Urol Res (1990) 18:61–86

Urological Research

Abstracts

Second European Symposium on Stone Disease, March 22–24, 1990, Basel, Switzerland

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Physicochemical pathophysiology

1

Investigations into the crystallization tendency of calcium oxalate in urines

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This new method is based on the addition of a well defined amount of ammonium oxalate (31.1 umol) to a fresh native urine sample (30 ml). The resulting clouding is photometrically measured after 20 minutes (E_{20}). It is sufficient to classify the urines as "slithtly", "moderately" and "readily crystallizing". Consideration of correlations and discriminant analytical computation with constant oxalate concentration show that calcium concentration is the decisive parameter in calcium oxalate crystallization. The so-called limit of oxalate tolerance as an indirect standard of crystallization tendency is not superior to the diagnostic value of the measuring value E_{20}. Discrimination results of 75 % correct classification are evidence of high specificity of the crystallization model. Tendencies of increased crystallization in urines from idiopathic stone formers can be demonstrated with standardized diet (drinking volumes!). The inexpensive procedure guarantees an acceptable accuracy of the analytical values (S % 4). It is helpful in finding risk constellations in urines and is recommended as an aid for decisions in metaphylaxis, particularly for borderline cases of calcium and oxalate findings.

2

EFFECTS OF TAMM-HORSFALL PROTEIN ON THE GROWTH AND ADHESION OF CALCIUM OXALATE CRYSTALS

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The effect of Tamm-Horsfall Mucoprotein (Uromodulin; THMP) on the crystal formation of calcium oxalate (CaOx) was investigated in different crystal growth systems.
Using the Gel Crystallization Method (GCM; Achilles et al.) no influence of THMP on the crystal growth rate of CaOx could be detected (17-170mg protein/l of artificial urine; ionic strength 50-400 mmol/l).
A special dynamic system was developed to study the influence of effectors on the formation of crystal phases, which simulates the process of stone formation as well as possible.
In this system, supersatured artificial urine without and with THMP (17 mg/l) was conducted through channels which contained a gel (1 wt% agar-agar) as a matrix for CaOx crystal growth.
The channels were cut in microtiter plates.
The artificial urine was formed by mixing of two different solutions just before entering the test plate.
Solution flow (1ml/min.) was maintained by using a multichannel peristaltic pump.
The duration of one experiment was 4 hours.
After that time, the crystal image of CaOx formed within the gel or on its surface was observed by light microscopy.
In the dynamic system under regard, THMP caused a considerable agglomeration and adhesion of crystals on the gel surface.
The results support findings of ROSE et al., who consider THMP as a potential promoter of CaOx formation in human urine.

3

The influence of three exogenous glucosamine glycans on the experimental induction of microliths in rats.

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The efficiency of three exogenous glucosamine glycans (Gags) isolated recently from seaweed are compared in their effect on the experimental induction of renal microliths. In control experiments such microliths could be induced in rats by an ethylene glycol/NH_4Cl regime in the drinking water for several days.
Two days prior to the onset of the stone inducing regime, to each group of animals, one of the exogenous Gags (G871, G872 and SPP) was given in the drinking water, leading to a consumption of about 10 mg/day, maintained over the remaining induction period. After elapse of the stone-induction period both kidneys were flushed by a retrograde arterial perfusion with a phosphate-buffered saline solution (PBS). Subsequently one of the kidneys was fixed by glutaraldehyde perfusion leaving the other unfixed. After dissolution of the tissue from the unfixed kidney, the crystalline fraction was collected and measured in a Coulter counter. From the aldehyde-fixed kidney slices were inspected in the light microscope in polarized light. The number of particles per square area was counted by transferring the birefringent image to an (IBAS-2000, Zeiss-Kontron Oberkochen, FRG) image analyzer. The mean number of particles per area was compared with the number of particles per volume for each experimental group of animals. The beneficial influence of the Gags on the experimental stone induction was objectively established.

4

An ultrastructural study of experimentally induced rat microliths, investigated by electron probe microanalysis.

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In a group of male rats renal microliths were induced by a dietary regime of ethylene glycol (0.8 %^{v}/v) and NH_4Cl (1% ^{w}/v) in the drinking water for 4, 8 and 24 days respectively. Microliths were isolated from the glutaraldehyde perfusion-fixed kidney slices by solving the tissue components in NaClO. $5H_2O$. The remaining mineral fraction was collected on a Millipore filter. Crystals were present in the tissue of all three groups of animals. Samples of this crystalline fraction were studied in the scanning electron microscope (SEM) and analyzed by X-ray microanalysis (XRMA).
Morphologically predominantly oxalate monohydrate and some dihydrate crystals were present in the crystalline fractions from all experimental groups. Calcium was the main detected component in all crystals, but in some instances additional chemical elements were detected like, iron and zinc.
Ultrastructural analysis of osmium tetroxide + potassium ferrocyanide postfixed tissues, revealed in all experimental groups the presence of intra-luminal crystals surrounded by organic material from cellular origin. At the baso-lateral sides of some proximal tubular cells pathological ultrastructural changes were noticed, some of which could be related to the calcium metabolism as revealed by the precipitates created by a potassium pyroantimonate treatment prior to postfixation.

5

KINETIC MICRODETERMINATION OF CRYSTAL GROWTH RATES OF CALCIUM PHOSPHATES IN GEL MATRICES

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The automated Gel Crystallization Method (GCM; Achilles et al.) was applied to the determination of relative crystal growth rates (Vcr) of octacalcium phosphate (OCP) in gel (0.5 wt% agar-agar) using 96-well microplates.
In order to optimize the measuring procedure, experimental conditions were varied using wide ranges of ionic strength (0-400 mM NaCl), pH-buffer (0-100 mM), concentration of seed crystals and total calcium (1-20 mM).
OCP grown in the gel was identified by FTIR spectroscopy, x-ray diffractometry and chemical analysis from independent experiments.
Because of the change of pH during crystal growth buffering of pH was absolutely necessary. The unprecision of measuring values (slope of kinetic curves) was in the range of 1-5% (RSD). Using volumes of the gel phase and measuring solutions of 100 and 200 µl, respectively, 120 kinetic determinations could be carried out per hour.
The following substances were tested with respect to their effects on the crystal growth parameter of OCP (Vcr) under defined experimental conditions: citrate, magnesium, pyrophosphate, polyphosphates, chondroitin sulfate. They could be shown to be effective inhibitors within the system under regard.
Conclusion: The GCM, which has been applied up to now predominantly to the study of calcium oxalate, may be succesfully adapted to the efficient determination of relative crystal growth rates of the biologically important calcium phosphates.

