, calculi, metabolic disease, factors, risk, incidence

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INTRODUCTION

Formation of concrements in the urinary tract is a pathologic condition that afflicts people in most parts of the world with a high prevalence. Urolithiasis thus causes a pronounced strain to the health care system. The recurrent nature of the disease makes it important not only to remove stones from the urinary tract and to assist in the spontaneous passage of stones, but also to offer these patients an appropriate metabolic care.

EPIDEMIOLOGICAL CONSIDERATIONS

The average lifetime risk of stone formation has been reported to be in the range of 5-10% with a considerable geographical variation (1,2). The annual incidence varies between 0.1 and 0.4% (3,4) and it is roughly estimated that in Europe stones form in 2000 persons of a population of one million (5). Of these patients 500 (25%) will require active stone removal. There are various figures in the literature on the risk of recurrent stone formation and it has been shown in some series that as many as 75% of the patients suffers the risk of repeated stone formation during a follow-up period of 20 years. Based on epidemiological studies in Swedish stone patients there was an expected recurrence rate of 70% after 10 years when those patients were considered who had formed at least 2 stones before the follow-up period (6). After 5 years, about 50% had formed new stones. In contrast
only less than 30% of the first time stone formers presented with recurrent stones during the following 10 years (7,8).

There is obviously a pronounced variation in the severity of the disease and in a recent review Strohmaier pointed out that the fraction of patients who formed more than 3 stones was only 11-14% (9). For interpretation of therapeutic results it is of importance to realize that the average individual annual rate of stone formation is in the range of 0.15 to 0.20 (9,10).

In almost all reports on stone composition there is a striking predominance of calcium oxalate stones with or without calcium phosphate (11). Approximately 70-80% of the stones has this composition. The remaining 20-30% of the stones are composed of magnesium ammonium phosphate (struvite), carbonate apatite, uric acid, ammonium urate and cystine. Stones composed of struvite and carbonate apatite are usually referred to as infection stones and also ammonium urate stones are in most cases associated with urinary tract infection. Cystine stones are found in 1-2% of the patients, whereas uric acid stones are subject to the most pronounced geographical variation. In Scandinavian countries uric acid stones occur with a frequency of not more than 4-5%, while the frequency might be as high as 30-40% in the Mediterranean and Arabic countries. Recurrent stone formation is a common problem with all these types of stones and recurrence prevention thus is an important part of the medical care of patients with stone disease.

For the preventive treatment of patients with stone disease it is fundamental to be as selective as possible. Thereby it is necessary to take into consideration the stone composition, the expected risk of recurrent stone formation for the individual patient and the abnormalities that are responsible for or might have contributed to the stone formation. In order to be successful in this regard it is important to take a careful medical history in order to identify those patients for further evaluation that are most likely to benefit from preventive measures. The intention of this paper is not to give a complete review of the world literature of metabolic risk factors and preventive treatment but rather to describe a few simple principles that can be followed in the clinical routine.

**CATEGORIES OF STONE FORMERS**

It is important that a program for evaluation and treatment of stone patients take the various aspects mentioned above into consideration. The factors responsible for formation of non-calcium stones are well identified and so are the therapeutic principles. The formation of calcium stones is unfortunately less well understood and this fact is of obvious concern because in most populations calcium stones constitute more than 70-80% of all stones.

For the therapeutic efforts, attention has to be paid to the variable course of the disease. It is thus necessary to adapt the evaluation and treatment to the presentation of the disease in the individual patient. In this regard, it is very helpful to subgroup the stone-formers in the categories depicted in Table-1 (12-14).

