Urinary Stones

Diagnosis, Treatment, and Prevention of Recurrence
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Foreword by
Hibbard E. Williams, Davis, California, USA

32 figures, 16 in color, 2002

2nd revised and enlarged edition
Nachsorge bei Harnstein-Patienten
Ein Leitfaden für die ärztliche Praxis
Herausgeber: A. Hesse, A. Jahnen, K. Klocke, A. Nolde, O. Scharrel
ISBN 3-334-60832-8
© Gustav Fischer Verlag, Jena, 1994
1. Auflage

Urinary Stones
Diagnosis, Treatment, and Prevention of Recurrence
Editors: A. Hesse, H.-G. Tiselius, A. Jahnen
ISBN 3-8055-6346-9
© Gustav Fischer Verlag, Jena, 1997
1st edition

Library of Congress Cataloging-in-Publication Data
Urinary stones: diagnosis, treatment, and prevention of recurrence/Albrecht Hesse, Hans-Göran Tiselius, Andrea Jahnen; foreword by Hibbard E. Williams, – 2nd rev. and enl. ed.
p.; cm.
Includes bibliographical references and index.
ISBN 3805573707 (soft cover: alk. paper)
RC916.N3313 2002
616.6'22–dc21 2002019341

Drug Dosage. The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

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© Copyright 2002 by S. Karger AG, P.O. Box, CH-4009 Basel (Switzerland)
www.karger.com
Printed in Switzerland on acid-free paper by Reinhard Druck, Basel
ISBN 3-8055-7370-7
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Renal stone disease is a most ancient and common affliction of man. Over a seventy-year life span, it is estimated that as many as 15% of some populations will develop renal stones. No age is spared and no country or ethnic group protected from this common clinical problem. Most, but not all, patients who develop a stone will eventually form others. Although very few individuals die as a direct result of stone disease, it does lead to substantial morbidity from pain, urinary tract infections and obstructive uropathy.

In the past few decades, substantial progress has been made in understanding the basic pathophysiologic mechanisms of stone disease, which has subsequently led to rational and effective programs for both its treatment and prevention of recurrence. Diagnostic study protocols to identify underlying mechanisms have now become available in most countries, thereby allowing for an accurate categorization of patients with renal stone disease.

This handbook to assist physicians in the diagnosis, treatment and prevention of stone disease has been developed by its three editors, each of whom has contributed significantly to our basic understanding of stone disease. Their handbook is oriented toward clinicians and health care professionals to help them quickly and effectively study and treat patients with stone disease and assist them in developing effective approaches to the prevention of further stone development. In addition, it is written in a manner that could make it very useful in explaining to patients the more important aspects of their disease. It is very well organized, making it simple to use as a reference work and its utility is strengthened by an outline format, which facilitates understanding of diagnostic studies and treatment plans. All of the major stone types are discussed in detail, including sections on the less frequent stones, such as those composed of xanthine and 2,8-Dihydroxyadenine. Of particular value is the discussion of diagnostic studies to be performed in those patients for whom a stone is not available for analysis, an increasingly common event now that lithotripter use has made it more difficult to recover stones.

With our ability to determine more accurately than ever the basic mechanisms of stone formation and, therefore, to develop more effective treatment programs, recurrent stone disease should become less and less common. The editors and authors of this text have made an important contribution to this effort with this handbook which should be of immense help to health care professionals who care for patients with renal stones in efficiently and effectively guiding them through the appropriate diagnostic studies and the development of safe plans for treatment and prevention. Their patients will be ultimate beneficiaries of this text. We are grateful to its editors and authors for such a useful and usable book.

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University of California, Davis, California, USA
Preface to the first edition

During the past 15 years, therapeutic procedures for urinary stone disease have undergone fundamental changes. Alternative methods of lithotripsy have made open surgery superfluous in most countries. Repeated treatment with extracorporeal shock wave lithotripsy (ESWL) is relatively free of side effects and, as a rule, does not interfere with kidney function. However, one should note that these modern methods of therapy serve only to treat the symptoms of the disease – the stone. The actual cause of stone formation – infection, malnutrition, metabolic abnormalities, etc. – frequently remains unnoticed, so that recurrence is bound to occur.

