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Abstracts of the 13th Urolithiasis Symposium Bonn – Vienna

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Editorial

Since 1972 W. Vahlensieck (Bonn) und G. Gasser (Vienna), supported by an advisory board of international experts have been organizing Urolithiasis Symposia alternating in Bonn and Vienna. Characteristics are lectures and discussions on epidemiology, pathogenesis, diagnostics and therapy. In the meantime these are internationally appreciated meetings with the great advantage of interdisciplinary discussions. In this year the main topic is the residual fragment after operation, ESWL and PCN. Of each symposium a report by Steinkopff-Publisher exists. To inform more interested searchers about the topics and to give the possibility to get in contact with the experts in this issue the abstracts of the 1987 Symposium in Vienna will be published, too.

G. Gasser

I. Epidemiology and Pathogenesis

1 Familial Incidence of Urolithiasis in Czechoslovakia

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An enquiry, in the form of a detailed personal interview, was made in a series of 857 probands with nephrolithiasis and in a control group of 400 subjects with no lithiasis, investigating the incidence of urolithiasis among the first-degree relatives.

The incidence of urolithiasis among the probands' parents was 5.9% (in the control group 2.1%), among their siblings 7.4% (2.0%) and among their children 3.0% (0.6%). The differences between the nephrolithiasis group and the control group were statistically highly singnificant in every case ($p < 0.001$). At least one case of lithiasis occurred in the families of 7.8% of the healthy subjects, whereas a further case – apart from the proband – occurred in the families of 23.6% of the stone-formers. The highest familial incidence was found in the group with cystine lithiasis (30.5%), followed by the oxalate group (24.3%), mixed and unidentified stones (23.8%), uric acid stones (16.1%) and phosphatic stones (14.1%).

The high figures for the familial incidence of lithiasis are a challenge calling for selective primary prevention among the members of these families.

2 An Epidemiological Study of Cystinuria

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A semiquantitative method for the determination of cystine was modified as a tablet test after Takemoto and Kinoshita. It is based on the splitting of cystine by means of dithionite ions and the formation of a nickel/cystine/sulfide-complex. The criteria of analytical reliability and applicability were established by comparison of methods. The procedure is suitable as an inexpensive rapid search test. It can be performed in every clinico-chemical laboratory and can be done by the patient for continuous cystine determination. Treatment of fresh urines is urgently recommended. A cystine screening test was performed with this method on 2,395 children in créches. In cystinuria patients, the determination in the morning urines after investigation of the circadian profiles proved most useful. In 8 children increased cystine levels [150 mg/l (0.62 mmol/l – 300 mg/l (1.25 mmol/l)] were confirmed by three consecutive analyses. This corresponds to a prevalence of 0.33%, which is in good agreement with the literature. Similar results were obtained in 1,000 children below 16 in a children's hospital. The results were checked by simultaneous thin-layer chromatography of the amino acid patterns of cystine, lysine, arginine and ornithine. Positive findings resulted in examination of the family for cystinuria.

On the basis of 460,000 children between the age of 1 and 3 years in the GDR, the prevalence 0.33% yields an interval of confidence between 800 and 3,000 with a mean value of 1,542 children with increased cystine levels. This might suggest the possibility of routine screening in young children.

3 Prevalence of Uric Acid Lithiasis in Israel and Other Parts of the World in the Last Decade

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The prevalence of uric acid stones in Israel was assessed by analysis of 425 stones, voided between January 1984 to March 1986. The results were compared to those reported from the same laboratory 25 years ago and to reports from different parts in the world in the last decade. In general, the prevalence of uric acid lithiasis is low in the modern industrialized countries and high in the less developed states. The lowest prevalence was reported from USA (2.1% of all stone patients), the Scandinavian countries (4%) and Belgium (5.3%). In Germany, the prevalence reported (17%) was the highest of all Western European countries reviewed. A relatively high prevalence was reported from Sudan (23%), Pakistan (27%), Thailand (30%) and Iran (37%).

In Israel, the prevalence of uric acid stones was found to be 19.4%, markedly lower than 25 years ago (39.5%). Moreover, only

0.7% of the stones, in comparison to 50% in the 1963 series were pure. 99.3% of the uric acid stones were mixed with calcium oxalate, but in 81.2% of the mixed stones, uric acid was the major constituent.

The results indicate a significant change in both the prevalence of uric acid stones and their composition in Isreal in the last 25 years, presumably reflecting the rise in the standard of living during this period.

4 The Tuebingen Urolithiasis Record

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Starting from the patient documentation system UROPAD which was developed in our department to record patients suffering from bladder cancer, we drew up a record for patients suffering from urolithiasis. As UROPAD is a data bank with maximum information, only a few stone-specific forms had to be supplied. To a large extent codification is done using the Systemized Nomenclature of Medicine (SNOMED). There is a special form at hand to answer statistical problems; correlations between different parameters can be examined in this way.

It is thus possible to evaluate complex relations – as they are met with in urolithiasis – rather easily and quickly. By means of the patients who had been treated in our stone-consulting hours we shall illustrate the evaluation of findings with patients suffering from infection stones.

5 Clinical Characteristics of Renal Stone Disease in Relation to Urinary Oxalate Excretion

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The purpose of this study was to compare clinical characteristics of patients with idiopathic stone disease in relation to urinary oxalate levels.

Methods. The 24-h urinary excretion of oxalate was measured in consecutive stone formers during three years in our out-patient stone clinic. Out of 233 patients with idiopathic stone disease two groups of 30 patients each with the lowest and highest urinary oxalate values, respectively, were compared.

Results. Urinary oxalate was higher among stone formers than controls. There were no differences in age or heredity of stone disease between patients with high or low urinary oxalate.

	Stone episodes per 100 patient-years	Stone operations per 100 patient-years
U-ox < 350 μmol/24 h	61	3.8
U-ox > 700 μmol/24 h	72**	6.9***

** $p < 0.01$, *** $p < 0.001$

Conclusion. These results suggest that hyperoxaluria causes a more severe stone disease with a greater frequency of operations.

6 To What Extent is Urine Composition Related to Stone Formation, and How Efficient Are We in Affecting Urinary Risk Factors?

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Urine composition and the clinical course of stone disease were followed in 856 patients with calcium stone disease. During a mean (± SD) period of 3.9 ± 2.9 years the patients were regularly seen at our out-patient stone clinic.

In addition we analysed urine composition in more than 800 patients subjected to ESWL treatment. The biochemical risk situation appeared to be related to the frequency of stone formation and the stone volume. Urinary citrate is evidently of considerable importance. A higher risk of forming a urine supersaturated with calcium oxalate was observed in those who formed new stones during the follow-up period.

All patients were given general advice to maintain a high urine flow, to avoid excessive intake of oxalate rich food, and to avoid daily ascorbic acid doses above 1 g. In many patients a usually selective medical treatment with thiazides, orthophosphate, alkaline citrate, magnesium, and allopurinol was added.

The risk of forming a urine supersaturated with calcium oxalate was reduced. Whereas urinary calcium and urine volume are favourably affected, there were no effects on urinary oxalate.

Our results so far emphasize previous evidence of the importance of urine composition for evaluation of stone formers, and also for conclusions on the clinical effect of different therapeutic regimens.

7 Intestinal and Renal Handling of Oxalate in Nutritional Deficiencies of Vitamins with Special Reference to Pyridoxine

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Nutritional deficiency of vitamins, i.e. vitamin A, B_1 and B_6 has been implicated to cause hyperoxaluria, leading to calculus formation in man and experimental animals. Molecular mechanisms involved in hyperoxaluria of pyridoxine deficient (PD) rats have been studied using intestinal and renal brush border membrane vesicles (BBMV). In pairfed controls (PC), ^{14}C-oxalate uptake was a linear function of substrate concentration. Induction of oxalate transport carrier in PD intestinal BBMV was observed by the biphasic transport characteristics of oxalate influx. Oxalate analogues, altered its intestinal transport in PD rats, whereas these test compounds had no effect on oxalate influx in PC.

In contrast to biphasic transport of oxalate in PC kidney cortex, PD rats exhibited a hyperbolic curve. The oxalate transport was significantly ($p < 0.001$) higher in PD rats. Monocarboxylic acids (acetate and pyruvate) did not effect the oxalate influx in cortical BBMV prepared from PD and PC rats. Dicarboxylic acids (fumarate, maleate and succinate) significantly ($p < 0.05$; $p < 0.01$ and $p < 0.001$, respectively) augmented the oxalate absorption in PC, whereas a significant ($p < 0.05$) decrease was observed in PD rats.

Na^+/K^+ ions were ineffective in altering the oxalate transport process in intestinal and renal BBMV. Thiol groups did not effect the oxalate influx in intestinal membranes, whereas renal epithelium required thiol groups for the translocation of oxalate across the tubular cells. Alterations in enzymic activity and lipid profile were observed in intestinal and renal BBMV in pyridoxine deficiency. The present data indicate that in pyridoxine deficiency, rat kidney cortex has a specific mechanism to increase the risk factor for calculus formation, as compared to oxalate influx through the intestine. Work on the mechanisms of oxalate transport in vitamin A and B_1 deficiency is in progress.

8 **Calcium Oxalate Crystal Growth: Influence of Natural Inhibitors**

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By the constant composition technique the following inhibitors of CaOx crystallization were investigated: dermatan sulfate, chondroitin sulfate, keratan sulfate, RNA and pentosan polysulfate.

In this system seed crystals of CaOx monohydrate are added to supersaturated solutions of calcium oxalate. The calcium and oxalate ion concentrations are kept constant by the addition of reagent solutions containing these ions and the rate of addition is controlled by a calcium ISE. The highest inhibition of CaOx crystallization was obtained by pentosan polysulfate. The natural inhibitors chondroitin sulfate and RNA which are found in human urine represent only a small part of the whole inhibitory activity of urine. Therefore urine must contain other unknown inhibitors of CaOx crystallization.

9 **Epithelial Adhesion of Urease-Induced Crystals in the Urinary Tract**

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The primary prerequisite for the formation of infection stones in the urinary tract is supersaturation of the urine with struvite and calcium phosphate, due to the action of urease-producing microorganisms. A second prerequisite for stone formation is retention of urease-induced crystals allowing crystal growth and aggregation to occur. The endothelial surface lining the urinary tract has a mucous coat containing glucosaminoglycans (GAGs). This study was performed to study the importance of the mucous coat to prevent adhesion of urease-induced crystals.

The adhesion of crystals was studied with chemical methods in rat bladders after incubation with a supersaturated slurry containing struvite and calcium phosphate crystals for one hour. Three experimental models were used: intact rat bladders, rat bladders pretreated with 0.1 M HCl (which disrupts the GAG layer without destroying the underlying urothelium) and rat bladders preincubated with non-urease-producing *E. coli* during 2 h. Efforts to restore the GAG layer with heparin, after HCl treatment and *E. coli* incubation, were performed.