**Table 1 - Definitions of different categories of stone formers.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non Calcium Stones</strong></td>
<td></td>
</tr>
<tr>
<td>INF</td>
<td>Infection stone disease</td>
</tr>
<tr>
<td>UR</td>
<td>Uric acid or ammonium urate stone disease</td>
</tr>
<tr>
<td>CY</td>
<td>Cystine stone disease</td>
</tr>
<tr>
<td><strong>Calcium Stones</strong></td>
<td></td>
</tr>
<tr>
<td>S₀</td>
<td>First time stone former without residual stone or fragments</td>
</tr>
<tr>
<td>S_res</td>
<td>First time stone former with residual stone or fragments</td>
</tr>
<tr>
<td>Rm₀</td>
<td>Recurrent stone formers with a mild disease (long intervals between episodes of stone formation). No residual stones or fragments</td>
</tr>
<tr>
<td>Rm_res</td>
<td>Recurrent stone formers with a mild disease with residual stones or fragments</td>
</tr>
<tr>
<td>Rs</td>
<td>Severe disease. Frequent stone formation. Specific risk factors.</td>
</tr>
</tbody>
</table>
STONE INCIDENCE AND PREVENTION

The number of patients in each category certainly is subject to a considerable variation from one geographical area to another, not only because of differences in stone incidence but also because of differences in principles for stone removal (2).

If the reasons for stone formation have not been eliminated, the rate of recurrent stone formation that occurs in patients with non-calcium stones, that is cystine, uric acid and infection stones, is so high that stone preventive treatment always should be considered. Treatment of these patients in most cases can be started following only a few specific analyses. For calcium stone patients who form stones of pure calcium oxalate, mixtures of calcium oxalate and calcium phosphate, or pure calcium phosphate, the situation is different inasmuch as in average only 25-30% of the patients can be expected to form another stone within a 10-year period (6,8).

For Swedish stone formers, and with generous application of shock wave lithotripsy for stone removal, it was noted that of patients presenting with a stone problem 55% were first time stone formers (S) and 45% recurrent stone formers (R). Although 8-10% of the first time stone formers will form new stones during the coming 5 years and 25-30% during 10 years, it is usually not possible at this stage to predict who will become a recurrent stone former and who will not (5).

It is difficult to derive exact figures for the fraction of patients belonging to each category but the figures in Table-2 might serve as a rough guide. For these data, the author have referred to category Rs those patients who had formed at least 4 stones or had an annual frequency of stone formation of at least 0.3. The definition of category Rs can otherwise be left to the discretion of the reader. In this respect, it is important to also include the patient’s attitude. If the patient is not interested in preventive measures there is of course no meaning to proceed with an extensive metabolic evaluation.

The reason for making a distinction between S and Rm patients with (res) and without (o) residual stone material is that the latter group theoretically is at greater risk of new stone formation (see Table-1, for classification).

Irrespective of their previous history of stone formation, patients with specific risk factors are referred to category Rs and treated accordingly. The following risk factors should be noticed in this regard: 1) Start of stone disease before the age of 25; 2) Pronounced family history of stone formation; 3) Single kidney; 4) Presence of brushite (calcium hydrogen phosphate) in the stone; 5) Disease or medication known to be associated with stone formation; 6) Anatomical abnormalities that have not been surgically corrected.

Despite our incomplete understanding of the exact mechanisms of calcium stone formation, a number of risk factors and abnormalities have been identified in stone formers. It is important to utilize this knowledge and the available tools in order to counteract new stone formation in those patients who are likely to benefit from such a treatment. For this purpose we need a program for identification of risk factors of stone formation in the individual patient, a program that take into account not only the mechanisms of stone formation but also the variability by means of which the disease presents (15-18).

According to the data in Table-2 approximately 20% of the calcium stone patients (Rs + Rm_{res} + S_{res}) should be offered a biochemical risk evaluation. It can be assumed that about half of these patients (10%), will be considered for pharmacological stone prevention (5,9).

Table 2 - Approximate fractions of calcium stone formers in each category.