6

The effect of three semi-synthtic glycosaminoglycans on the zeta potendial on the surface of Calcium oxalate (CaOx) crystals

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Application of exogenous GAGs to prevent stone growth or recurrence has been actively studied. Three exogenous GAGs, G871, G872, and G873, extracted from marine algae and prepared through physicochemical modification, have been developed by us. The GAGs have a heparin-like molecular structure (mol.Wt. 5000). The poupose of this study is to examine the effect of three new GAGs on the zeta potencial (ZP) on the surface of CaOx crystals, and to affirm the machanisms of their action. According to Scurr and Robertson (1986) the ZP on the surface of CaOx seed crystals are measured with the MDP-II zeta meter. The results are summarized in tablel:

Table 1. The influence of three GAGs on the Zeta potential on surface of calcium oxalate cryatal (-mv)

Drug group	Concentration mg/L						
	0.0	1.0	10.0	25.0	50.0	75.0	100.0
G-871	24.3	35.8	41.1	46.5	55.0	60.2	60.4
G-872	16.5	18.3	23.5	27.2	29.0	31.1	38.4
G-873	24.3	40.1	47.8	52.3	57.0	57.7	59.5
G-873+Cit	24.3	33.6	49.1	56.9	60.3	57.4	61.8

Table 1 shows the effect of increasing concentrations of the three GAGs (within range:0-100mg./l.) on the ZP on the surface of CaOx crystals in 10% artificial urine. The three GAGs caused the ZP to become more negative. This suggests that the GAGs can be absorbed to the surface of CaOx crystals, it therefore leads to a reduction in the tendency of CaOx crystals to agglomerate in vitro.

7

INFLUENCE OF INDOMETHACIN ON THE ADHERENCE OF UREASE-INDUCED CRYSTALS TO RAT BLADDER EPITHELIUM

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Urine supersaturation with respect to struvite and calcium phosphate is necessary for the formation of infection stones. Another prerequisite is the retention of formed crystals in the urinary tract. An intact mucous coat lining the uroepithelium prevents formed crystals from adhering to the epithelial cells. It is well known that prostaglandin synthetase inhibitors decrease the production of mucins in the stomach. This study was performed to evaluate if the anti-adhesive properties of the urinary tract mucous coat is influenced by prostaglandin synthetase inhibitors.
Material and methods: A potent prostaglandin synthetase inhibitor (indomethacin) was given to female Wistar rats. Fifty animals received intraperitoneal injections of indomethacin twice daily for three days. Doses between 0.8 and 8 mg/kg b.w./24 hrs were given. Twenty rats were given indomethacin orally, 1 mg/kg b.w./24 hrs, dissolved in the drinking water. Ten of these rats received the drug for three days and the other ten received the drug for 6 weeks. The crystal adherence was then studied by incubating the rat bladders with a slurry of urease-induced crystals.
Results: The adherence was significantly higher ($p < 0.05$) in animals given indomethacin intraperitoneally compared to control animals. The increase varied from 54 to 187%. The group that received oral indomethacin for three days had a mean increase in crystal adhesion of 43% (n.s.). The group that received the drug for 6 weeks showed an increase of 114% ($p < 0.05$).
Conclusion: An increased crystal adherence was found in the bladder of rats pretreated with indomethacin. This may be due to a reduced mucin production. An increased crystal adherence may thus enhance the risk for stone formation.

8

Measurement of calcium oxalate monohydrate solubility, crystal growth and crystal agglomeration in undiluted urines.

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We have shown previously, that urines form healthy subjects are capable to increase the solubility and inhibit the growth and the agglomeration of calcium oxalate monohydrate crystals. Urines from calcium oxalate urinary stone formers, in contrast, have a defective or even absent ability for inhibition of crystal agglomeration. The degree of this defect is related to the severity of the stone disease, expressed as stone formation rate. These data were obtained from growth kinetics measured with a seeded crystal growth system. For an exact interpretation of these kinetic data the solubility of calcium oxalate in the sample used must be known exactly. Measurement of the solubility in our system requires the construction of a concentration range around the solubility product. Up to now we therefore used urines diluted 1:5. We have now tried to obtain undersaturated urines without a dilution step, by dialyzing them against a calcium chelator. This effectively removes bivalent cations, mainly calcium and magnesium. The magnesium content is then restored to pre-treatment values. Levels of other cations, like Fe++, are not corrected, since they are present in minor quantities only and thus do not significantly affect the solubility of calcium oxalate (the urines used for the kinetic experiments are not treated). The validity of the procedure is confirmed by comparing treated and untreated 1:5 urine dilutions. The mean values of the solubility are 0.253 ± 0.013 mM and 0.254 ± 0.013 mM respectively, r=0.999 n=14. This new procedure opens the way for testing undiluted urines in our system.

9

Urinary crystal surface binding substances on calcium oxalate crystals.

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In order to study the effect and characteristics of urinary crystal surface binding substances (CSBS), we extracted the naturally existing CSBS from large volume of healthy urine. CSBS was obtained by conducting massive homogeneous crystallization of calcium oxalate in a whole urine, separating and washing crystals formed, dissolving it in EDTA 4Na solution, and ultrafiltrating with cut-off molecules of 6,000. In our whole urine assay system, CSBS was not proved to be promoters but was proved to be strong inhibitors of calcium oxalate crystal growth and aggregation. In other words, CSBS was not a cement substance of stone formation but was inhibitors of its process. As for the characteristics of CSBS, we found 9 peaks of peptide by gel filtration study and 11 peaks by reverse-phased liquid chromatography. The molecular weight ranged from 5,800 to more than 300,000 dalton. Every peaks obtained from reverse-phased liquid chromatography contained both peptide and saccharide although the amount of them varied widely. Furtheremore, it was proved that CSBS themselves contained acid glycosaminoglycans which did not correspond to commercially available AGAGs completely.
These results suggest us that CSBS are a mixture of various kind of glycoproteins and/or proteoglycans and act as strong inhibitors of calcium oxalate crystallization.