Pretreatment of the bladders with 0.1 M HCl or preincubation with *E. coli* increased the adhesion of struvite and calcium phosphate crystals 5–6 times compared to that of untreated rat bladders with an intact mucous coat ($p < 0.001$). Heparin completely abolished the increased adhesion produced both by HCl treatment and incubation with *E. coli.*

An intact mucous coat prevents the adhesion of urease-induced crystals. Infection with non-urease-producing *E. coli* eliminates this protection. This indicates a so far unknown property of *E. coli* to enhance the formation of infection stones in the urinary tract.

10 **Stone Formation in the Kock Pouch**

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The introduction in recent years of the Kock pouch ("continent stoma") in urology revealed a problem that was seen infrequently before, that is stone formation on staplers exposed to urine. In this operation, these staplers are used for the construction of the nipples.

In a group of 17 patients (8 male, 9 female) with a Kock pouch, stone formation on staplers in the pouch was seen 7 times (2 male, 5 female patients) (follow-up 6–27 months). Only 1 patient had passed stones before this operation. After the operation 4 patients passed stones spontaneously; in the other patients the stones were seen on X-rays and on endoscopy.

Almost all patients with a Kock pouch had positive urine cultures. In the stone former group *Proteus, Pseudomonas, Klebsiëlla* and *E. coli* were predominant; in the non-stone former group, *E. coli* was predominant, besides *Klebsiëlla* and *Enterococ.* There is a clear distinction in the incidence of pyelonephritis in both groups: in the former group it was diagnosed in 4 out of 7 patients, in the latter group in 2 out of 10 patients.

24h-urine investigations revealed no significant metabolic disorders. The average urine pH in the former group was 6.46, in the latter group 6.30.

It is evident that urinary tract infections with urease producing bacteria in the presence of foreign bodies are the main cause of the stone formation. This is emphasized by the stone-analysis: sometimes 100% triplephosphate stones were found. Also combinations were found of triplephosphate (20–85%), calciumcarbonate (25–65%) and calciumoxalate (max. 30%).

We started to treat these patients with regular Renacidin irrigations in the pouch.

11 **Urolithiasis and Atherosclerosis – Is There an Association?**

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Idiopathic urolithiasis and coronary artery disease have been described as diseases of the affluent communities. Both conditions are strongly influenced by environmental factors such as diet. During the course of an investigation of the effects of various nutrients on risk factors for stone in normal subjects and idiopathic stoneformers, opportunity also arose to assess the risk factors for arteriosclerotic disease.

11 normal subjects and 9 male stoneformers were studied. The tests were performed on 4 separate days on each individual. On day 1, after overnight fasting, venous blood samples were obtained just before 9.00 h when 400 ml of distilled water was given by mouth. Blood samples were obtained at 2 h-intervals over the ensuing 8 h. On days 2, 3 and 4 the test was repeated in a similar fashion except for a test meal, at 9.00 h, of isocaloric quantities of glucose, animal protein and fat respectively. The blood samples were analysed for cholesterol, Triglycerides and apolipoproteins A1 and B.

Stoneformers were found to have higher plasma cholesterol and triglyceride levels when compared to normal subjects. The levels of cholesterol, triglycerides and apolipoproteins A1 and B showed an increase in both groups after the ingestion of animal protein and fat.

The results suggest that the dietary risk factors for urolithiasis and degenerative arterial disease are similar and stoneformers may be at an increased risk of arteriosclerosis and related conditions. These indicate a need for prospective epidemiological studies to investigate the relationship between the two disorders.

II. Diagnostics

12 **Improved Discrimination Between Stone-Formers and Controls**

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In a long-term clinical study, up to 108 single urinary samples per patient (and control, respectively) were collected and over 20 parameters determined. The results were compiled by special SPSS/Fortran-Programs on Cyber 175/CDC.

Here, the clear differentiation between stone-patients and controls as well as between moderately recurrent (1 stone/year) and

severely recurrent stone-formers (more than 1 stone/year) will be shown, based on two urinary crystallization inhibitors (magnesium and citrate) and on some urinary parameters, characterizing the acid-base balance regulating capacity of the kidney (titratable acidity. TA, equivalent of org. anions in urine: A_{4-6}, ammonium ion: NH_4^+, total acid excretion: TA = NH_4^+, inorganic phosphate "corrected" TA: TA-P7.4).

In addition, some mathematical terms ("quotients") and some parameter-dependent characteristic treshold values, bringing about an essentially improved discrimination between stone-formers and controls, compared with single urinary parameters, will be presented.

The clear differentiation between stone-patients and controls as well as between moderately and severely recurrent stone-formers, based on repeated determination of the same parameter in urinary samples of a the same person, can be deduced e.g. from the mean values for urinary magnesium (2.3 mmol/l in severely recurrent, 3.28 mmol/l in moderately recurrent stone-patients and 4.2 mmol/l in controls), urinary citrate (0.6 mmol/l in severely recurrent, 1.28 mmol/l in moderately recurrent patients and 1.90 mmol/l in controls), further for NH_4^+ (23.8 mmol/l in severely recurrent, 39.21 mmol/l in moderately recurrent patients and 44.0 mmol/l in controls), for TA (17.5 mmol/l in severely recurrent, 33.9 mmol/l in moderately recurrent stone-formers and 51.7 mmol/l in controls), further for A_{4-6} (19.9 mmol/l in severely recurrent, 29.8 mmol/l in moderately recurrent patients and 35.3 mmol/l in controls) and finally for TA + NH_4^+ (41.3 mmol/l in severely recurrent, 73.1 mmol/l in moderately recurrent patients and 95.7 mmol/l in controls).

The essential improvement in the discrimination between stone-formers and controls by the introduction of special "quotients" can be demonstrated by some examples: (TA-P7.4) (citrate) (5.2 in stone-formers, 69.0 in controls); (TA-P7.4) (TA + NH_4^+) (citrate) (402.0 in stone-formers and 9,222.9 in controls!); further Ca^{++}/(citrate) (TA) (152.8 in stone-formers and 14.1 in controls).

13 Urinary Supersaturation or Risk Index Calculations in the Assessment of Urinary Stone Formers

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Objectives. Since ion activity products reflect the thermodynamic pressure for urinary crystal formation calculated 24h-urine supersaturation (SS) values for stone salts (EQUIL-program) were compared to empirical risk indices and concentration – or excretion values in 113 stone formers (SF) and 32 healthy controls (C).

Results. 1) Calculation of ionized Ca^{++} concentrations and of calcium oxalate (CaOx) ion activity products correlated very well (r = 0.9) with direct Ca^{++} measurements and simplified estimations by the Tiselius AP(CaOx)Index. 2). There was no significant difference between SF and C regarding SS-CaOx, -brushite, -hydroxyapatite the average urine volume in SF being slightly larger. 3) SS for calcium phosphate salts was much more dependent on urinary calcium concentration than SS-CaOx. Since the probability of being a stone former increased with calcium concentration more than SS-CaOx, increases of urinary calcium could induce calcium phosphate crystalluria and heterogenous CaOx nucleation. 4) Normo- and hypercalciuric SF could be separated significantly from C by increased values of the Tiselius Risk Index. Patients with "no metabolic anomality" could not be differentiated from C by 24h-urine analysis. 5) If a specifity of 80% was assumed while distinguishing SF from C by no parameter a sensitivity of more than 50% could be calculated the diagnostic parameters being different in hyper- and normocalciuric SF. 6). Following thiazide or allopurinol treatment Ca-, H2U-excretion and SS-NaU, -H2U decreased significantly. No significant decrease of SS-CaOx could be calculated.

Conclusions. Through 24h-urine analysis the risk of urinary stone formation can only be assessed with a high margin of error. Cofactors other than urinary SS must play an important role in the pathogenesis of sterile calcium urolithiasis.

14 Urinary Pyrophosphate (PPi) in Patients with Recurrent Calcium Urolithiasis (RCU) and in Healthy Controls (C)

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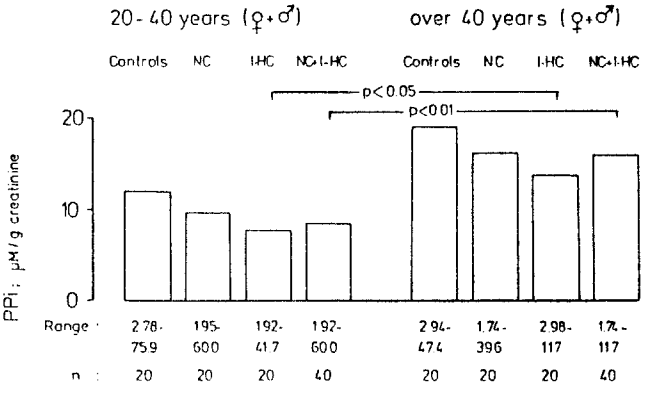
PPi is excreted in human urine in amounts up to 100 µmol/d. It is considered an inhibitor of nucleation, growth and aggregation of calcium oxalate and -phosphate crystals [1]. A urinary PPi deficit might favour RCU, but data on PPi excretion in RCU are contradictory, possibly due to the fact that mostly 24 h urines were evaluated. We studied PPi excretion in 24h-, 2 h fasting and 3 h postprandial urine (after an overnight fast) of normocalciuric (NC), hypercalciuric (I-HC) RCU patients (n = 80; ♂:♀ = 40:40) and age- and weight-matched healthy controls (n = 40; ♂:♀ = 20:20). Both populations were subdivided into younger (< 40) and older (> 40 years) individuals. All were studied under outpatient conditions.

Results. In general, urinary PPi increased with age, although the difference between younger and older NC and C was not significant (see table for pooled ♂ + ♀ data). While in younger male RCU patients, median PPi was not different from C in any of the urine portions, younger female NC and I-HC patients exhibited a significant postprandial PPi deficit. In older male RCU patients, PPi was significantly lower than in C in 24 h and 3 h postprandial urine. In older female patients, PPi was unchanged from C in any of the urine portions.



Conclusions. Decreased urinary PPi is not a general feature of RCU. It may be found predominantly in the postprandial urine of older male and younger female RCU patients, in the older males also in 24 h urine. Only subclassification of RCU patients with respect to sex, age, type of calciuria, and consideration of additional urine portions besides 24 h urine may help to uncover states of urinary PPi deficit.

1. Wilson JWL et al (1985) J Urol 134:1255

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15 Urinary Parameters in Hyperuricemic Patients (a) With Oxalate Lithiasis, (b) Urate Lithiasis and (c) Without Lithiasis

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As is well known, the gouty patients are characterized by a markedly increased stone incidence (about 20%), compared with the average population (1–4%). A high percentage of calculi, formed by gouty patients, are Ca-oxalate concrements.