<table>
<thead>
<tr>
<th>Category</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>S_0</td>
<td>51</td>
</tr>
<tr>
<td>S_{res}</td>
<td>4</td>
</tr>
<tr>
<td>Rm_0</td>
<td>29</td>
</tr>
<tr>
<td>Rm_{res}</td>
<td>2</td>
</tr>
<tr>
<td>Rs</td>
<td>14</td>
</tr>
</tbody>
</table>

EVALUATION OF RISK FACTORS

Stone Analysis

Knowledge of which salts that build up the stone is of fundamental importance for correct decisions regarding the preventive treatment. In every patient steps should be taken so that at least one stone
can be analyzed for its composition. The recommended methods for stone analysis are x-ray diffraction or infrared spectroscopy.

Unfortunately a stone is not retrieved from every patient and conclusions have to be made from indirect evidence. A positive urine culture and a high pH might reflect a condition typical for formation of an infection stone. A positive cystine test (Brand’s test; sodium nitroprusside reaction) is diagnostic for cystinuria. Uric acid stones develop in acid urine and although this process can occur at a completely normal metabolism of urate, a high blood level of urate supports the diagnosis.

**Medical History**

Information on the previous medical history is of great help in the further work-up procedure. It is necessary to know if the current stone is the only one that the patient has formed and if not, how many stones there have been. The age at which the initial stone was diagnosed might give a clue to the severity of the disease and it also gives a possibility to calculate the frequency of stone formation. The latter estimate is not always easy to derive and the stone age index (SAI) might serve the same purpose. SAI is calculated as follows: 100 x [total number of stones formed / age of the patient] (7). A high SAI is associated with a higher prospective recurrence risk than a low index. This is in accordance with the observations that patients with a history of more than one stone have a higher future recurrence risk than those who have formed only one stone (19).

Information on previous surgical procedures for stone removal as well as on any other disease the patient might suffer from is important. We know that abnormalities in intestinal function associated by malabsorption give a high risk of stone formation. Other causes of stone disease are hyperparathyroidism, hyperthyroidism, Cushing’s disease, hyperuricosuria due to chemotherapy of malignant diseases, renal tubular acidosis and immobilization.

Some forms of medication can contribute to stone formation for example: acetazolamide, calcium supplements taken between meals, vitamin D, indinavir (resulting in indinavir precipitation) and possibly very large (> 4g) doses of ascorbic acid.

**Radiographic Examination**

A plain x-ray film together with a pyelography usually is the standard procedure for description of the current stone situation in terms of size and number of concrements. The plain film of kidney, ureter and bladder (KUB) gives the necessary information on whether the kidney is stone free or has residual stones or fragments after treatment or after an acute stone episode. This step in the work-up of the stone forming patient also discloses any contributing anatomical abnormalities. Moreover, the radiographic image of the stone can be used for conclusions on the stone composition.

**BIOCHEMICAL ANALYSES**

**Blood Analyses**

A limited set of samples should be part of the early examination of all patients with stone disease. It thereby is recommended to measure the plasma concentrations of either calcium and albumin or ionized calcium. This analytical step makes it possible to diagnose or rule out hyperparathyroidism as a cause of stone formation. It is the author’s routine to measure the parathyroid hormone level only in those patients who have an albumin-corrected calcium level of 2.6 mmol / litre or higher. Furthermore, creatinine should be measured as a rough estimate of kidney function. Plasma urate also should be included in the analysis. It is of note, however, that an increased creatinine occurs together with a high urate. Analysis of potassium also might be motivated particularly for patients treated with diuretics, because hypokalemia is one cause of hypocitraturia.

**Spot Urine Analysis**

A spot urine sample is useful for the diagnosis of bacteriuria and cystinuria. In cases of unknown stone composition, microscopic examination of the urinary sediment can give valuable clues. Although information of the pH level is of great importance, random spot urine is of doubtful value in this respect. To tell anything about the acidification of urine the measurement has to be made in a fasting morning sample. The 8-hour night urine collection is another way to get a standardized estimate of the pH level (see below).
A spot urine sample should be analyzed in all patients, but when the stone composition is known its major purpose is to demonstrate the presence or absence of bacteria.