With a yearly incidence rate of 0.5% in Europe, the number of recurrences approximates 80%. However, with detailed knowledge of the causes of urinary stone formation, recurrences can largely be prevented. To achieve this goal, there is a need for laboratory diagnostics, including stone and urine analyses. Furthermore, it is necessary to investigate the dietary (nutritional) habits of the patient so that they can be given comprehensive guidelines for their specific kind of stone disease. Finally, the most appropriate post-operative follow-up care must be provided including, if necessary, the use of drugs. The patient should be encouraged to take part in a two-year therapy with regular checks. This may spare the patient further and repeated illness and can reduce the costs of therapy quite considerably.

The present book is a manual for physicians in charge who, in the course of practice, encounter urinary stone patients. It provides appropriate diagnostic procedures as well as general advice for recurrence prophylaxis. To start with, there is a survey of outpatient diagnosis and treatment of acute urinary stone disease as it occurs in emergency medicine. If no stone analysis is available, general and unspecific therapeutic measures may be used. If, however, the type of stone is known, the indication as described in the respective chapter should be applied. The layout of the book is arranged so that on the right-hand pages, concise and distinct information is presented, while on the left-hand pages the respective detailed explanation is given. We trust that this book serves as a useful and practical guide to all physicians treating their urinary stone patients.

July 1996                                            The authors
Preface to the second edition

The first edition of our book and an unamended reprint stimulated great interest world-wide. Karger Publishers consequently asked us to prepare a second revised edition. We are pleased to comply with this request, and are grateful to the staff of the publishing house for their excellent cooperation.

A recent epidemiological survey revealed that 5.5% of all men and 4% of all women in Germany already had urinary stones (prevalence). In the case of men, 10% of those aged 50 or above were stone-formers. Acute disorders were recorded in 1.5% of the population in year 2000 (incidence). The high incidence of this disease makes it clear that modern methods of lithotripsy (ESWL, PNL, URS) have led to the continued disregard of metabolic diagnosis and the prevention of recurrent stone formation. It is in the vital interest of both patients and health economics that prophylactic measures are undertaken for each stone patient in order to prevent recurrences.

During the revision of this book due attention has been paid to the current literature (see references) as well as the European and international guidelines on urolithiasis. Certain special methods of metabolic clarification have been supplemented in the appendix. Detailed tables referring to the oxalate, calcium and uric acid content of food have been added. We assume that the reference values for urinary excretion derived from healthy children will help to improve the treatment of children with urinary stones.

We trust that this book will prove to be helpful to both doctors and their patients.

September 2001

The authors
Introduction

Urinary stones

- belong to the group of biominerals
- are the final product of a multifactorial process

Symptoms of different abnormalities

- occur today with a prevalence of 4–10%

Widespread disease

- the recurrence rate which depends on the stone composition is in untreated patients 50–100% and in treated patients 10–15%

Metaphylactic treatment is undoubtedly necessary
Introduction

General aspects of urinary stone formation

The biomineralization resulting in a urinary stone has a multifactorial origin in which socio-economic, genetic and constitutional factors as well as diet, pharmacologic treatment and metabolic abnormalities might act in concert.

A supersaturation of urine with the stone forming salt(s) is of fundamental importance and a prerequisite for the necessary precipitation. The solubility of the different stone components depends on the urinary pH and the excretion of other urine constituents. Accordingly, a saturation of urine above the solubility product (SP) and the associated risk of crystallization are determined by the urinary concentration (mmol/l) of the solutes taking part in the crystal formation and the pH. When the SP has been exceeded, the supersaturation is metastable. At this level of supersaturation the crystals can grow and aggregate (agglomerate) but new crystal formation is not possible. In order to start the formation of new crystals, the supersaturation has to be further increased to a level termed the formation product (FP). The isolated findings of increased concentrations are not diagnostic for stone disease but might reflect only the concentration capacity of the kidney. Normal values of urine constituents are usually expressed as the total excretion during a 24h period or a fraction of a 24h period.

There is often an overlap in terms of urine supersaturation between stone-formers and normal subjects indicating that factors other than the supersaturation have to be considered in the process of stone formation. In this respect, substances which inhibit the nucleation, growth and aggregation of crystals are thought to play an important role. Furthermore, anatomical and functional abnormalities might contribute either by fixation of crystals or by reducing their excretion. Such a retention of crystals is necessary for the development of a clinically significant crystalline deposit.