To get more details, explaining the increased oxalate lithiasis in gouty patients, we carried out a long-term study in (a) hyperuricemia patients with oxalate lithiasis (b) hyperuricemia patients with uric acid lithiasis, further in (c) hyperuricemia patients without lithiasis and (d) controls. Over 30 urinary samples per patient (and control, respectively) were collected and analyzed (osmolarity, specific weight, Ca, pH, uric acid, phosphate, uric acid and Ca-oxalate crystalluria, erythruria, proteinuria).

In addition, the effect of Zyloric (Allopurinol) on uric acid and Ca excretion as well as on urate and oxalate crystalluria, erythruria and proteinuria was studied.

The pH was slightly decreased in all patients with hyperuricemia, especially in the group of hyperuricemic patients with oxalate lithiasis, showing a lower pH than the patients with urate lithiasis.

The phosphate was increased, especially in hyperuricemic patients with oxalate lithiasis and without lithiasis.

The calcium was elevated in hyperuricemic patients with oxalate lithiasis and in those without lithiasis, but reduced in patients with uric acid lithiasis.

Interestingly, the uric acid crystalluria showed the highest frequency in hyperuricemic patients with oxalate and not urate lithiasis, as would be expected.

Ca-oxalate crystalluria was, interestingly, in some analogy to the urinary calcium, markedly reduced in the group of hyperuricemic patients with uric acid lithiasis, being lower than in controls.

From these results it could be concluded that hyperuricemic patients tend to form Ca-oxalate calculi in normocalciuric and hypercalciuric basic constellation and tend to form uric acid calculi only if hyperuricemia is combined with hypocalcuria. The extreme uric acid crystalluria in hpyeruricemic patients with Ca-oxalate lithiasis and not those with uric acid lithiasis, as expected, supports the basic idea of uric acid involvement in oxalate calculogenesis. The dramatic reduction of urate, urate/oxalate and oxalate crystalluria as well as erythruria by Zyloric strongly supports the own concept of calculogenesis.

16 Determination of Hydroxyproline in the 24-h Urine of Ca-Oxalate-Stone Patients and Healthy Persons

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There is a possibility that the formation of glyoxalate from hydroxyproline may be linked to hyperoxaluria in Ca-oxalate-stone disease.

Material and Method. A quantitative determination was made of hydroxyproline excretion in the 24-h urine and in the circadian rythm of 10 healthy test subjects and 10 patients suffering from recurrent Ca oxalate stones. Measurements were taken on both controlled and uncontrolled diets.

Determination was effected according to column chromatographic separation in amino acid analyser 4,400 (LKB). Both the free and the bound hydroxyproline was determined.

Results. Six of the ten stone patients of uncontrolled diets excreted free hydroxyproline, but only two of the control subjects. Levels of bound and total hydroxyproline were much higher in stone patients than was the case with healthy persons. On uncontrolled diets, the male patients excreted statistically significantly higher levels of hydroxyproline than the females. On standardised diets, the amounts of hydroxyproline excreted by Ca-oxalate-stone patients decreased.

Resumée. Diet can cause an increase in hydroxyproline excretion in stone patients. A possible link with hyperoxaluria does exist.

	Uncontrolled diet	Controlled diet
	Total hydroxyproline (μmol/24 h)	
Stone patients	106 ± 89	91 ± 47
Healthy subjects	52 ± 35	89 ± 57

17 Some New Aspects of the Oxalate-Tolerance-Method

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A) Urinary Inhibitors. In 1985 we presented first results of our oxalate-tolerance-method at the congress in Vienna. In the meantime the influence of inhibitors and of other urinary components was examined. Thereby magnesium showed the most distinct effect of inhibition in our system. Also citrate gave a good inhibition with increasing concentration. Other known inhibitors like pyrophosphate and chondroitinsulfate showed only little or non-detectable effect in their physiological range. Additionally the urinary compounds urea, creatine and creatinine were tested in the same way.

B) Oxalate-Tolerance and Ionic Strength. Further experiments showed that the oxalate-tolerance is dependent on the ionic strength of a urine sample. At constant calcium concentration the added oxalate quantity required for precipitation becomes higher when the ionic strength of the urine sample is increased. This means that the hitherto existing standard-curve (ionic strength ≈ 0.2 M) is not valid for all those urine samples with different ionic strengths. For this reason the oxalate tolerance-values of a new standard curve and of all collected urine samples were determined at a fixed ionic strength. The conductivity of each urine sample is a good and easily measurable parameter for the ionic strength. Therefore all samples were fixed at 40 mS/cm by addition of NaCl. A comparison of urines of stone formers and of other persons with regard to the new standard curve is in preparation and will be presented at the symposium.

18 Are the Values of the Oxalate Tolerance Test in Correlation to the Values Calculated by EQUIL?

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1985 at the congress in Vienna we presented our first results concerning the oxalate tolerance values of stone and non stone formers. Further studies investigated the possible correlation between the oxalate tolerance values and the relative urine saturation calculated by EQUIL I (Finlayson et al.).

Methods. Urine probes (sampled in the morning and/or afternoon) of recurrent stone formers and non stone formers (in both groups out- and inpatients) were investigated by the originally described oxalate tolerance test and in an aliquot pH, volume, sodium, potassium, calcium, phosphate, uric acid, magnesium. Oxalate and citrate were measured. Urin saturation with respect to calcium oxalate was calculated using EQUIL I. Values of oxalate tolerance were plotted against values calculated by EQUIL I. Results will be presented at the symposium.

19 Ion-Chromatographic Determination of Urinary Phosphate and Sulphate

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Ion-chromatography seems to be the method of choice for measuring urinary oxalate if a medium number of samples has to be analyzed daily. The same technical equipment used there also allows

the determination of other urinary anions like inorganic phosphate and sulphate. Although the importance of the latter for urolithiasis is still unknown, both are measured routinely in some laboratories working on urolithiasis research. We compared an ion-chromatographic application for the simultaneous determination of urinary phosphate and sulphate with the molybdenum blue method (Merckotest 3331, Merck, Darmstadt, FRG) for determining phosphate and the turbidimetric method from Berglund and Sörbo (1960) for sulphate. For the chromatographic procedure the samples simply were acidified and diluted.

The conventional methods as well as the ion-chromatographic method were found to be of good reliability and practicability. Within-run imprecision was below 5% and between-run imprecision below 10% in case of all methods. The recovery of 6 mmol/l phosphate and sulphate was near 100% with the chromatographic and the conventional methods. The statistical evaluation of parallel determinations carried out on 80 urine samples showed, that both methods for determining phosphate gave identical results. For sulphate, however, a significant difference between the two methods was proved. On the average the results produced by the chromatographic procedure were about 8% less than those from the turbidimetric method, which possibly overestimates the sample concentrations.

Although the ion-chromatographic procedure is most easily performed in terms of practicability the conventional methods seem to be more advantageous than the ion-chromatographic as it was performed here, since they allow analyzing more samples per day at lower costs. From this point of view the ion-chromatographic determination of phosphate and sulphate could only be an alternative if it would allow the simultaneous determination of urinary oxalate, which, however, seems possible.

20 Single-Dose Response to Ethacrynic Acid in RTA I

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A single dose of ethacrynic acid (ETA, Hydromedin®, 100 mg) was given orally to 5 pts. with incomplete distal renal tubular acidosis (RTA I) and recurrent stone formation (group 1) and to 5 controls with recurrent urolithiasis (group 2).

Before and in hourly intervals after medication ph, K^+, Na^+, Ca^{++}, phosphate, creatinine, ammonia, titrable acidity and bicarbonate were measured in the urine. Serum Na^+, K^+, Ca^{++}, phosphate, creatinine, acid-base data and parathormone were determined before and 3 h after ETA-medication.

ETA had a similar effect in both groups: urine ph decreased significantly not only in the controls but also in the RTA cases. Urinary net acid excretion decreased in 2 pts. of each group and increased in the others. Urine calcium concentration decreased in 4 pts. of group 1 and in 3 of group 2. Urinary phosphate excretion showed no significant change. Serum parathormone increased in all patients.

Decrease of urine ph and calcium-phosphate-concentration-product combined with only a slight rise of serum ph and parathormone are the criteria to use ETA in prevention of recurrent stone formation in pts. with RTA I.

21 Some Urinary Parameters in Immobilized Patients

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To get more information about the factors influencing the considerably increased stone formation in immobilized patients, we started a long-term study measuring during 12 weeks after immobilisation in the (a) morning (b) midday and (c) evening urinary samples repeatedly the following parameters: osmolarity, specific weight Ca^{++}, Ca (total), Mg (total), Na, Zn, pH, NH_4^+, Cl^-, citrate, phosphate, uric acid, urinary anions (org. acids), excreted in the pH-ranges 3.0–6.0 (SÄ3-6), 4.0–6.0 (SÄ4-6) and 3.0–10.0 (SÄ3-10), and titratable acidity (TA). In addition, the osmolarity and specific weight "correctures ' of single parameters were calculated.

Some quotients, based on analytical data in urine, were introduced to underline the differences between immobilized patients and controls, in dependence also on the post-immobilization week.

The study was carried out in cooperation with the Berufsgenossenschaftliche Unfallklinik in Murnau/FRG. In this abstract, only some examples can be presented. So, in the midday urinary samples the Ca-values dropped to 1.48 mmol/l (control value: 3.67 mmol/l) in the 1st week after immobilization, reached 3.59 mmol/l in the 6th week and increased to 3.86 mmol/l in the 12th week. On the contrary, the Mg-values increased to 5.18 mmol/l (control value: 3.67 mmol/l) in the 1st week, fell to 2.69 mmol/l in the 6th week and reached a value of 3.78 mmol/l in the 12th week after immobilization. The Zn-values (control: 0.0094 mmol/l) increased to 0.0215 mmol/l in the 1st week, reached the value of 0.0389 mmol/l in the 6th week and 0.0345 mmol/l in the 12th week. NH_4^+-values (control: 26.53 mmol/l) increased to 46.05 mmol/l immediately (1st week) after immobilization, fell to 20.34 mmol/l in the 6th week and reached the value of 31.04 mmol/l in the 12th week. Citrate (control: 1.80 mmol/l) fell immediately after immobilization to 0.72 mmol/l, increased in the 6th week to 0.92 mmol/l and in the 12th week to 1.07 mmol/l. The Ca (total)/Mg (total)-quotient (control: 0.9768) fell in the 1st week to 0.4514, increased in the 6th week to 1.8291 and in the 12th week to 1.4272. The Ca (total)/citrate-quotient (control: 2.20) increased slightly in the 1st week to 2.62, in the 6th week strongly to 13.38 and in the 12th week to 8.32. The mechanism of stone-formation in immobilized patients is discussed.