**Analysis of Urine Collections**

The major risk factors for calcium stone formation are supersaturation with calcium oxalate, calcium phosphate or both salts. Moreover, it has been demonstrated that stone-forming urine very often is deficient in its inhibiting power with regard to crystal growth and crystal aggregation. Although promotion of nucleation and crystal-cell interaction probably also are of importance, there are no methods by means of which these variables easily can be assessed.

Urine analysis for demonstration of risk factors of calcium stone formation is only indicated for patients belonging to categories Rs, Rmres and Sres (see Table-1). The rational for including the latter 2 categories is that the combined presence of residual fragments or stones and a high supersaturation occasionally might call for preventive measures irrespective of the previous stone history.

Analysis of urine composition can be carried out in 24-hour urine samples as well as in samples collected during shorter periods of the day. It is the author’s preference to split the 24-hour collection in one 16-hour daytime sample and one 8-hour night sample. Repeated sampling in at least two collections is recommended (12, 20).

**16-hour Urine**

The 16-hour urine produced between 6:00h and 22:00h should be collected in a bottle containing 20-30 ml of 6 mol/l of hydrochloric acid. This acidification is necessary to maintain the calcium salts in solution and to prevent ascorbic acid from being oxidized to oxalate. The 16-hour urine sample should be analyzed for its content of calcium, oxalate, citrate and creatinine. The additional analysis of magnesium and phosphate makes it possible to get approximate estimates of the ion-activity products of calcium oxalate and calcium phosphate (11,21-25). Although the individual urine variables are useful for selecting the appropriate form of treatment, it is the combined effect in terms of supersaturation (ion-activity product) that gives us an idea of the risk of crystallization.

The following formulas can be used to derive approximate estimates of the ion-activity products by inserting the recorded urine volumes, and there is no doubt that the urine volume is of fundamental importance for the supersaturation with both calcium oxalate and calcium phosphate. The volumes recorded in the urine samples, however, do not necessarily reflect the normal situation. Estimates of the ion-activity product of calcium oxalate therefore have been standardized to a 24-hour urine volume of 1.5 litres (16-hour volume = 1 litre):

\[
\text{AP(CaOx)-index}_s = \frac{A \cdot \text{Calcium}^{0.84} \cdot \text{Oxalate} \cdot \text{Citrate}^{0.22} \cdot \text{Mg}^{0.12} \cdot \text{Volume}^{1.03}}{\text{Citrate}^{0.22} \cdot \text{Mg}^{0.12} \cdot \text{Volume}^{1.03}}
\]

For the 24-hour period \(A = 1.9\) and \(V = 1.5\) litres and for the 16-hour period \(A = 2.3\) and \(V = 1.0\) litre (11).

The index thus obtained corresponds numerically to \(10^{8} \cdot \text{AP}_{\text{CaOx}}\) (where \(\text{AP}_{\text{CaOx}}\) is the ion-activity product of calcium oxalate).

In a similar way it is possible to derive an estimate of the ion-activity product of calcium phosphate (\(\text{AP}_{\text{CaP}}\)). In addition to standardized volumes of 1.5 and 1.0 litres for the 24-hour and 16-hour periods, respectively, the pH is set to 7.0:

\[
\text{AP(CaP)-index}_s = \frac{B \cdot \text{Calcium}^{1.07} \cdot \text{Phosphate}^{0.70} \cdot (\text{pH} 7 - 4.5)^{6.8} \cdot \text{Citrate}^{0.22} \cdot \text{Volume}^{1.31}}{\text{Citrate}^{0.22} \cdot \text{Volume}^{1.31}}
\]

In this formula, \(B\) should be set to 0.003 for a 16-hour sample and to 0.0027 for a 24-hour sample. The \(\text{AP(CaP)-index}_s\) index approximately corresponds to \(10^{15} \cdot \text{AP}_{\text{CaP}}\) (where \(\text{AP}_{\text{CaP}}\) is the ion-activity product of calcium phosphate) (11).