10

THE IN-VIVO EFFECT OF FARNOLITH(R) ON THE CRYSTAL GROWTH RATE OF CALCIUM OXALATE AND OTHER PARAMETERS IN HUMAN URINE

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In a pilot study with 7 male healthy volunteers, the dietary fibre preparation FARNOLITH(R) was tested with respect to its effect on a series of parameters which characterize the risk of stone formation in human urine.
Urine samples were investigated in periods without and with application of 2x15 g of the preparation per day.
In both periods, the volunteers kept to the same diet and fluid intake.
As the most essential parameter, the relative crystal growth rate (Vcr) of calcium oxalate (CaOx) was determined in 3-h-fractional and 24-h urines of both periods using the Gel Crystallization Method (GCM; Achilles et al.).
No significant decrease of Vcr could be demonstrated during administration of FARNOLITH(R).
This lack of a benificial action could be interpreted by counteracting effects of Vcr-decreasing (i.e., decline of calcium excretion) and increasing factors (i.e.,decrease of citrate and phosphate).
Significant differences ($p<0.05$) of parameters in 24-h urine collections before and during therapy, respectively, were only found for pH (5.70/6.00) and total phosphate concentration (38.7/28.0 mmol/l).
The useful application of FARNOLITH(R) as a prophylactic measure in CaOx urolithiasis seems to be limited to stone formers with absorptive hypercalciuria as could be demonstrated by others.

11

LOCALIZATION OF NEPHROCALCIN, A MAJOR CRYSTAL GROWTH INHIBITOR, IN HUMAN KIDNEYS.

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Nephrocalcin (NC) is a urinary glycoprotein with a molecular weight of 14 k which inhibits the growth and aggregation of calcium oxalate monohydrate crystals in the kidney and the urinary tract of mammals. We investigated the localization of NC in the nephron and used a highly specific polyclonal antibody to perform immunohistochemistry examined by light microscopy and transmission electronmicroscopy.
The cytoplasm of proximal tubules and thick ascending limb of Henle's loop stained equally. EM-micrographs demonstrated a predominantly apical immunoreaction and showed staining in the golgi apparatus. The brush border and the lumen also stained whereas the glomeruli and the cytoplasm of the collecting duct cells failed to stain.
We conclude that cells of the proximal tubule and thick ascending limb contain immunoreactive material. They may produce NC and secrete this crystal growth inhibitor into at least two separate nephron segments as a protection against crystal formation.

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PURIFICATION OF NEPHROCALCIN BY IMMUNO-AFFINITY CHROMATOGRAPHY FROM HUMAN URINE.

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Nephrocalcin (NC) is a protein containing 10-15 % carbohydrate which is excreted by mammals in the urine. It shows extremely high inhibitory activity to crystal formation. An anti-NC-antibody must be able to recognize urine inhibitors and should remove inhibitory activity from the urine.
We have raised NC antiserum in rabbits. This polyclonal antibody did not crossreact with major urinary proteins including Tamm Horsfall protein, albumin, beta 2-microglobulin, chondroitinsulfate, hyaluronic acid and alpha 1-antitrypsin but recognizes NC at > 1:15.000 by ELISA. An affinity column was prepared by immobilizing purified anti-NC-IgG to CNBr-activated Sepharose.
Dialyzed urine passed through this column had about 90 percent of its immunoreactivity and crystal growth inhibitory activity removed. The column eluate had a dissociation constant of 10^{-8} M in a spectrophotometric crystal growth assay. Western analysis of this eluate showed 3 main bands that correspond to the aggregated forms of NC.
The production of a NC antibody and the isolation of this major crystal growth inhibitor will be valuable for further studies on the pathogenesis of stone disease in the kidney.

13

Heavy metals in urinary calculi.

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The formation of urinary calculi grows by complex patholocical processes and may lead to a multitude of different chemical products. In these processes also the heavy metals are incorporated into the calculi. Specially the role of the trace elements (Cd, Pb, Cr, Ni, Cu, Zn, Hg, etc.) and their important significance in pathogenesis and therapy are not clarified.

In a DFG-research project, above all, environmental trace elements of 200 calculi (since 1987) will be quantitative recorded and evaluated in connection with the case histories of patients referring to the inorganic and organic phases.

In this study the analytical results will be presented and the statistical evaluation, compared to the case histories of the patients, will be discussed.

14

DISTRIBUTION OF TRACE ELEMENTS IN WHEWELLIT KIDNEY STONES AND CRYSTAL MORPHOLOGY.

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Three different layers in the ultrastructure of Whewellit kidney stones were described by Iwata (1985*). Assuming a possible interrelationship between crystal growth and trace elements, we expected a homogenous distribution of elements, as we presumed the various layers of Whewellit kidney stones to be of the same age, according to Iwata's model. We examined the Whewellit stones' ultrastructure by means of a Scanning Electron Microscope. The measurements of element distribution was determined by Energy Dispersive Xray analysis (EDX), and varied ultrastructures which had developed contemporarily were observed in the layers. Although we found concentration levels of most trace elements to be below EDX detection limits, it was possible to detect differing levels of elements within the same layers. In random samples, variations in crystal morphology as well as an inhomogenous distribution of trace elements were observed.

* H. Iwata: J. Urol., 133: 334, 1985.

15

Calcium oxalate crystallization properties in urine samples from patients with calcium oxalate stone disease.

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The formation of calcium oxalate (CaOx) crystals occurs in urine that is supersaturated with respect to CaOx. A deficient inhibitory activity of crystal growth and/or aggregation is considered important for the subsequent development of large crystals, crystal aggregates and stones.

Direct measurements of the risk of CaOx crystallization in only slightly diluted urine showed higher values in stone forming (SFM) than in normal men (NM). On the other hand different methods to determine the macromolecular inhibitory properties of bladder urine disclosed only minor differences between SFM and NM.

These results indicate that, from a clinical point of view, great emphasis still has to be put on determination of the supersaturation level. A modification of the simplified ion-activity product index [AP(CaOx)index] is presented, adjusted to the results obtained by the EQUIL 2 program. By overhauling previous experimental data a risk level for CaOx crystallization was established.

16

Change of promotive effect of urine from patients with primary hyperparathyroidism on calcium oxalate crystal aggregation after parathyroid surgery

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We have recognized primary hyperparathyroidism as an model of in vivo stone formation and have investigated and reported about the promotive effect of urine from patients of primary hyperparathyroidism on calcium oxalate crystal aggregation in whole urine crystallization system. Herein, we investigated about the change of promotive effect in post-parathyroidectomy patients.