22 The Importance of Crystal Growth Rates and Other Urinary Parameters in Diagnosis and Therapy of Urinary Stone Formation

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The following parameters potentially relevant in stone formation were determined or estimated from 24-h collected urines of 275 unselected stone formers: crystal growth rates of calcium oxalate (CaOx) and phosphates, degrees of supersaturation for CaOx, brushite and uric acid, excretion volume, pH, total concentrations and excretions of Ca, Mg, Na, K, oxalate, phosphate, citrate, uric acid and creatinine.

1) The data were grouped corresponding to the kind of stone formers (CaOx, CaOx/Ca-phosphates, uric acid) and compared one to another by tests of significance in order to elucidate their potential role in stone formation. Kinetic data of crystal growth for CaOx, calculated supersaturations for brushite and uric acid, pH and Ca excretion seemed to be of highest diagnostic value.

2) Multiple linear regression analysis was applied to detect the dependence of CaOx crystal growth rate (Vcr(CaOx)) on other parameters as well as interrelationships between all parameters determined. The strongest correlations were found between Vcr(CaOx) and free ($r = 0.83$) or total calcium concentrations ($r = 0.79$).

3) The results obtained from these experiments (correlation matrix) were compared with those from artificial urines and independent studies on the effect of different therapeutic measures on risk factors of stone formation. It has been confirmed that the growth rate of CaOx as determined by the Gel Crystallization Method (GCM) is a very useful means and definitely superior to calculated supersaturation.

23 The Crystalline Urinary Sediment/Long-Term Observation

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Long-term observations at the Surgical clinic in patients with renal stones and other illnesses. When comparing the sedimental slides of surgical patients having other illnesses it was to be seen that the crystals in the urine sediment differed from those patients who had had renal stone attacks earlier.

III. Basic Research

24 Investigations on the Crystallization Tendency in the Urine of Calcium Oxalate Stone-Formers and of Stone-Free Patients and in Artificial Urine with AC-Impedance Measurements (Frequency Response Analysis)

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Nucleation as well as crystal growth and aggregation are primary the effect of electrophysical properties and the dielectric reaction of outer phase limit layers (eg. cell tissue), and of inner phase limit layers (eg. molecule cluster, solvate formation etc.) of an electrolyte. Our investigations had to settle the question whether it is possible by determination of the complex resistance to discriminate in "high stone formation tendency" and "low stone formation tendency" urines. For this we used an AC-impedance analyzer for the frequency range 10^{-2} to 10^5 Hz (frequency response analysis). We examined so-called artificial urinelike urine of calcium oxalate stone-formers and stonefree persons. The urine of stone patients examined up to now shows a clear influence through DC-polarization in the low frequency range 0.01 to 10 Hz; a DC of +0.2 V or −0.2 V already leads to an obvious decrease of resistance in the whole frequency range, i.e. to an increase of substance transport rates and therefore to a higher crystallization tendency. The fact that the measurements in artificial urine of variable supersaturation were quite different from those in natural urine shows that there are some other substances in natural urine strongly influencing crystallization. Our present investigations make us hope that the impedance measuring will enable us to discriminate urine in view of its "stone risk" and to check the efficiency of medical and other metaphylactic measures.

25 The Effects of Zinc and Citrate on Urease-Induced Crystallization in Synthetic and Human Urine

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Colonization of the urinary tract by urease-producing microorganisms can result in the formation of concrements composed of magnesium ammonium phosphate and calcium phosphate. Clinical observations and recent experimental studies indicate that the concrement forming process is not only determined by the urease-induced pH-increase but influenced by as yet unidentified components. Zinc is excreted in urine and has been shown to inhibit urease enzymatic activity as well as the crystallization of calcium phosphate. Citrate has been described to act as an inhibitor of calcium phosphate crystallization. How zinc and citrate influence urease-induced crystallization is, however, unknown and the subject of the present investigation.

Method. Human and synthetic urine with and without added zinc or citrate was incubated with urease at 37 °C during continuous stirring. Synthetic urine of a composition described by Griffith containing 11 solutes was used. The precipitation of magnesium ammonium phosphate and calcium phosphate on glass rods immersed into the urine was measured.

Results. In synthetic urine the addition of zinc (0.9–7.2 mg · l^{-1}) reduced the urease-induced pH-increase and the precipitation of calcium phosphate but the precipitation of magnesium ammonium phosphate was increased. The addition of citrate (0.6–11.4 mmol · l^{-1}) augmented the pH-increase with a marked influence on the precipitation of both magnesium ammonium phosphate and calcium phosphate. In human urine the addition of the same amounts of zinc or citrate gave but a minimal influence on the pH-increase and had no effect on the precipitation of neither magnesium ammonium phosphate nor calcium phosphate on the glass rods.

Conclusions. The results obtained in synthetic urine demonstrate that both zinc and citrate markedly influence urease-induced crystallization. Why the same effects could not be reproduced in human urine remains to be investigated. Our findings stress the fact that one should be careful when extrapolating from studies using synthetic urines to the conditions for human urine.

26 Studies on the Kinetic and Thermodynamic Effect of Citrate on the Crystal Growth Rate of Calcium Oxalate in Urine

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The automated Gel Crystallization Method (GCM) was used to study the effect of citrate (0–8 mmol/l) at varying calcium concentrations (0–8 mmol/l) on the relative crystal growth rate of calcium oxalate, Vcr(CaOx), within a gel matrix of agar-agar. Cit_T and Ca_T were varied in an artificial urine keeping pH at 6.0 and other total concentrations at constant normal values.

It could be shown that Cit_T did not only reduce the nearly linear slope of $Vcr = f(Ca_T)$. It increased also the total calcium concentration which is necessary to induce crystal formation within the gel phase thus demonstrating its thermodynamic action via an alteration of complex chemical equilibria.

Plotting of Vcr as a function of (Ca^{2+}) (Ox^{2-}) (= ion or activity product of calcium oxalate) at different Cit_T revealed a significant kinetic effect on crystal growth of CaOx in addition to the thermodynamic impact mentioned before. The solubility product of CaOx, however, is not affected by this action.

The results obtained from these in-vitro measurements could be confirmed by an in-vivo study using alkali citrates as alkalinizing agents.

The GCM has proven to be a reliable method in order to detect thermodynamic and kinetic effects of effectors of crystal growth processes in gel matrices.

27 Changes of Urine Parameters by Intake of Full-Cream Milk and Cocoa

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Overconsumption of milk and milk products is thought to be a predisposing factor of calcium oxalate stone formation. So far there are no quantitative studies on the actual changes of urine parameters.

Material and Method. Under a standard diet 9 healthy subjects received 1 l of fullcream milk and cocoa in an acute loading test. Urine samples were collected for 24 h in portions of 2–3 h. In each sample the following parameters were measured: sodium, potassium, calcium, magnesium, phosphate, sulfate, chloride, creatinine, uric acid, citric acid, oxalic acid, pH and specific gravity.

Results. Full-Cream Milk: pH is not affected. Calcium, potassium, phosphate and sulfate excretion rises statistically significantly. Oxalic acid excretion is significantly reduced. In the circadian rhythm and over the 24 h period the relative supersaturation for calcium oxalate is elevated.

Cocoa: pH is not changed. Sodium, potassium, chloride, phosphate, sulfate and citric acid excretion also shows an increase. The relative supersaturation for calcium oxalate rises significantly shortly after the intake of cocoa.

28 Influence of Test Conditions on the Results of the Measurement of Urinary Inhibitor Activity

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Various approaches to measure inhibition of crystallisation processes by urine and by inhibitory substances reveal contradictory results because these results are not only dependent on inhibitors but also on test conditions. Inhibition of crystal aggregation shows only differences between stone formers and controls at high urine dilution and seems to be lost in whole urine. The formation product for spontaneous nucleation often used as measure of inhibitor activity is influenced by the incubation time and often is lower in whole urine than in control solutions, probably due to the action of promotors which can not be separated from the action of inhibitors by this test method. High supersaturations overwhelm the effect of potent inhibitors in low concentration. The relative influence of low molecular inhibitors change essentially with the amount of seed crystals given to test systems measuring secondary nucleation and growth.

From these observations we conclude that more research should be done in whole urine with test systems adapted to crystallization conditions in the kidney and the urinary tract.

29 The Effects of Low and High Molecular Weight Substances on the Citrate-Induced Changes of Growth and Agglomeration of Calcium Oxalate Crystals

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Growth (CG) and agglomeration (CA) of calcium oxalate crystals are important processes in renal stone-formation and can be measured independently. We have previously shown that in stoneformers with high recurrence rate, there is lack of inhibition of CA in the presence of normal inhibition of CG. This was associated with low citrate excretion rates and increase in the citrate content of urine either in vitro or in vivo led to correction of this abnormality. In order to study further the role of citrate on the crystallization processes we examined first its effect on CA and CG in vitro. Citrate inhibited both CA and CG in a dose dependent manner. However, as other substances may also influence the crystallization processes, we studied the effects of high and low M.W. substances (heparin and magnesium resp.) on the citrate-mediated responses.

Heparin had no effect on CA by itself and its presence did not change the citrate-induced CA inhibition. It produced, however, a strong inhibition of CG which in turn was not affected by the presence of citrate in increasing concentrations. Magnesium had only a small effect on CA and inhibited CG to the same extent as citrate. When magnesium and citrate were tested together, a strong potentiation of the citrate induced CA inhibition was found, while no further effect on CG inhibition could be detected. Citrate, therefore, affects mainly the CA process and this action can be potentiated by low M.W. substances, such as magnesium, while high M.W. substances, as heparin, do not inhibit CA. In contrast, CG is probably modulated by high M.W. substances.

30 Human Atrial Natriuretic Peptide (H-ANP) Plasma Levels in Idiopathic Renal Calcium Stone Disease – Preliminary Report

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The recently recognized H-ANP from cardiac atrial tissue is discussed as a factor involved in the renal regulation of sodium, and possibly other electrolytes like calcium. Fractional excretion (FE) of both sodium and calcium (FE-Na, FE-Ca) in fasting urine of patients with so-called Renal Hypercalciuria (R-HC) is elevated from unknown reasons [1, 2]. In controls and stone patients we measured H-ANP in plasma extracts, FE-Na and FE-Ca, all during clearance conditions after an overnight fasting period (12 h). Results (table): FE-Na is higher-than-normal (not significant) in male and elevated in female patients with R-HC and normocalciuria (NC). FE-Na and FE-Ca are significantly correlated in females ($n = 14$; $r = 0.571$; $p < 0.05$), while for males the correlation is not significant ($n = 13$; $r = 0.362$). H-ANP is significantly lower in female than in male controls, and it is increased in female R-HC. FE-Na and H-ANP in females, not in males, are significantly correlated ($n = 14$; $r = 0.672$; $p < 0.05$). Plasma sodium, creatinine clearance, 24 h urinary sodium (not shown), all are unchanged.