It is of note that there is a relationship between \(\text{AP(CaP)-index}_s\) derived from analysis of voided urine and \(\text{AP}_{\text{CaP}}\) in the distal part of the distal tubule, where the initial nucleation of CaP might take place (26).
It has been shown that patients with a high AP (CaOx) index have a higher recurrence rate than those with a low index (7). A higher rate of recurrent stone formation in patients with more advanced biochemical abnormalities was recorded also in other studies (16).

8-hour Urine
The urine produced between 22:00h and 6:00h is collected in a bottle containing 10 ml of 0.3 mol/l sodium azide as a preservative to avoid bacterial growth. Provided this sample is delivered to the laboratory within the first few hours after collection, it gives a good opportunity to measure pH in a standardized way. Moreover, the sample gives an idea of the night urine volume. The 8-hour urine sample also with advantaged can be used for urate analysis.

Because the 8-hour urine sample does not contain any destructive preservative, it opens the possibility to measure inhibitory properties as well as the risk of crystallization (27-30). Such procedures are, however, not commonly used in most laboratories and these analyses will not be further considered in this paper.

RECURRENT PREVENTIVE TREATMENT

Calcium Stones
The recurrence prevention can be carried out at 3 different levels: 1)- General advice regarding fluid intake and diet; 2)- Specific advice regarding fluid intake and diet; and 3)- Pharmacological treatment.

General Advice
Without sufficiently supersaturated urine there will be no risk of crystallization and without crystals, no stones will develop. The easiest way to reduce urine supersaturation is to keep the fluid intake at a level so that the 24-hour urine flow is at least 2000 ml (31-34). The patient should be advised to refrain from excessive intake of animal protein that is to avoid eating meat products every day (33). There should be no restriction in calcium intake unless this is at a very high level (12), and the minimal daily requirement of 800-1000 mg (20-25 mmol) should be fulfilled. There is usually no need to restrict oxalate intake, but if dark chocolate and nuts are commonly ingested snacks, such a habit should be stopped. General advice is given to patients in categories S₀ and Rᵐ₀.

Specific Advice
This type of advice has the purpose of correcting one or several abnormalities recorded in urine. The analytical findings provide the basis for this regimen.

The drinking habits should be adapted to a urine volume required for an AP (CaOx) index of 1.5 or less. The 24-hour volume necessary for this can be calculated from the AP (CaOx)-index. For example with an AP(CaOx)-index of 2.65 obtained from analysis of the 16-hour urine sample, a 24-hour urine volume of about 2.6 litres would be necessary to get an AP(CaOx)-index of 1.5.

The limit of 1.5 has been chosen because experiments have shown that an AP(CaOx) of 1.5-1.7 was enough for calcium oxalate crystallization, induced by calcium phosphate (35). There are no experimental data available to select a corresponding limit for AP(CaP)-index, but a value of 50 had at least some discriminating power when stoneformers and normal subjects were compared (7). Both AP(CaOx) and AP(CaP) are useful parameters in the follow-up. They are excellent tools for recording the therapeutic effects on the risk of forming urine critically supersaturated with these salts.

It is highly important to teach the patients that the fluid intake should be evenly ingested during the day and that an abnormal loss of water needs to be replaced by an extra load of fluid.

Animal protein increases urinary calcium, oxalate and urate and decreases pH and citrate. It is therefore obvious that in the presence of such findings a careful dietary history should be taken and the necessary corrections made. In patients with a urinary pattern reflecting an excessive intake of animal protein, meat and sausage should be avoided 2-3 days a week.

Restrictions in oxalate intake is usually without meaning in patients with a normal urinary
oxalate, but intake of oxalate-rich food stuff should be restricted if the oxalate excretion is above normal, as for instance in patients with enteric hyperoxaluria. The latter group of patients might benefit from calcium supplements which, however, always should be taken together with meals.