Morning-urine samples were collected from 20 post-parathyroidectomy patients, whose were all stone type. 10 ml of each urine sample, which was filtered through 0.22 micrometer millipore filter priorly, was added to 90 ml of previously treated pooled urine collected from healthy adult males. The mixture was adjusted to pH 5.40 by adding 1N HCl and filtered through 0.22 micrometer millipore filter again. 5ml of 5mM sodium oxalate and 0.5ml of 1M calcium chloride were added to the mixture for introducing spontaneous crystallization. After incubation at 37°C for 3 hours, the particle size distribution was assayed by Coulter Counter Multisizer.

In all 20 urine samples, we could not recognize the promotive effect on calcium oxalate crystal aggregation in contrast to the promotive effect of pre-parathyroidectomy urine previously reported. This result suggested that removal of parathyroid adenoma corrected the ability to form crystal aggregation and recurrent urolithiasis in patients of primary hyperparathyroidism.

Reference

1. T. Koide et al., J. Urol. 140:1571, 1988

Metabolism

17

Peroxyoxalate-Chemiluminescence - a new efficient method for the determination of oxalate in urine in comparison to an enzymatical and a RP-HPLC-method

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A new sensitive method for the determination of oxalate in urine is presented. By using the chemiluminescence decay of monoperoxyoxalate acid very low concentration of oxalate can be determined. Optimized reaction conditions and präanalytical factors also permit oxalate determinations in native urine without calcium oxalate precipitation (measure time: 0,3-0,4 s per sample).
We've investigated 30 patients suffering from oxalate stone diathesis with a high recurrence rate and a control group of 30 healty persons.
The plausibility and reproducibility of this new chemiluminescent method will be discussed in comparison to an enzymatical method and a modification of a RP-HPLC-method described by HUGHES et.al. (Anal. Biochem. 119 (1982) 1-3).

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BACTERIOLOGIC AND METABOLIC FINDINGS IN PATIENTS WITH INFECTED URINARY STONES

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Urinary tract infection (UTI) with urea splitting bacteria is regarded the major cause of so-called infected urinary stones. Hyperammonuria due to urea splitting results in a supersaturation of magnesium ammonium phosphate resulting in struvite crystallization. As infected urinary stones usually do not consist only of struvite but also of apatite the role of metabolic disorders as hypercalciuria has to be discussed as well.
To further define the role of bacteriologic and metabolic disorders the following findings of n = 43 consecutive patients with infected urinary stones (stones consisting of 50% % struvite/apatite) were analyzed: Urine culture including sensitive test for urea splitting (UREA-test), urinary pH profiles, serum parameters and urinary excretion of stone relevant parameters. These findings were compared with other stones (oxalate, uric acid etc.).
As has been expected the incidence of UTI positively correlated with the percentage of struvite/apatite defined by stone analysis. Urea splitting bacteria have been found almost only in infected stone patients. On the other hand metabolic evaluation showed significantly higher calcium excretion in infected stone patients compared to oxalate or uric acid stone formers. The calcium excretion positively correlated with the percentage of struvite/apatite.
Our findings demonstrate that metabolic disorders as hypercalciuria are not uncommon in infected urolithiasis. Thus metabolic examinations should be done also in these patients being more important for correct metaphylaxis.

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Primary Hyperparathyroidism: Frequency in 4000 Renal Stone Formers.

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The reported incidence of primary hyperparathyroidism (pHPT) in urolithiasis patients varies from 0,2% to 7%. The purpose of this paper is to determine the frequency of pHPT in 3680 (final paper: about 4000) renal stone formers treated by ESWL between 1983 and 1989.

In all patients treated by ESWL serum calcium, phosphorus and parathormone were determined three times and stone analysis was made when the amount of collected stone particles was not too small. The constellation of serum parameters was typical of pHPT in 53/3680 (1,4%), 43% men and 57% women. 53% of patients with pHPT were recurrent stone formers. 72% were more than 50 years of age and only 4% under 30 years. Neck surgery was performed in 15 patients (0,4%) and 12 of this group (80%) showed recurrent stone disease or multiple stones.

The conclusion is that today the incidence of pHPT is far lower than usually described in the literature. High percentages propably result from selection of patients with suspected pHPT referred to specialised centers . Investigation for pHPT should be done in all patients with recurrent or multiple calculi. Patients will benefit from surgery by an experienced parathyroid surgeon: surgery of parathyroid adenoma will prevent occurence of calculi and other complications, i.e. hypercalcemic crisis. Patients whith pHPT accompanied by only few signs however may not accept neck surgery as an adequate form of treatment. A follow up is mandatory in these patients.

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Bone mineral density of lumbar spine, femoral neck and distal tibia in patients with calcium nephrolithiasis.

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Bone mineral density (BMD) was measured with X-ray densitometry (Hologic QDR 1000) in 94 patients with recurrent stone disease (51 men, 43 women) in a cross-sectional study. Lumbar spine (mostly spongious bone) femoral neck (mostly cortical bone) BMD results, expressed as Z-score (SD from mean BMD of 171 age and sex-matched controls from Berne) are displayed in table (x±sem). Patients were analyzed in 2 groups, ≤45 and >45 years-old, respectively. Statistics were performed with one way ANOVA (p values vs. healthy controls).

	Lumbar spine	p	Femoral neck	p
Men ≤45 y.o. (n=26)	-0.54±0.19 SD	0.03	-0.01±0.31 SD	ns
Men> 45 y.o. (n=25)	0.02±0.13 SD*	ns	-0.2±0.18 SD	ns
Women ≤45 y.o. (n=18)	-0.57±0.19 SD	0.02	-0.23±0.25 SD	ns
Women >45 y.o. (n=25)	+0.3±0.24 SD**	ns	+0.02±0.35 SD	ns

*p=0.03 vs men≤45 y.o. **p=0.01 vs women ≤45 y.o.