We conclude that 1) net tubular reapsorption of sodium in fasting urine of R-HC and NC appears generally low; this may contribute to

	n	Age years	Weight kg	Fasting blood			Fasting urine: 2 h		
				Calcium mM/L	Sodium mM/L	h-ANP pg/ml	C_{Cr} ml/min	FE-Ca	FE-Na
Males									
Controls	4	44 ± 2	86 ± 4	2.42 ± 0.16	143 ± 1	61 ± 12	86 ± 9	0.79 ± 0.24	0.80 ± 0.26
NC	4	44 ± 2	79 ± 3	2.36 ± 0.04	144 ± 1	43 ± 11	87 ± 6	1.55 ± 0.57	1.03 ± 0.23
R-HC	5	43 ± 7	71 ± 4	2.40 ± 0.04	143 ± 1	20 ± 3[b]	95 ± 9	2.61 ± 0.20[c]	1.01 ± 0.20
Females									
Controls	5	46 ± 1	66 ± 4	2.27 ± 0.03	142 ± 1	23 ± 3[+]	101 ± 27	0.84 ± 0.23	0.43 ± 0.14
NC	5	48 ± 3	66 ± 5	2.41 ± 0.02[c]	142 ± 1	16 ± 1	95 ± 12	1.23 ± 0.10	0.85 ± 0.16[a]
R-HC	4	46 ± 4	71 ± 2	2.26 ± 0.07	141 ± 2	42 ± 9[a]	114 ± 14	2.88 ± 0.41[b]	1.09 ± 0.12[b]

C_{Cr}: creatinine clearance; FE-Na, FE-Ca: (C_{Na} or $C_{Ca} \cdot C_{Cr}^{-1} \cdot 100$; [a, b, c]: $p < 0.05, < 0.01, < 0.001$ vs controls
[+]: significantly ($p < 0.01$) different from male controls

the higher calcium in NC and fasting hypercalciuria in R-HC; 2) in females with R-HC high H-ANP and elevated FE-Na suggest a close interdependence of the two variables during limited time periods within a daily cycle. – Supported by Deutsche Forschungsgemeinschaft; Schw 210/4-3.

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31 Kinetics of Precipitation of Calcium Phosphates and Oxalates From Solutions Supersaturated to Both Solid Phases

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The kinetics of precipitation of calcium oxalate trihydrate (COT) and calcium hydrogenphosphate dihydrate (DCPD) under conditions comparable to those in urines (pH ~ 5, ionic strength 0.26, made up with sodium chloride) has been investigated. The respective supersaturations were as in patients with disorders of calcium metabolism (S_i (COT) = IP/K_{sp} = 6.86, S_i (DCPD) = 2.10–3.57) which have a high propensity to form renal stones.

Under the experimental conditions employed, COT precipitated first (induction period t_i = 10–12 min) and effectively initiated the precipitation of DCPD from the above solutions which, without COT, were metastable for more than three hours.

By following the kinetics of precipitation of COT under conditions at which the respective induction periods, $t_{i(COT)}$ and $t_{i(DCPD)}$ differed by more than one hour, and interpreting the data in terms of quantitative parameters characterizing crystal growth and aggregation, information of the influence of phosphate ions on these processes was obtained. It is shown that phosphate ions inhibit crystal growth of COT but have no influence on the mode, rate constant and transport mechanism of aggregation. The efficiency of aggregation to inhibit crystal growth, however, is enhanced by the presence of excess calcium ions as follows from a comparison with the results of previous kinetic experiments carried out at equimolar total calcium and oxalate concentrations.

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32 Influence of Various Substances on Growth and Agglomeration of Calcium Oxalate Monohydrate

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To determine the influence of various concentrations of citrate, magnesium and pyrophosphate on growth and agglomeration of calcium oxalate monohydrate, the uptake of radioactive ^{45}Calcium was measured in seed crystals grown in metastable oversaturated solution. The used growth model was introduced by Bijvoet and Blomen (Bijvoet 1978; Blomen 1982). This model permits the determination of agglomeration independent of growth.

The effect of citrate was examined in equimolar and nonequimolar calcium oxalate solutions. The effect of magnesium and pyrophosphate was tested in nonequimolar solutions. Each additive showed inhibitory effect on growth. Agglomeration of the crystals was slightly inhibited by citrate and slightly promoted by magnesium. Pyrophosphate had a strong inhibitory influence on agglomeration.

33 Phosphate Adsorption on Calcium Oxalate Calculi

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According to previous work of our laboratory, a non-apatitic phosphate has been found in "pure" calcium oxalate monohydrate calculi by means of infrared spectroscopy. The observed absorption band near 1,100 cm^{-1} was confirmed to be associated to $H_2PO_4^-$ ions by the infrared and Raman studies of "in vitro" obtained samples. From the results attained we concluded that the phosphate ions could be adsorbed on the calcium oxalate monohydrate crystals.

In the present work, a series of both whewellite and weddellite stones previously selected by their infrared spectra, have been examined by scanning electron microscopy and electron dispersive X-ray analysis in order to determine how the phosphate ions are distributed. In opposition to the case of small apatite nuclei or apatite zones easily recognized by their spherical microcrystalline structure, this type of non-apatitic phosphate cannot be observed by SEM. The EDAX gives P/Ca ratio values of ca. 0.01. Phosphorus seems to be inhomogeneously distributed throughout the stone.

This type of phosphate is absent from the weddellite calculi, at least in the cases we have hitherto studied.

34 Precipitation and Solubility of Calcium Hydrogene Urate Hexahydrate

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The composition, conditions of precipitation and solubility of calcium urate are of considerable interest because of their possible occurrence in renal calculi. However, solubility data are not yet available and there is, moreover, considerable confusion in the literature concerning the exact chemical composition of such a compound.

In this work calcium hydrogen urate hexahydrate, ($Ca(C_5H_3O_3N_4)_2 \cdot 6H_2O$); $Ca(HU)_2 \cdot 6H_2O$) was prepared by dissolving anhydrous uric acid in aqueous solutions of calcium hydroxide and hydrochloric acid. Pure crystals of the compound, as characterized by X-ray diffraction powder patterns, chemical and thermogravimetric analysis, were obtained in the range of $pH\ 7 \leqslant pH \leqslant 10$ and uric acid concentration $10^{-2} \geqslant [H_2U] \geqslant 10^{-3}$ at calcium/uric acid molar ratios 1.1–1.5 [1]. Exact conditions of preparation of $Ca(HU)_2 \cdot 6H_2O$ and data on its solubility in aqueous solutions are given. The anhydrous form, $CaC_5H_3O_3N_4$, has also been prepared and characterized.

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35 Structure and Composition of Oolitic Granules of Milk of Calcium Sand

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Some specimen of milk of calcium, composed by oolitic granules, were analyzed by i.r. spectroscopy, stereoscopic and polarization microscopy, SEM and EDAX. The most typical granulates are composed by mainly spherulitic but also compact and microcrystalline calcium phosphate; some others show calcium oxalate in the nucleus and compact calcium phosphate in the outer layer. A third pattern, on the contrary, is composed by apatite in the central part and calcium oxalate in the cortex of the granule. We have found granules with whewellite, crystalline in the core and again compact and

microcrystalline in the outer part. Another type was observed to be composed by either uric acid or complex urate containing potassium in the central part enveloped by compact calcium oxalate. Finally some renal oolitic sands were wholly composed by uric acid or by struvite. Micrographs and infrared spectra are shown. According to our results, there is not a common composition for this oolitic or milk of calcium sand.

36 Phase and Elemental Analysis of Cystine Stones

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24 cystine stones of 18 patients have been re-analysed using the scanning electron microscope equipped with x-ray microanalysis to determine the texture and distribution of the crystalline phases present. Subsequent x-ray diffractometry was performed for a phase analysis.

In contrast to the common opinion that cystine stones are monomineralic, 7 of the stones (34%) contained additional compounds. In 5 stones apatite besides cystine was detectable. One stone showed some disseminated whewellite crystals and in another concretion whitlockite together with apatite and cystine was present.

The localisation and arrangements of apatite layers seem to be the metabolic answer to an overalkalisation of the urine by oral medication to prevent the formation of cystine stones.

One concentration as an extreme consisted only of a central core of cystine (total mass about 10%) surrounded by a thick crest of apatite. A significant urinary tract infection with *E. coli* additionally could be established.

Due to the fact that Ca-phosphates (apatite, whitlockite) are easily precipitated in alkaline urine, oral alkalisation of the urine of patients suffering from cystinuria has to be performed very carefully with exact pH controls. Additionally, infection controls of the urine are mandatory.

37 The Efficient Microdetermination of Urinary Constituents by Vertical-Light-Path Photometry in Microtiter Plates

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Automated photometric measurements in microtiter plates have been used in our laboratory for years to determine kinetic parameters in gel matrices. We have now extended vertical-light-path photometry to quantify various urinary constituents in aqueous solution at definite measuring wavelengths. For this purpose, automated pipetting of samples and reagents was combined with automated measurement in 96-well microplates.

Experimental Device. Computer controlled pipetting station TECAN 505 (Fa. Zinsser Analytic, FRG) with IBM PC and microreader MR 600 (Dynatech) with IBM PC-XT. Programs for evaluation of measuring data were written in BASIC.

The following assays were adapted to the special conditions of determination in microplates: 1) citrate (enzymatic UV-test, Boehringer), 2) isocitrate (enzymatic UV-test, Boehringer), 3) uric acid (enzymatic color test "Peridochrom^R", Boehringer) and 4) creatinine (enzymatic test combination "PAP", Boehringer).

In general, measuring volume was about 300 µl per well for all tests. Mean unprecision within series was smaller than 2%. The agreement of results obtained from corresponding macro- and microtests was good or excellent. About 90% of reagents could be saved and manual work was reduced drastically. The analytical principle described here is characterized by efficiency, flexibility and economy.

38 Lactose Induced Urolithiasis in Rats

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A total of 25 female Wistar rats were subdivided into two collectives: 1. diet rich in lactose (n = 15); 2. control diet (n = 10). The animals were kept for 9 months, pool-urine was determined in the third and ninth month and blood taken at the end of the experiment. The urine was examined on the following parameters: calcium, phosphate, magnesium, citrate, uromucoid and creatinine. Calcium, magnesium, phosphate and creatinine were determined in the blood.

The following results were obtained: The administration of a diet rich in lactose resulted in a distinct urolithiasis or nephrocalcinosis respectively. The excretion of calcium and magnesium was significantly increased compared to the control group. An increased intestinal calcium absorption is supposed to be the cause of hypercalciuria or urolithiasis respectively. Thus the experimental setup is a practicable animal model of absorptive hypercalciuria.

39 Cystinuria in Dogs

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Cystinuria is a congenital metabolic disorder which is not confined to human beings. Animal tests provide an opportunity to study this disease.