Details regarding the dietary influence on urine composition and the effects of dietary manipulations is extensively summarized elsewhere (33).

Pharmacological Treatment

Extensive reviews of the literature have shown that thiazides, alkaline citrate and allopurinol are the only useful pharmacological agents for calcium-stone prevention (12,36). Although there is no definitive proof that a selective treatment is superior to a non-selective treatment, there is no proof for the opposite view either (5). When the literature was scrutinized, patients treated in a selective manner had a lower recurrence rate than those who were treated non-selectively (5,37). According to these observations, it is recommended that pharmacological treatment should be instituted selectively according to the principles outlined in Table-3 (12).

During the last years, treatment with citrate has become very popular. The reasons for this is that hypocitraturia is a common abnormality in calcium stone formers and, moreover, the fact that citrate influences a number of important steps in the crystallization process (38-41). Recent results have shown that a single evening dose of sodium potassium citrate is not sufficient to effectively prevent recurrent stone formation (42). Potassium citrate should be chosen instead of sodium potassium citrate in order to avoid the hypercalciuric effect of sodium.

For patients who need a calcium reducing treatment and do not tolerate thiazides, orthophosphate might be an alternative. The problem with phosphate treatment is, however, that the side effects are bothersome and that this drug has to be administered at least three times daily.

Potassium-magnesium citrate represents a new and promising alternative form of treatment but this preparation is not yet universally available (43), and it remains to be shown that this form of treatment is superior to treatment with potassium citrate.

It is usually wise to start a recurrence preventive regimen with conservative measures and to

Table 3 - Principles for recommended pharmacological treatment of patients with calcium stone disease.

<table>
<thead>
<tr>
<th>Biochemical Abnormality</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>High calcium excretion</td>
<td>Thiazide + potassium or Thiazide + potassium + magnesium (Orthophosphate in case of thiazide intolerance)</td>
</tr>
<tr>
<td>High oxalate excretion (moderately increased)</td>
<td>Oxalate restriction</td>
</tr>
<tr>
<td>Enteric hyperoxaluria</td>
<td>Oxalate restriction + calcium supplements (together with meals) + alkaline citrate Reduced intake of fat might be useful.</td>
</tr>
<tr>
<td>Primary hyperoxaluria</td>
<td>Pyridoxine can be tried. These patients should be treated by a specialist on primary hyperoxaluria</td>
</tr>
<tr>
<td>Low citrate excretion</td>
<td>Alkaline citrate (potassium citrate)</td>
</tr>
<tr>
<td>Low pH</td>
<td>Alkaline citrate</td>
</tr>
<tr>
<td>High urate excretion</td>
<td>Allopurinol</td>
</tr>
<tr>
<td>High phosphate excretion</td>
<td>Restricted intake of animal protein</td>
</tr>
<tr>
<td>Low magnesium excretion</td>
<td>Magnesium oxide or magnesium hydroxide supplements</td>
</tr>
<tr>
<td>No abnormality</td>
<td>Alkaline citrate</td>
</tr>
</tbody>
</table>
institute pharmacological therapy only when the conservative approach for some reason fails. The compliance to the long-term treatment regimens necessary for these patients is low.

In order to maintain compliance at a reasonable level it is necessary to see these patients regularly and to check the therapeutic effect by repeated follow-up examination of urine composition and stone formation.

In the literature there are very few controlled studies of sufficient duration to provide a solid basis for conclusions on the real efficacy of the various forms of preventive treatment. In Table-4 the data from recurrent stone formers treated in a selective way have been used to derive an approximate average estimate of the stone free rate after 3 years (5). The stone free rates obtained from patients treated selectively, which varied between 77 and 86%, were obviously better than those 49 to 73% recorded in patients treated in a non-selective way. The expected stone free rate in an untreated group of recurrent stone formers is about 65% (7).