In addition, 13 patients' distal tibia was scanned using a soft tissue compensator device (Casez 1989, VIIth International Workshop on Bone Densitometry). Tibial shaft (cortical), tibial metaphysis (spongious) and tibial epiphysis (spongious) were examined separately.

	tibial shaft	tibial metaphysis	tibial epiphysis
Men (n=7)	-0.23±0.3 SD	-1.37±0.8 SD	-0.42±0.8 SD
Women (n=6)	-0.36±0.4 SD	-0.84±0.4 SD	-0.57±0.4 SD
All patients (n=13)	-0.29±0.3 SD	-1.1±0.48 SD*	-0.5±0.5 SD

*p=0.04 vs control

Comments: In both sexes, stone formers under 45 y.o. have a lower vertebral BMD than controls. Explanation for BMD increase after 45 may be spine osteoarthritis due to excess weight, especially in women who were found to be 5.5kgs heavier than controls (p=0.04). Femoral neck density does not appear to be significantly lower in nephrolithiasis. Preliminary data on 13 patients show a lower BMD Z-score at tibial metaphysis than at lumbar spine (p=0.005) and femoral neck (p=0.05). This suggests higher sensitivity of this artefact-free area for detection of early bone loss, as we recently showed in dialysis and kidney transplanted patients. It remains to be seen whether subgroups of renal stone formers are particularly prone to osteopenia.

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Plasma pyridoxal phosphate levels in normal subjects and in patients with mild metabolic hyperoxaluria and type 1 primary hyperoxaluria.

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Since some patients with type 1 primary hyperoxaluria (PH) and mild metabolic hyperoxaluria (MMH) respond to pyridoxine with a fall in urinary oxalate, whereas others do not, it was thought desirable to study vitamin B6 metabolism in these patients. Plasma B6 metabolites were measured by HPLC in normal subjects, in 8 patients with MMH and 7 patients with PH, all of whom were on various doses of pyridoxine.

In normal subjects the plasma pyridoxal phosphate (PLP) level was independent of dose between 10 and 800 mg per day of pyridoxine. The mean PLP for normal subjects taking these doses was 626 nmol/L (SD 184) and this was significantly higher than the mean level of 396 nmol/L (SD 142) in MMH who had responded well to pyridoxine, while MMH who showed only partial response to pyridoxine showed even lower mean levels of PLP of 282 nmol/L (SD 129). These differences were statistically highly significant. In PH the mean plasma PLP level was 514 nmol/L but this was statistically not different from normal.

These results seem to show first that there is a resistance in conversion of pyridoxine to PLP in MMH, and second that MMH is metabolically distinct from PH.

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THE FREQUENCY OF MEDULLARY SPONGE KIDNEYS AND THEIR ROLE IN RENAL STONE DISEASE.

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To evaluate the role of medullary sponge kidneys (MSK) in nephrolithiasis, the frequency of MSK was measured in two populations of patients, by using, in both groups, identical diagnostic criteria at intravenous pyelography. 280 consecutive renal stone-formers were studied and results compared with those obtained in 280 patients who had never formed a stone.

The frequency of MSK was 12,5 % in renal stone-formers, versus 1 % in the control population (Chi-square = 27,1; $p < 0,001$). In addition, whereas in renal stone-formers without MSK, metabolic disorders potentially accounting for the lithiasis were noted in 93 % of the cases, in stone-formers with MSK such metabolic disorders were present in only 60 %; moreover, in one third of the latter patients, the only detectable metabolic abnormalities were disorders classically regarded as possible consequences of MSK : renal hypercalciuria (6 patients), distal renal tubular acidosis (1 patient).

In conclusion, the frequency of MSK is higher in a population of stone-formers than in a control population. MSK appears as a potential cause of nephrolithiasis, via simple urine stagnation in dilated collecting tubules, via renal hypercalciuria or via distal renal tubular acidosis.

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URINARY CITRATE EXCRETION IN RECURRENT CALCIUM STONE FORMERS, PATIENTS WITH A SINGLE STONE EPISODE AND NORMAL CONTROLS

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Hypocitraturia is considered as risk factor for urolithiasis. Low urinary citrate excretion might result in the precipitation of calcium oxalate and -phosphate and the formation of renal calculi. However, for urinary citric acid excretion in stone formers and normal subjects different concentrations within a wide range are reported in the literature.

In our study 24 hour urinary citrate levels of 100 normal males and females were examined and compared with those of 150 male and female calcium stone formers. Stone formers were devided into 2 groups: recurrent stone formers and patients with a single stone episode. Recurrent stone formers presented significant lower urinary citrate levels whereas in patients with a single stone episode no statistical significance to the control group could be found. The results for citrate excretions were also related to urinary calcium excretions.

According to these results sodium-potassium citrate metaphylaxis seems to be indicated only in recurrent calcium stone formers.

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RESOLUSION OF CALCIUM OXALATE STONE FORMATION IN VITAMIN B_6 DEFICIENT RATS

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The mechanism of calcium oxalate stone formation was studied in hyperoxaluria rats by autoradiography, using radioisotope-labelled oxalate and calcium. Hyperoxaluria was induced in rats after feeding them a vitamin B_6 deficient diet for 4 weeks. Urinary excretion of oxalate was 448±129 µg/day/100g body weight in hyperoxaluria rats, about 3 times higher than that in normal rats. Renal clearance of oxalate was higher than that of inulin in normal and hyperoxaluria rats, indicating that oxalate is secreted at the proximal tubules. On the other hand, fractional excretion of oxalate in hyperoxaluria rats was higher than that found in normal rats. This result confirmed that secretion of oxalate is increased in hyperoxaluria rats. Renal content of oxalic acid in hyperoxaluria rats was 38.1±7.9 µg/g wet weight, about 1.3 times higher than that in normal rats. Autoradiographic study showed that focal depositions of radioisotope, not found in normal rats, were observed in the renal papilla not only after injection of ^{14}C-oxalate but also after injection of ^{45}Ca. The deposits shown by the autoradiograms of hyperoxaluria rats, fed on the diet specified above for 8 weeks, increased in number and size over time. These facts indicate that calcium oxalate crystal deposits in the renal papilla result in the formation of calcium oxalate stone.

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Renal stone disease and chronic renal failure due to small bowel resection.