Material and Method. Analysis of 741 canine urinary stones (IR spectroscopy) revealed that in 20.4% of all cases cystine was the main component. A quantitative amino acid analysis was conducted in the spontaneous urine of 40 dogs with cystinuria and 11 healthy dogs.

Results. Cystine calculi are only formed by male dogs. 70% of dogs with cystinuria were found to have a cystine concentration in excess of 150 mg/l. In the amino acid sample, in addition to cystine, lysine and arginine, statistically significant rises in threonine, citrulline, taurine and cystathionine were also observed. These amino acid samples, however, vary greatly from group to group of the animals. Thus, for example, at 12.5% only the cystine concentration was found to be raised.

Resumée. The male dog with cystinuria seems to be a good model to study pathogenesis, diagnosis and therapy of the cystine urolithiasis.

IV. Therapy

40 More on Mild (But Clinically Significant) Metabolic Hyperoxaluria and Its Response to Pyridoxine

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This syndrome was previously described at Vienna in 1985. Three of the cases mentioned then have been selected for further review because of certain interesting features. One has been controlled without difficulty on 800 mg per day of pyridoxine. One responded well to 800 mg per day of pyridoxine but then relapsed and remains hyperoxaluric with raised urinary glycollate. One who also had primary hyperparathyroidism, responded to 20 mg per day of pyridoxine, relapsed when it was stopped and responded a second time with the same dose of pyridoxine and now has a normal urinary oxalate, glycollate and calcium. A fourth new case with raised urinary oxalate and glycollate in a young girl will also be described. She responded at first to 10 mg per day of pyridoxine but now requires 40 mg a day. There are three lessons to be drawn:

1) Urinary oxalate should be measured in all cases of calcium oxalate urolithiasis even if another cause is apparent.

2) Urinary glycollate should be measured once hyperoxaluria is recognized.
3) Mild metabolic hyperoxaluria with raised urinary glycollate may respond to pyridoxine although it is impossible at the moment to predict the dose required.

41 The Effect of Different, Orally Applied Magnesium Preparations on the Crystal Growth Rate of Calcium Oxalate and Other Parameters in Human Urine

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In the present work, three different magnesium preparations (I: Mg-citrate / Mg-Levulinate / citric acid / vitamins B1, B2, B6; II: Mg-citrate / Mg-yhdrogenglutamate / Mg-nicotinate; III: Mg-L-aspartate-hydrochloride-trihydrate) were applied to 7 healthy probands under controlled diet (dosage: 12 mmol Mg^{2+} per day). The crystal growth rate of calcium oxalate, Vcr(CaOx), measured by the Gel Crystallization Method (GCM), was determined in 4-h collections of daily urine and 8-h collections of night urine with and without therapy. Other parameters (pH, Ca, Mg, Na, K, oxalate, citrate, phosphate, uric acid, creatinine, supersaturations) were determined in corresponding 24-h collections.

No significant impact on the important crystal growth rate of CaOx could be observed for I and II while III increased Vcr(CaOx) significantly.

The results demonstrate the essential effect of the different anions combined with the metal ion.

The failure of the anticipated benificial effect of magnesium compounds on the measured factors of stone formation risk could be clearly accounted for by the overlapping actions of increased magnesium and citrate and the counteracting increase of calcium excretions.

42 The Influence of Oral Alkali Citrate on Intestinal Absorption of Calcium (CaA) in Healthy Men

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In recurrent calcium stone formers, decreased urinary excretion of calcium (Ca) is observed after treatment with oral alkali citrate (AC). This finding has been attributed to AC-induced metabolic alkalosis, but the latter has never been verified under acute or long-term AC treatment. Animal studies revealed dose-dependent decreasing effects of oral AC on CaA. Since a fall in intestinal CaA might help explain decreased urinary Ca excretion, the present study was designed to determine the influence of AC on intestinal CaA of healthy males, using a ^{85}Sr, ^{47}Ca double tracer method [1].

An oral load containing 5 mmol $CaCl_2 \times 2\ H_2O$ and 21 mmol citrate as a sodium potassium salt (Oxalyt-C), pH 5.6, or a pH- and cation-corrected calcium, sodium- and potassium chloride load (vehicle) was administered. Each load was labelled with 0.55 MBQ ^{47}Ca. After its ingestion, 0.075 MBQ ^{85}Sr were given intravenously. The cumulative CaA over 3 h was calculated using a computerized deconvolution method.

10 min fractional CaA fell significantly under AC from 30 to 110 min post-load. 3 h cumulative CaA decreased from 76.3 ± (SEM) 4.5% of the total dose under vehicle to 54.6 ± 6.1% under AC ($p < 0.002$). Under AC, serum and urinary citrate increased, while the blood acid-base status and serum parathyroid hormone were unchanged. Urinary specific activity of ^{47}Ca correlated significantly with 3 h cumulative CaA under both loads, while urinary Ca decreased only slightly under AC as compared to vehicle.

Our data suggest that in man, oral AC can inhibit CaA without major systemic acid base changes. This action is probably due to intraluminal complexation of Ca^{++} by $Citrate^{3-}$ and indicates preferential absorption of ionized Ca as opposed to Ca complexed by citrate. The finding might help explain the fall in urinary Ca excretion observed in patients treated with AC for recurrent Ca urolithiasis.

I. Wooton R, Reeve J (1980) Clin Sci 58:287–293

43 Influence of Different Alkaline Salts on Urinary Citrate and Calcium Excretion in Healthy Subjects

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44 Alkalisation of the Urine by Mineral Water in Calcium-Oxalate Urolithiasis

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In recent years a successful recurrence prophylaxis of the calcium-oxalate disease with citrate mixtures (e.g. Oxalyt^{R}) has been reported on repeatedly. These preparations effect an alkalisation of the urine and an increase in citrate excretion. In this way the risk of a calcium-oxalate-crystal formation is reduced. The administration of a citrate mixture in the form of a granular powder is problematic with some patients – particularly with long-term administration. That was why we tested in $n = 10$ patients suffering from calcium-oxalate stones whether an alkalinisation with mineral water rich in bicarbonate is possible for recurrence prophylaxis. The patients were directed to drink one liter of Adelheidquelle a day. pH was measured continuously as were the following substances in the 24-h urine: calcium, sodium, phosphate, uric acid, citrate and magnesium.

Our results are presented and their relevance for the metaphylaxis of calcium-oxalate stone disease discussed.

45 The Influence of Calcium-Containing Mineral Waters on the Urinary Composition

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The use of mineral waters especially with high content of calcium in renal stone formers is still controversial. Therefore we investigated the influence of a Na-Mg-Ca-HCO_3-Cl-CO_2-water (Wildunger Helenenquelle) on the urinary composition in 12 healthy subjects undergoing 24 h constant bed rest. The food consisted of equally distributed portions of a standardized low-protein diet. The mineral water was given in three portions: 700 ml at 9.00, 350 ml at 13.00 and 17.00. For controls tap water was administered to the same test persons under the same conditions. The urine was collected during 24 h in 6 4-h-probes. Beside urinary volume, pH, and osmolarity the content of Na, K, Ca, Mg, urate, oxalate, phosphate, citrate, sulfate, and Cl were measured.

The results showed compared with tap water an increase of osmolarity during forenoon, which was compensated by lower values in the night. The urinary calcium concentration was significantly increased from 15.00 to 3.00, however, the concentrations of magnesium and citrate were significantly increased as well. The oxalate excretion values were altogether very low according to the low nutritional oxalate intake, however, the oxalate concentrations were higher in the night after the application of the mineral water. The calculation of the quotient Ca x Ox : Mg x Cit as well as of the AP (CaOx) showed that the higher Ca-concentration is overcompensated by the increased Mg- and citrate-values, however, the differences were not significant. Calculating the quotient Ca : Mg x Na x Cit the values were significantly decreased during 24 h after the first mineral water application. It is concluded, that a mineral water with high Ca-content, containing additionally HCO_3, Mg, and Na, does not increase the risk of stone formation.

46 Sulfate Content in Mineral Water and Sulfaturia

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Drugs inducing sulfaturia are used in the treatment of phosphate stones. Mineral water with high sulfate content seems to have an osmotic laxative effect which is attributed to poor absorption of sulfate salts in the gut. The objective of this study was to evaluate the influence of sulfate content in mineral water on urinary sulfate excretion.

9 patients with recurrent idiopathic calcium stone disease entered the study which was performed under standard diet in hospital. On day one the patients received 2.4 liters of a mineral water with a low sulfate concentration (SO_4 0.07 mmol/l, HCO_3 1.05 mmol/l, calcium 0.25 mmol/l, magnesium 0.25 mmol/l) and on day 2 the same amount of a mineral water with a high sulfate concentration and also with a higher content of other ingredients (SO_4 9.17 mmol/l, HCO_3 5.66 mmol/l, calcium 9.65 mmol/l, magnesium 2.08 mmol/l). Urine was collected during the day for 10 h and during the night for 14 h. Each patient contributed 4 urine samples in which the sulfate was measured with ion chromatography.

The sulfate excretion increased from 18.5 ± 7.9 mmol/24 h on day 1 up to 35.3 ± 6.3 mmol/24 h on day 2 when the sulfate rich mineral water had been ingested. The significant increase of sulfaturia ($p < 0.001$) corresponded to 67% of the sulfate ingested with mineral water. Urinary pH decreased from 6.31 ± 0.47 on day 1 to 6.08 ± 0.36 on day 2 ($p < 0.05$). Linear regression analysis revealed a correlation coefficient of −0.58 between pH and sulfate concentration in urine ($p < 0.001$).

It is therefore concluded that a significant portion of sulfate ingested with mineral water will be absorbed and excreted in urine, which leads to a mild urinary acidification.

47 The Influence of Rye Bran on Urinary Composition

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In order to test its suitability for applications in urinary stone prophylaxis, an investigation has been conducted into the influence of rye bran on the composition of urine.

Material and Method. 12 female test subjects were directed at random into a bran group and a control group. The bran group ingested 30 g of rye bran daily. After a habituation phase of 7 days, both groups were placed on a standard diet for 8 days. In the first 4 days, 800 mg calcium/day were administered, and on the 5th to the 8th day, an additional 1,000 mg calcium in the form of cheese. The 24-h urine was collected daily. The following urine parameters were determined: density, pH-value, Na, K, Ca, Mg, NH_4, Cl, P, S, Kr, Ox, Cit, GAG and the relative supersaturation for CaOx was calculated.

Results. Provisional calculations reveal the following trends (mean values over 4 days; statistical calculations follow on completion of all measurements)

	Standard diet 800 mg Ca/d		Standard diet 1,800 mg Ca/d	
	control group	bran group	control group	bran group
Ca	4.13	3.92	5.27	4.99
Cit	2.96	3.04	2.75	3.74
K	66.75	66.30	60.85	70.20
pH	6.47	6.42	6.26	6.28
	mmol/d	mmol/d	mmol/d	mmol/d

Calcium excretion in the bran group is consistently below that of the control group. However, increased calcium intake leads to an inevitable rise in calcium excretion. An overall assessment will be provided in our presentation, once all the measurements have been completed.