![pH-dependence of the urinary solubility of lithogenic substances](image-url)
### General aspects of urinary stone formation

<table>
<thead>
<tr>
<th>Age</th>
<th>Profession</th>
<th>Nutrition</th>
<th>Climate</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Mentality</td>
<td>Constitution</td>
<td>Race</td>
<td>Genetic factors</td>
</tr>
</tbody>
</table>

- **Abnormal renal morphology**
- **Disturbed urine flow**
- **Urinary tract infection**
- **Metabolic abnormalities**
- **Genetic factors**

- Increased excretion of stone forming constituents
- Decreased excretion of crystallization promoters
- Decreased excretion of crystallization inhibitors
- Decreased urinary volume

**Physico-chemical change in the state of supersaturation**

**Abnormal crystalluria**
- Crystal aggregation
- Crystal growth

**Urinary stone**
Urinary stones occur in all parts of the renal collecting system. The sites of occurrence and formation are not necessarily identical. In the industrialized part of the world,

- 97% of all urinary stones are localized in the:
  
  | Parenchyma | Pelvis |
  | Papilla | Pelvis + calices |
  | Calyces | Ureter |

- only 3% are found in the bladder and the urethra.

The anatomy of the collecting system at the site of stone development is an important determinant for the shape of the stone inasmuch as there frequently is an adaptation to the surrounding structures.

### Composition and occurrence of the different crystal phases in urinary stones

Urinary stones belong to the group of biominerals. Different inorganic or organic substances with a crystalline or amorphous structure are the major constituents of the stones. Only about 1/3 of all urinary stones has a monomineral composition. There is frequently a structure with layers of varied composition or a homogeneous mixture of different crystal phases. Calcium oxalate is by far the most common stone constituent, and is considered to be the major mineral in at least 65% of all stones.

<table>
<thead>
<tr>
<th>Major constituent</th>
<th>The only mineral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate</td>
<td>70.4</td>
</tr>
<tr>
<td>Uric acid</td>
<td>11.0</td>
</tr>
<tr>
<td>Struvite</td>
<td>6.0</td>
</tr>
<tr>
<td>Carbonate apatite, Whitlockite</td>
<td>4.8</td>
</tr>
<tr>
<td>Brushite</td>
<td>1.0</td>
</tr>
<tr>
<td>Cystine</td>
<td>0.4</td>
</tr>
<tr>
<td>Ammonium urate</td>
<td>0.5</td>
</tr>
<tr>
<td>Protein</td>
<td>0.8</td>
</tr>
<tr>
<td>No major constituent</td>
<td>5.1</td>
</tr>
</tbody>
</table>
**Location and shape of urinary stones**

- Staghorn stone
- Pelvic stone
- Caliceal stone
- Ureteral stone
- Bladder stone

**Composition of the most important stone constituents**

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Mineral name</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxalate</strong></td>
<td></td>
</tr>
<tr>
<td>Calcium oxalate monohydrate</td>
<td>Whewellite</td>
</tr>
<tr>
<td>Calcium oxalate dihydrate</td>
<td>Weddellite</td>
</tr>
<tr>
<td><strong>Phosphate</strong></td>
<td></td>
</tr>
<tr>
<td>Carbonate apatite</td>
<td>Dahllite</td>
</tr>
<tr>
<td>Calcium hydrogen phosphate dihydrate</td>
<td>Brushite</td>
</tr>
<tr>
<td>ß-tricalcium phosphate</td>
<td>Whitlockite</td>
</tr>
<tr>
<td>Hydroxyapatite</td>
<td></td>
</tr>
<tr>
<td>Magnesium ammonium phosphate hexahydrate</td>
<td>Struvite</td>
</tr>
<tr>
<td><strong>Uric acid, Urate</strong></td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>Uricite</td>
</tr>
<tr>
<td>Uric acid dihydrate</td>
<td>–</td>
</tr>
<tr>
<td>Mono ammonium urate</td>
<td>–</td>
</tr>
<tr>
<td>Mono sodium urate monohydrate</td>
<td>–</td>
</tr>
<tr>
<td><strong>Stones associated with inborn errors of metabolism</strong></td>
<td></td>
</tr>
<tr>
<td>L-cystine</td>
<td>–</td>
</tr>
<tr>
<td>Xanthine</td>
<td>–</td>
</tr>
<tr>
<td>2,8-Dihydroxyadenine</td>
<td>–</td>
</tr>
</tbody>
</table>