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A 58 years old female patient with a 40 years old history of M. Crohn had obtained the usual drug treatment and had undergone ileocoecal resection. Nevertheless chronic diarrhea persisted. Consequently calcium-oxalate stones in the urine were repeatedly observed ultimately. Progressive renal failure developed necessitating chronic dialysis. No other cause of chronic renal failure could be found in the patient except for the presence of calcium-oxalate stones. Therefore an extensive investigation of the patient was performed to elucidate the pathophysiologic mechanism of chronic renal failure. The work-up revealed a severe steatorrhoe of 43,3 g/d (5-7g/d), pronounced hyperoxaluria of 0,7mmol/d (below 0,5mmol/d), decreased vitamin B-12 serum concentration of 115pmol/l (125-500pmol/l) and a severe chronic interstitial nephritis with intratubular and interstitial calcium-oxalate cristalls in the renal biopsy. All other investigations were within normal limits, especially no activity of the Crohn's disease could be found. In the pathogenesis of renal stone disease the concentration of lithogen substances may play an important role. In the case of small bowel resection there is an interruption of the enterohepatic bile-acid circulation leading to a loss of bile salts and steatorrhoe. Due to the loss of bile salts, oxalate absorption is increased inducing hyperoxaluria. The increased concentration of oxalate in the urine plays the main role in the pathogenesis of calcium oxalate stone formation. Secondary oxalosis and bacterial infections lead to a chronic interstitial nephritis and chronic renal failure. **Conclusions:** In case of small bowel resection the digestive function must be investigated. If steatorrhoe or other types of malabsorption syndromes are observed, oxalate excretion is to be measured. To normalise oxalate absorption, drug and dietary therapy must be performed to prevent calcium oxalate stone formation and finally renal failure.

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CORRELATION BETWEEN COMPOSITION AND THE CAUSAL REASON OF FORMATION OF URINARY CALCULI.

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In 473 urinary calculi the presumable causal reason for stone formation could be evaluated. These include 128 stones of patients with some kind of hypercalciuria classified by the "Pak-test". For the other stones, the causal reasons were specified by the attending urologist on a form sheet. Besides for trivial cases (e.g. cystinuria, 2,8-dihydroxyadeninuria or infection stones), no unequivocal correlations could be found. Even using additional methods of phase distribution and texture analysis (scanning electron microscopy), only tendencies can be evaluated. With special regard to the most frequent but very complex class of the Ca-stones, these are as follows:

- **Whewellite-rich stones:** Inhibitor deficiency of Mg and/or citrate; uric acid irregularity (especially when there exists an apatite nucleus)
- **Weddellite-rich stones:** Hypercalciuria (often in connection with a primary hyperparathyreoidism); intestinal diseases
- **Apatite-rich stones:** Renal tubular acidosis; primary hyperparathyreoidism; infection with non-urea splitting bacteria; immobilisation
- **Brushite-rich stones:** Urinary flow disturbances (especially in bladder stones due to adenoma of the prostate)

Uric acid stones are produced not only because of uric acid irregularities, but also due to urinary flow disturbances. In some cases, a diabetes mellitus may be thought of as the causal reason.
Taking these results into account, many unnecessary laboratory tests can be omitted and a more precise and direct stone prophylaxis can be started.

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RENAL HANDLING OF CITRATE IN CHRONIC RENAL INSUFFICIENCY

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Citrate (Cit) is a relevant factor of the inhibitory potential of urine environment. Its excretion has been widely studied in subjects with normal renal function, but little is known about its behaviour in chronic renal insufficiency (CRI). We have investigated on renal handling of Cit in 40 patients with different degrees of CRI and 30 healthy subjects (HS) with normal renal function. The patients were subdivided into two groups: A, 30 pts with 40 < GFR < 80 ml/min and B, 10 pts, with GFR < 40 ml/min. The results are listed in the Table.

	HS	Group A	Group B	p
GFR[a]	113.2(19.6)	63.1 (8.6)	31.2 (6.2)	<0.001
Serum Cit[b]	95.7(28.1)	115.7(33.7)	110.9(44.2)	n.s.
Urine Cit[c]	2.6 (1.2)	2.4 (1.3)	1.2 (0.8)	<0.01
Cl Cit[a]	19.1 (9.2)	16.5(10.7)	8.5 (6.6)	<0.02
UF Cit[d]	11.0 (4.2)	7.3 (2.2)	3.5 (1.5)	<0.001
FE Cit(%)	17.5 (9.9)	26.4(17.1)	26.9(17.5)	<0.05

[a] ml/min, [b] µmol/l, [c] mmol/24 hr, [d] µmol/min

Serum Cit was independent of GFR, while urine Cit was low only in more advanced CRI. Renal clearance (Cl Cit) and ultrafiltered load (UF Cit) gradually decreased with GFR, whereas fractional excretion (FE Cit) increased. The increase in FE Cit depended on the impairment of GFR ($y = -1.5x + 35$, $p < 0.001$).
These data show that reduced tubular reabsorption of Cit blunts hypocitraturia ensueing from both reduced filtered load and increased renal metabolism induced by CRI. We suggest that high FE Cit might contribute to the reduced risk of stone formation observed in CRI.

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Patterns of glycosoaminoglycans excretion in the urine of stone-formers and controls after vitamins A and protein loading.

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Until now there have been many controversies about glycosoaminoglycan (GAG) excretion of stone Pts. in comparison to healthy control subjects. Part of this discrepancy may originate from the decisive influence of dietary habits on GAG excretionn. Vitamins, proteins and energy levels are said to affect GAG synthesis and/or their metabolic break-down but few reports are available on the effects of a diet rich in these components on the pattern of GAG excretion in the urine. It's the aim of this study to find out the quantitative effects of vitamins (A) and animal protein on urinary GAG composition in healthy and stone-forming subjects. 10 healthy subjects and 10 stone-formers were examined. They were divided into two groups: 1)vitamin A (a) normal uptake (3000 I.U./day) for the first week and (b) (5000 I.U./day) for the subsequent one; 2) protein group (a) normal uptake and (b) protein concentrate administration, following the same time schedule used for 1). 24 h urinary total GAG output was measured. The The GAG were also subjected to electrophoretic separation and quantitation on cellulose acetate strips. A significant increase in the excretion of GAG was registered in both groups after the massive administration of both vitamin A and protein. The relative electrophoretic proportion of the single GAG fraction as percentage of total GAG among the different study groups is illustrated. The relevance of diet as relative to the macromolecules excreted will be discussed.