48 Sequential Radionuclide Scanning After Percutaneous Kidney Stone Removal and Pyelolithotomy

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Percutaneous kidney stone removal has been performed on 125 patients between 1984 and 1986. 250 MBq 99m Tc-DTPA study on Dynacamera was done to evaluate changes in renal function. 25 patients were investigated before and on the 5th day after surgery. Only slight loss of renal function was found. Thereto in another study 25 patients had been investigated preoperatively, immediately after percutaneous nephrostomy, 1 and 5 days after litholapaxy. There was only 3–4% loss of renal function immediately after surgery and nearly normalisation on day 5 after procedure. Complete normalisation of renal function was found 6 months after surgery. These results are compared with data collected from 10 patients after pyelolithotomy.

49 Toxicological Studies of Stone-Solving Solutions

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To compare the toxic activity of clinically used litholytic solutions like N-acethylcysteine and Renacidin with some new substances of higher lytic capacity, we studied the effect of Fe(III)-citrate, Al-lactate, malonate, Fe-EDTA, Mg-EDTA, Na_2-EDTA, and CDTA to porcine ureters and to porcine kidney cells (PK 15).

Results. All solutions are bacteriostatic. Renacidin, Fe-EDTA, and CDTA have a lethal effect of 50–80% on cultured kidney cells, not causing the cell detachment. N-acethylcysteine, Mg-EDTA, and Na_2-EDTA (only at the lowest concentration of 0.001 moles/l) show no damaging to the ureter or just small changes on the cell viability and cell adhesion. This effect of mentioned solutions, except the CDTA, agrees well with the slight damaging effect on the uroepithelium of porcine ureters. Fe(III)-citrate and Al-lactate kill the cultured cells without or with a minimum cell detachment, showing a moderate damaging effect on ureters. Malonate, a very potent litholytic compound, shows a lethal effect on cultured cells as well as considerable histological alterations of the ureter.

50 Zeiss Loop Stone Extractions in Epidural Analgesia

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In our clinic continuous epidural anaesthesia has been used for facilitating spontaneous passage of impacted ureteric calculi and analgesia for Zeiss loop stone extractions. In 23 cases Zeiss catheter was maneuvered past the stone and formed into a complete loop in the renal pelvis in epidural analgesia. Giving various doses of epidural bupivacain we maintained continuous analgesia with retention of motor activity so that the patient could walk. Within 3 days the loop and the calculi measuring 5–14 mm passed spontaneously without any complication in all cases. Comparing this method with the one formerly used without analgesia, we could extract larger stones and in addition remove stones from the upper third of the ureter as well. The time of the treatment became shorter, the patients were painless and did not need any other analgetic.

51 The Responsibility of the Internist in the Fight Against Urolithiasis

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V. The Residual Fragment

52 The Endoscopically Visible Radiologically Non-Recognizable Residual Fragment

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The diagnosis "renal stone, residual fragments after ESWL or percutaneous nephrolithotomy or kidney free from calculus" is usually yielded by flat plate and by excretory urogramm.

In some cases, however, tiny stone fragments are visible during percutaneous endoscopic inspection of the renal collecting system, although the flat plate doesn't show residual stones. In experimental studies the size of kidney stones, which are radiologically recognizable, was investigated.

Flat plate of human body was simulated: A water bath was placed on an x-ray table. Small bowls, filled with calcium oxalate stones in different sizes, were installed in the water bath 15 cm over the x-ray table. X-ray pictures were performed with 65 KV.

The results suggested that calcium stones with a size – 1 mm are not visible on the flat plate.

Based on radiological and endoscopic observations radiologically stone free kidney units must be distinguished from endoscopically stone free kidney units.

In order to get free the renal collecting from tiny stones after percutaneous lithotripsy a special endoscopic stone suction apparatus was developed. With this procedure the kidney can be cleaned endoscopically from small residual stones.

53 Persistent Nephrolithiasis According to Anatomical and Metabolic Influences

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In cases of residual stones after percutaneous litholapaxy and open stone surgery the course in terms of spontaneous passage of stones and stone growth was investigated. The possible impact of metabolic disturbances on stone growth was evaluated. Moreover the influence of metaphylactic regimen on stone growth was studied.

54 The Importance of Residual Calculi on Recurrence in Patients With Infection Stones

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In patients with infection stones it is often difficult to achieve complete removal of all stones even after treatment with open surgery. Today, with modern techniques (percutaneous lithotripsy, ESWL) small residual fragments often are left behind in the kidney. The aim of this investigation was to study the recurrence in 37 stone patients with recurrent UTI treated with open surgery related to the presence of residual calculi and/or postoperative urinary tract infection (UTI).

Material. Out of 796 consecutive stone patients from our stone clinic 52 patients were found where recurrent UTI was considered to be of pathogenic importance for stone formation. Forty-nine out of those patients had been submitted to surgery and in 37 of these data were available concerning residual calculi, postoperative UTI and recurrence. The follow-up period was 4.6 years.

Results. In 12/37 patients small residual calculi were left behind postoperatively. New stones were found in 5/12 patients with residuals and in 9/25 without residuals.

We found equal frequency of new stones in patients with or without residuals. In patients without postoperative infection only 4/15 had new stones while 10/18 patients with postoperative infection had new stones.

Conclusion. The presence of postoperative UTI seems to be more important for the recurrence than for the residual calculus.

55 Residual Concrements and Urinary Tract Infections

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It is from the symptoms and history difficult to determine if a urinary tract infection involves the upper urinary tract or not. This problem can be true also for patients with urinary tract infections and residual renal concrements. It is thus important to establish that the stone is infected before stone surgery is performed if the stone does not cause other symptoms which indicate operative stone surgery. This study addresses this problem and presents the results of operative stone removal in patients where the infection was preoperatively localized to the residual concrement.

Nineteen patients, 7 men and 12 women, aged 30–77 years (mean age 56 years) were studied. All had previously been operated on for renal concrements 2–15 years earlier and had residual concrements postoperatively. Although they had been given many courses of antibiotics the infection had relapsed. Seven patients had recurrent periods of dysuria and frequency, 3 had episodes of loin pain and fever while 9 patients were asymptomatic. Mean size of the residual concrements was 8 mm (range 3–20 mm).

All patients were examined with retrograde bilateral ureteric catheterisation and culturing or ureteric urine according to Stamey in order to localize the infection. Sixteen patients were found to have a high, i.e. stone-related infection, while 3 had a low infection. In 12 of the 16 patients with high infection, stone surgery was performed, 6 percutaneously and 6 by open surgery. After operation antibiotic treatment according to culture and sensitivity tests was instituted for 4 weeks. Four patients were not operated. Two of these patients had Ureaplasma urealyticum infection in the upper urinary tract and were treated with doxycyclin for 4 weeks without surgical removal of the concrements. At follow-up (6–36 months postoperatively) 9 of the patients who were operated were rendered free from their infection. Three patients had persistent infection postoperatively and one of these had still residual concrements. The two patients with Ureaplasma urealyticum infection were cured from their infection without operation and their urine has remained sterile for 3 years and the concrements have not grown.

Conclusion. In patients with residual concrements after stone surgery it is recommended that the infection is localized to the stone before surgery is undertaken. If the infection is traced to the concrement its removal will eradicate the infection in the majority of the patients (in 9 out of 12). If an ureaplasma infection is traced to the upper urinary tract it is worth trying to treat it with doxycyclin since in 2 patients we were able to eradicate it with this treatment only.

56 Cause of the Residual Stone in Patients with Complete Staghorn Calculi Treated by Nephrotomy or Percutaneous Litholapaxy

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Residual renal stone can be observed mainly in patients treated for complicated nephrolithiasis. Complete, radiographically dense staghorn calculi were found in 27/357 patients (2× bilaterally) treated for nephrolithiasis in 1963–1975. In all 27 patients nephrotomy

was carried out (29 procedures), residual stones were left in 6 of them. Poor technical facilities being at disposal for preoperative check-up are thought to be a cause of this surgical failure.

Complete, radiographically dense staghorn calculi were also found in 32/315 patients treated by percutaneous litholapaxy in 1985–1986. Staghorn calculi were removed completely in 25 patients. During the endoscopic procedure residual stone has already been seen but found as technically not approachable and therefore left in situ in 7/32 patients. These residual stones were neither dislocated fragments nor partially disintegrated stones, they were remnants of staghorn calculi located behind the narrow infundibulum of the terminal calyx. Unfavourable configuration of the calyx with the consequent feature of the stone are thought to be a cause of residual stones in patients treated by percutaneous litholapaxy.

57 Residual Stones After Endourologic Treatment of Staghorn Stones

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Since June 1984 over 120 patients with partial or complete staghorns of the renal pelvis and the calices have been treated in the Urological Department of the Frankfurt University Medical School. By means of a percutaneous litholapaxy the central mass of the stone was reduced or completely removed. The residual mass of the stone was then disintegrated by means of shock wave lithotripsy. Three percutaneous litholapaxy sessions and up to three shock wave lithotripsy treatments were required per patient. The patients were discharged either completely stone-free or with residual stone fragments that could be passed spontaneously.

In the course of follow-up examinations we checked in particular those patients who had left the clinic with residual stones. We will also report on the rate of residual stones independently of the stone analysis and infections of the urinary tract. We intend to evaluate the value of this operational technique in the framework of the therapy of staghorn stones on the basis of the pre- and postoperative Iodine-Hippuran-Clearance.

58 Recurrence Rate of Phosphate Stones After Open Surgery and PCN

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In the period from 1975 to 1984, 777 renal stones were removed by open surgery or PCN, 173 being pure struvite and/or apatite concrements and 279 comprising mixed stones, containing infectious stone fractions.

The Rocco-classification, based on clinical data and radiographic analysis, showed in 81.7% stones or pads of large concrements in the lower calix.

Questioning of patients, of family doctors and attending urologists provided the following late postoperative data: urinary infection: (a) open surgery: 49.6%, (b) PCN: 46.9%. Stone recurrences: (a) open surgery: 24.8%, (b) PCN: 18.4%. This high recurrence rate, observed in both, the open surgery and PCN, can be significantly reduced by Renacidin irrigation.

59 Prognostic Factors for Success of ESWL-Treatment – A Critical Review

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The introduction of percutaneous stone surgery and ESWL has changed many requirements for documentation of kidney stones. To accurately assess the efficacy of ESWL – treatment-prognostic series of well documented material must be evaluated. For this purpose a modified ESWL adjusted kidney stone classification is used. This classification includes important prognostic factors such as singularity and shape of the kidney (i.e. horseshoe kidney), exact stone localisation, type of stone (i.e. pelvic stone or staghorn stone), number of stones, obstruction (i.e. ureteral pelvic junction), renal function, radiographic density of the stone, stone mass (i.e. critical stone mass).