**Uric Acid**

The determinants for precipitation of uric acid are a low pH, a small urine volume, a high uric acid concentration or any combination of these variables. The risk of uric acid crystallization can be reduced by an increased pH. This is accomplished with alkaline citrate. Both sodium potassium citrate (5g twice or three times daily) and potassium citrate (6.5 mmol twice or three times daily) are acceptable alternatives. The 24-hour urine volume should be at least 2000 ml. In case of hyperuricosuria, allopurinol should be part of the therapeutic regimen.

Uric acid stones can be dissolved with a similar treatment. In these cases allopurinol (300 mg once daily) should always be given. Sodium potassium citrate and potassium citrate should be given in doses higher than those used for prevention (7.5g 3 times daily and 10 mmol 3 times daily, respectively). The duration of this treatment depends on the stone volume but at least 2-3 months are usually required.

**Cystine**

The genetic defect in cystine stone formers causes an abnormal excretion of the aminoacids cystine, lysine, ornithine and arginine. The solubility of cystine increases with increasing pH and with dilution of the urine. The basic therapeutic steps are generous fluid intake giving a urine volume of at least 3000 ml per 24-hour and an alkalinization of urine to pH 7.5 if possible.

The cystine concentration should be lower than 300 mg or 1.25 mmol per litre and the currently most used compound to achieve this goal is α-

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**Table 4 - Approximate average stone free rate after 3 years for patients treated selectively and non-selectively. The figures were obtained by recalculation of literature data (ref. 5).**

<table>
<thead>
<tr>
<th>Form of Treatment</th>
<th>Percent of Stone Free Patients Treated Selectively</th>
<th>Percent of Stone Free Patients Treated Non-selectively</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazides</td>
<td>86</td>
<td>73</td>
</tr>
<tr>
<td>Alkaline citrate</td>
<td>78</td>
<td>72</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>85</td>
<td>68</td>
</tr>
<tr>
<td>Dietary advice</td>
<td>77</td>
<td>49</td>
</tr>
</tbody>
</table>

**Infection Stone**

Radical clearance of stone material is a mainstay for treatment of these patients. Long-term (3-6 months) of low-dose antibiotics helps to eradicate the infection after stone removal. Prevention...
of struvite and carbonate apatite precipitation can be accomplished by acidification of urine either with ammonium chloride or with methionine. The author has successfully used intermittent acidification with 1g of ammonium chloride 3 times one day each week.

CONCLUDING COMMENTS

Risk evaluation and preventive treatment of patients with stone disease have been a neglected area during recent years. One reason for this is the opinion by many urologists that stones better were removed with the new convenient methods than treated medically. There are, however, several problems with this attitude. The new methods, which are neither completely without risk nor without cost, have not reduced the recurrence risk. On the contrary, about 25-30% of patients treated with shock wave lithotripsy is left with residual fragments in their kidneys and these patients are thus potential candidates for new stone problems. Of all stone-formers 70-75% pass their stones during an acute stone episode, where methods for active stone removal usually have no place. Finally, the risk of being afflicted by an unannounced stone colic means a real threat to these patients.

It thus makes sense that steps should be taken to offer patients with urolithiasis an individualized preventive care in proportion to the severity of their disease. Undoubtedly there are serious shortcomings both in terms of our knowledge of the mechanisms of stone formation and the preventive possibilities. There are, however, some obvious risk factors that can and should be corrected in patients with a severe disease. It is important to detect these abnormalities with a rational system for biochemical evaluation and to make attempts to overcome the problem of a low compliance. One prerequisite for being successful in this respect is to give these demanding activities an appropriate place within the frame of everyday urologic practice.

REFERENCES

13. Tiselius HG: Metabolic evaluation of patients

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Correspondence address:
Dr. Hans-Göran Tiselius
Depart. of Urology, Huddinge University Hospital
Karolinska Institute
SE-141 86, Stockholm, Sweden
Fax: + (46) (8) 5858-7760
E-mail: hans-goran.tiselius@urol.hs.sll.se