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INCREASED COMPLEX BINDING OF SERUM CALCIUM (Ca) IN IDIOPATHIC CALCIUM UROLITHIASIS WITH NORMO- (NC) OR HYPERCALCIURIA (HC)

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The nature of idiopathic hypercalciuria (I-HC) is incompletely understood (increased intestinal absorption, renal loss of Ca?), and the possible role of enhanced Ca complexuria has found little attention. We evaluated the state of serum calcium fractions and relationship of calcium complexes to calciuria in calcium urolithiasis in male control, NC and I-HC subjects (n=12 each), ideally matched for age, weight, body mass, body water, kidney function, metabolic activity of stone disease. Techniques for sampling of fasting blood and 2 h fasting urine (after 12-15 h fast), anaerobic ultrafiltration, measurement of total (Ca-t), ultrafiltrable (Ca-UF), ionised calcium (Ca^{2+}), and other variables were extremely standardized and reliable. Mass equilibria and complexes were computed as based on established equations (K) and software (EQUIL-II).
Results (table; mean values): measured mean Ca-t, Ca-UF and Ca-k* were higher-than-normal in both patient groups, whereas Ca^{2+} and PTH were low. Both, protein-bound Ca (not shown) and K_{CaProt} were unchanged, as were the filtered load and tubular reabsorption of Ca, when based on Ca-UF. Urinary Ca and sulfate were elevated in I-HC and could be ascribed to increased filtered load of Ca-K. The complexes contributing quantitatively to Ca-K were identified as (same order): $[CaCit]^-$, $[MgCit]^-$, $CaHPO_4$, $CaSO_4$. However, $U_{SO_4}V$ was most influential to $U_{Ca}V$ (r=0.62, p<0.001, by multiple stepwise correlations, and different slope).

	Ca-t[1]	Ca-UF[1]	Ca^{2+}[1]	Ca-K[1]	Ca-UF[2]	Ca^{2+}[3]	Ca-K[3]	K_{CaProt}[4]	PTH[5]	$U_{Ca}V$[6]	$U_{SO_4}V$[6]
Controls	9.31	5.58	4.70	0.89	60	84.4	15.7	0.010	269	1.9	12
NC	9.34	5.79	4.58	1.21	61.4	79.3*	20.8*	0.009	168	2.4	15
I-HC	9.63*	5.77	4.63	1.27	60.1	80.9	21.7*	0.009	78*	3.3*	16*

[1]: mg/dl; [2]: per cent of Ca-t; [3]: per cent of Ca-UF; [4]: Dissociation constant (M/L); [5]: amino-terminal, pg-equiv/ml; [6]: µmol/min; *: p<0.05 or smaller, vs Controls

Conclusions: 1) high Ca-K is a prominent feature of males with idiopathic Ca urolithiasis; 2) the interplay of Ca complexes filtered by glomeruli and $U_{SO_4}V$ appears critical in determining $U_{Ca}V$; 3) fasting hypercalciuria in I-HC may me a sequel. Supported by Deutsche Forschungsgemeinschaft, Bonn. - *: complexed Ca

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Mineral metabolism and solution depletion studies in fasting urine and serum of pre-ESWL kidney stone patients - Results of a pilot trial

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Bedside studies on metabolism in patients undergoing ESWL are desirable, because they may be helpful in reducing both duration of hospital stay and number of attendances in specialized laboratories. However, the presence of stones of varying surface can influence the variables measured in urine, e.g. by depletion of the urinary inhibitor concentration. This work in (n=172; ♂/♀ = 98/74) pre-ESWL patients without urinary tract infection and with normal renal function was based on 1) fasting serum (creatinine, calcium, parathyroid hormone) and "spot urine" (pH, creatinine, cyclic AMP, magnesium, pyrophosphate, citrate), 2) computerized simulation of stone surface from X-ray appearance of urinary tract (mainly renal pelvis) concretions, 3) stone analysis. The key data for ♂ and ♀ are listed in the table showing that apart from serum total calcium the two sexes did not differ statistically. Stratification according to stone surface yielded differences in terms of parathyroid gland function (PTH, cAMP), pH, small-molecular inhibitor (Cit, PPi, Mg) concentration, with the trend being into the direction that surface controls measurable inhibitors. The main conclusion was that studying mineral metabolism and stone-forming processes principally is possible under pre-ESWL bedside conditions. Similar work may offer advantages over other types of clinical stone research.

	S-Cr	S-PTH[1]	S-Ca-t[2]	U-pH	U-Cit[3]	U-PPi[4]	U-Mg[5]	U-cAMP[6]	Surface[7]
♂	0.95±0.02[8]	311±15	9.42-0.05	6.74±0.08	214±9	15±1	3.7±0.2	4.7±0.3	596±107
♀	1.23±0.05[8]	328±26	9.14±0.07	6.78±0.09	212±12	16±2	3.3±0.2	4.5±0.4	703±152

S - serum; U - urine; [1]: pg-equiv/ml; [2]: total calcium (mg/dl); [3]: citrate (mg/l); [4]: pyrophosphate (µmol/l); [5]: magnesium (mmol/l); [6]: cyclic AMP (µmol/l); [7]: surface of stone(s) present (mm^2); [8]: x ± SEM; *: p<0.01

- Supported by Deutsche Forschungsgemeinschaft (Schw 210/4-3).

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Serum parathormone and nephrogenous cyclic adenosine monophosphate in stone formers

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The data for parathyroid gland activity in stone formers are controversial. Therefore we evaluated parathyroid function by determining nephrogenous cyclic adenosine 3,5-monophosphate (NcAMP) and serum parathyroid hormone (c-terminal) by radioimmunoassay in 206 patients with nephrolithiasis and in 70 normal controls. The study was carried out on outpatients basis. Each individual collected a 24-h urine sample on free diet and a 2-h fasting urine sample after 15 hours of fasting. A fasting venous blood sample was taken. The stone formers with daily calcium excretion exceeding 7.5 mmol for males and 6.25 mmol for females were assigned to be hypercalciuric. Eighteen of the 206 patients were diagnosed as having primary hyperparathyroidism (pHPT). Normocalcaemic stone formers (n = 188) were placed into a normocalciuric group (NN, n = 128) and a hypercalciuric group (n = 60). The hypercalciuric stone formers were further classified according to the criteria reported by Berlin, based on fasting urinary calcium / creatinine molar ratios and renal threshold phosphate concentrations, into hyperabsorbers (AH, n = 34) and renal hypercalciuric patients (RH, n = 26). The parathyroid function as assessed by mean fasting NcAMP in NN, AH and RH groups as well as in the pHPT group was significantly increased as compared with that in the normal controls. However, on the basis of serum iPTH parathyroid activity was estimated to be significantly higher in the pHPT group than in controls and depressed in NN and AH groups.

Stone analysis

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COMPOSITION OF URINARY STONES IN CHILDREN IN FRANCE : A QUANTITATIVE STUDY OF 415 PEDIATRIC CALCULI.