42% of treated patients had calyceal stones, 51% pelvic stones with or without calyceal stones and 7.1% staghorn stones respectively. The size of the treated stones was smaller than 1 cm in 46%, 1–2 cm in 33%, more than 2 cm in 21%. Auxilliary procedures were necessary in 12.7% of the treated patients. The basic data of prognostic value to discuss the outcome of ESWL-treatment are presented.

60 Residual Stones After ESWL – Correlation of Incidence and Symptoms with Pretherapeutic Stone Localization and Stone Composition

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Since the introduction of extracorporeal shockwave lithotripsy at the Urological Department, University of Ulm in January 1986, more than 800 stone patients have been treated. In the period from August through October 1986, 265 treatments were performed in 233 patients. 25% of the patients suffered from ureteric calculi which are of minor interest regarding residual concretion. Patients with calyceal (57%) or pelvic (18%) stones are currently being reexamined (3–4 months after treatment), to answer the following questions:

- How is the influence of the pretherapeutic stone size and localization on the rate of residual stones?
- Which are the symptoms of residual fragments with regard to the stone composition?
- Is there an indication to treat asymptomatic patients with calyceal calculi?

61 Prognosis of Residual Concretions Following ESWL

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To evaluate the importance of residual stone particles in the urinary tract after the treatment with ESWL we initiated a retrospective study. Up to now 810 patients could be analyzed who were treated with ESWL between May 1982 and May 1984, yet at a wide range of indications for ESWL.

At dismissal from hospital (mean 7.6 days after ESWL) 45% of the patients, 6 months after ESWL about 84% were free of stones. Calyceal stones in 77%, pelvic stones in 85% and ureteral stones in 94% passed spontaneously within 6 months after ESWL. Performing repeated treatments with ESWL in 14% of all patients only 1% of the series had residual concretions too big for spontaneous discharge. Despite using higher number and energy of shock waves increasing stone size resulted in a higher rate of insufficient stone disintegration. The success rate after 6 months therefore diminished from 89% (stones smaller than 1 cm) to about 79% (stones bigger than 2 cm). The remaining residual stone particles accumulated preferably (60% after 6 months) in the lower calyces. Available further results of the study, especially follow-up over a period of several years will be presented. The knowledge about the dynamics of stone discharge after ESWL permits prognostic recommendations in regard to the residual stone particles and enables the establishment of a schedule for further control and treatment.

62 Residual Stones After ESWL: A Long-Term Follow-up in 1,000 Patients

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From July 1984 until September 1986 more than 3,000 extracorporeal shock wave lithotripsy (ESWL)-treatments were performed at our department. We re-evaluated 1,000 patients with a follow-up of more than one year (mean follow-up 19.1 months).

Stone-treatments comprised primary renal and ureteral calculi; occasionally adjuvant procedures like retrograde stone manipulation, percutaneous nephrolithotomy or open surgery preceded ESWL (68.5% caliceal, 44.4% renal pelvis and 19% ureteral stones: 6.6% branched calculi). In 38.5%, more than 1 stone was treated.

On discharge, 35.2% were stone-free, whereas in 42.4% stone particles less than 3 mm in diameter were found. During the follow-up period of more than 1 year, 80% of the patients were free of symptoms, 46% reported discharge of further stone particles. After more than 1 year of follow-up, 72.3% were stone-free. Recurrent stones were found in 35 patients and half of them proved to be disintegrated (< 3 mm in diameter).

Post-discharge ancillary procedures (transurethral, endourological manipulations) became necessary in 57 patients. 6% proved to have significant bacteriuria. Follow-up IVPs were graded normal in 94%.

Despite adequate disintegration at the time of discharge, every fourth patient revealed residual stones, that represent a nidus for recurrent stone-growth. Stone metaphylaxis as well as adjunctive post-ESWL procedures will have to be implemented to increase the overall long-term success rate defined as stone-free.

63 Painless Piezo-ESWL: The Solution of the Residual Stone Problem

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Previous therapeutic modalities of renal calculi, including less invasive techniques such as ESWL and percutaneous nephrolithotripsy, required analgesia, at least by local anesthesia and sedation. This forced the urologist to attempt complete stone removal in one session to reduce morbidity. Residual stones too large to be passed required another intervention and added morbidity, or, when left behind, had the potential of needing this at a later time. The advent of Piezo-ESWL, which is absolutely pain-free, abolished the problem. in 146 patients with renal calculi treated with the Wolf Piezolith 2200 since September 1, 1986 only 2 patients required intravenous analgetics; in all others no analgetics, sedation or anesthesia was needed. The stone could not be focussed in 2 patients; in all others complete fragmentation was achieved. Complications were not observed, apart from a 9% rate of renal colics from passing debris. As staging lithotripsy does not add to the morbidity of the procedure, we now find it more advantageous to reduce larger stones in steps, always just producing so much debris as is passed without problems. Clusters of fragments that at follow-up are found not to disperse rapidly are simply treated with another series of shots. Residual stones after other treatment modalities are treated as they are diagnosed, and the sampe approach has also been adopted for newly diagnosed calyceal stones. The minimum morbidity of the procedure and the extremely low cost justify treatment of any stone large enough to be identified by ultrasound, and should eliminate all problems with residual stones in the future.

64 Secondary ESWL-Treatment

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Between January 1984 and April 1986 2,000 patients were treated by ESWL. Within that time period a secondary ESWL became necessary in 5% because of residual stones in 93 and recurrencies in 7 cases. Most of these 100 stones were primarily well suitable for ESWL with 74% of them having a diameter below 14 mm. An outflow obstruction at the calyceal necks or the ureteropelvic junction was suspected in only 29%.

Stone localization at the first/second ESWL was: upper calyces: 12%/8%, mid calyces: 6%/10%, lower calyces: 29%/46%, pelvis: 33%/14%, ureter: 19%/22%.

The result of the first/second ESWL was considered a success in 44%/90%, but only 2/21 patients were discharged without residuals.

The energy product of the first/second ESWL was 30,000 (kVx shots)/26,000 (kVx shots).

A careful selection of the patients for ESWL leads to a low frequency of secondary ESWL treatments, which can be accomplished with a high success rate. The most frequent localization of stones requiring a secondary ESWL is the lower calyceal group.

65 Prevention and Therapy of "Steinstrasse"

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ESWL transforms a pelvic stone in many small pelvic and later on ureteral stones. For prevention of residual stones on the one hand a sufficient passage especially in case of extensive stone mass on the other hand a prompt passage of the stone debris for prophylaxis of urinary stasis and infection is of great importance. The necessary conservative and endourological measures before and after ESWL treatment will be discussed, whereas the prophylactic use of endoprosthesis shall be deemed as of increasing importance.

The partly combined therapy of the "Steinstrasse" with ESWL and endourological treatment made operations rarely necessary even in case of complication. By means of 80 cases out of 800 ESWL treatments this problem will be discussed.

66 Treatment of Residual Fragments of Cystine by Chemolitholysis with Tromethamin-E

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67 Painless ESWL with the Dornier-Lithotrypter HMIII – Experience with 300 Patients

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68 ESWL Treatment of Infected Complete Staghorn Calculi-Effect of Remaining Disintegrates on Stone Recurrence and Infect

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Patients and Methods. A total of 21 complete staghorn calculi in 19 patients were treated; UTI was evident in all of them (18/19 *Proteus mir.*, 1/19 *Pseudomonas aerug.*). The treatment, whether ESWL-monotherapy or combined therapy (operation/ESWL), depended on stone mass and anatomy of renal pelvis and calyces.

(7× ESWL-mono, 13× combined OP/ESWL, 1× only OP). No septic complications were observed after adequate antibiotic pretreatment (Pipril 2 × 4 g/d, resp. Claforan 2 × 2 g/d). Auxiliary measures in ESWL-monoth.: urethral catheter/ Zeiss loop 2×, URS 2×) and in combined OP/ESWL: operative nephrostomy in all cases, renacidin irrigation 4×. The spontaneous passage of disintegrates without

major pain in the post ESWL period was provided by an approved drug regimen (Baralgin, Voltaren, Urol). Stone analysis (r-diffr.) showed struvite-apatite in 19/21 and apatite-whitlockite-whewellite in 2/21 stones.

Results (follow up: x = 9.5 months (4–16)). Completely stone free: 7/21 kidneys, remaining disintegrates (spontaneous passable): 13/21; remaining stone 1/21 infect free (without antibiotics for 3 weeks): 16/19 patients; persistent UTI: remaining stone 1x, remaining desintegrates 2x (1 *Proteus mir.*, 1 *Pseudomonas aerug.*).

Up to now no evidence (plain x-ray) for stone growth or stone recurrence.

Conclusions. 1) In infected complete staghorn calculi ESWL (mono resp. combined therapy) results in a high rate of stone free kidneys. 2) In more than 2/3 definite curing of UTI is possible even in presence of spontaneous passable desintegrates. 3) Stone recurrence rate after ESWL seems to be markedly reduced compared to surgical procedures alone.

69 Residual Stones After Percutaneus Litholapaxy

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Between 1986 and 1987 in our Urological Department we performed 74 percutaneous stone removals from the kidney with Storz instrument. The intervention was done in one session. After the stone removal or disintegration we have registered residual stones in 11 cases. Different routes proved to be useful to remove the stones. Three of them were noticed outside the kidney, two were removed at the time of intervention under fluoroscopy, the third, a single stone, has been still located beside the kidney without any tissue reaction for more than one year. We try to solve the residual struvite stones in two solitary kidneys. In one case the ureteral stone passed spontaneously.

In four cases we had to remove rest stones with surgical intervention. Once we have successfully extracted a small residual stone after open surgery with the help of percutaneous lithotriptor. We make strict efforts not to leave rest stones during the operation. Extrarenal rest stones are not removed but residual stones in the renal cavity – in case of complications – are candidates for reoperations.

70 Remaining Concrements after ESWL

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In our clinic kidney stone operations are only performed when ESWL is not indicated. Since many kidney stone patients are referred directly by their home urologists to ESWL-centers we observe a decreasing number of such patients at our clinic.

The few patients referred to us having ESWL-indicated kidney stones during the last year are presented here. Ureteric stone patients who are the largest proportion of our patients are not evaluated here.

We consider 33 pelvic or calyceal stones which were subjected to ESWL at four different centers. In ten cases remaining concrements were observed, two of which had a subsequent indication for nephrectomy. We regard this a disappointing result despite of the low number of cases.

By means of slides some cases are presented and the state after partial removal via a percutaneous or retrograding flushing is demonstrated.