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To study the present composition of urinary calculi in children, with respect to age and sex, we quantitatively analyzed by infrared spectroscopy 415 stones from children (280 male, 135 female) aged 0.1 to 15 years referred from 1975 to 1988. Calculi were classifed upon their main component (> 50% of the total content of stone)

Children aged 0-4 years were the largest group (180 cases, or 46.4%), with a striking male predominance (145 M, 35 F, M/F ratio 4.1). In this group, there was a striking preponderance of phosphatic stones with 63.3% of carbonate-apatite (CA) and 10% of struvite (Str) in the first year of life, 42% of CA and 36.3% Str from 2 to 4 years. Ammonium urate (AmUr) represented 20% in the 1st year of life and 9.6% from 2-4 years. In children aged 4.1-10 years (66 M, 41 F) and in those aged 10.1-15 years (62 M, 39 F), the male preponderance markedly decreased (M/F ratio 1.61 & 1.59, respectively). Calcium oxalate (CaOx) was the predominant main component (44.9 & 48.7%), whereas prevalence of CA (29/9 & 25 %), Str (14 & 14.5 %) and Am Ur (1 % in both) markedly declined.

We conclude that the peak prevalence of calculi in children is observed until the 4th year of life, with a marked preponderance of CA and/or Str stones especially in males whereas CaOx stones tend to become predominant, as in adults, after the age of five in both sexes.

Clinical investigation

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The significance of daily urine pH profiles in the prevention of urinary stone recurrence.

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The importance of urine pH as a parameter in the development and prophylaxis of urolithiasis is undisputed as is its significance, along with citrate excretion, in the treatment of this disorder. Eating habits at home and at work play a significant role in outpatient treatment of stone-forming patients. Under these conditions the recording of urine pH is thus essential to identify high risk patients. A urine pH profile was therefore performed on 30 outpatients in a study lasting for at least 7 days. Throughout the study the patients remained in their usual environment at home and at work.
Pathological changes were evident in over 70% of patients who had experienced urinary stone recurrence and in 50% of those in whom stone formation occurred for the first time.
The pH of morning urine in particular, frequently showed values of below 5.8, but urine pH also often dropped below 5.8 during circadian pH fluctuations, although the average pH in the 24 hour urine remained within the physiological range. Lithogenic substances such as calcium, uric acid, phosphate and oxalic acid as well as the inhibitory substances citrate and magnesium were also determined in the 24 hour urine of these patients.
The investigations show that even at daily citrate concentrations of more than 2.0 mg critical variations in urine pH can occur which must be considered responsible for the formation of stones. Since urine pH decreases particularly at night, single doses of citrate (Oxalyt-C) can and should be therapeutically used in the evening.

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Compliance in stone patients. An experimental and multivariate approach on predicting variables.

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To predict compliance of Ca stoneformers referring to metyphylactic measurements a multiple threedimensional set of variables (medicial, psychological and social) was investigated in a prospective study*; the criterion- variables were also multidimensional (urine-, serum-parameters, behavioral data etc.).
The aim of the study was to identify the variables in a multivariate system which predict alone or in combination a redefined compliance. Compliance was not seen dichotomic but as a continuum ranging from dismissing all appointments to a complete follow-up and including changed behavior according to the given recommendations. Urolithiasis in this context is a illness with exceptional possibilities for modelling this question in a quasi-expertimental desgin. Because of methodological demands patients were selected according to a strict catalog of in- and excluding criteria.
After stone-removal the predictor-variables were collected before hospital discharge. In an outpatient stone clinik a dual baseline (metabolic data in urine and serum) were taken. Extensive verbal and written metaphylactic recommendations (no drugs) were then given in order to the model of multifactoriell risks. After 3 and 6 month the criterion variables were re-evaluated.
Between 6/1988 and 6/1989 from 146 patients informed consent was received and the predictor-variables were collected (98 ♂, 48 ♀, $\bar{x}$ = 49ys, 85 single, 61 recurrent stone formers). To date rate of compliance measured by attending the appointments shows that from obviously motivated patients 95/146 after 3 and only 75/146 after 6 month came to the follow-up. The dead-line of investigation is 11/1989. No statistical analysis were done before data collection is completed (methodological demands). The hierachical multivariate statistical analysis (canonical correlation analysis, multiple regression analysis, Hotelling's T^2 etc.) will be finished up to february 1990.
*Financially supported by the Bundesministerium für Forschung und Technologie (No 0701628/2)

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BENEFITS OF COMPUTER-ASSISTED FOLLOW-UP IN RECURRENT STONE FORMERS

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To increase the efficiency of follow-up in recurrent stone formers , we developed a computer-assisted database system, which allows data storage and documentation as well as statistical and scientific anaylsis. With a systematic approach, and thereafter an accurate evaluation of numerous clinical or laboratory findings and imaging tests, urological survey and follow-up were significantly improved. Since the introduction of our computer system, the main benefits were:

- systematic and controlled input of our findings.
- easy and rapid output of essential data in every patient (or patients with similar findings).
- lowered time for analysis and a most helpful tool in planning clinical studies.
- enhanced patient compliance and recurrence survey due to an computerized call-up system.

Metaphylaxis of calcium oxalate stones

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The acute effect of Sodium-Potassium Citrate (Oxalyt-C) on the urinary saturation of calcium oxalate.

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Low risk factors for calcium oxalate crystallisation are of importance in the prevention of recurrent calcium oxalate stone formation.

Patients with calcium urolithiasis (n=23) and normal subjects (n=12) were admitted to the Clinical Research Center for 6 days. Two different doses of Na-K-Citrate (Oxalyt-C) were administered (3x3g,4x3g/d). Consecutive 24 hour-urine collections were used to measure the major ion species: pH, Na, K, Ca, Mg, Cl, P, SO_4, uric acid, oxalic acid, citric acid, creatinine. A modified version of the iterative computer-program EQUIL was used for the calculation of free ionic activity and relative supersaturation.

Na-K-Citrate therapy (4x3g/d) reduced the extent of urinary supersaturation with respect to calcium oxalate significantly below levels encountered in normal subjects without stones (3.22 ± 0.25 to 1.89 ± 0.39).

The possible effect of Na-K-Citrate on dissolution of "Calcium-sand" after comminution by ESWL is discussed.

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Urine alkalinization with mineral water.

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Several preparations are applicated for urine alkalinization in case of calcium oxalate, uric acid and cystine urolithiasis. As an alternative or a support of the therapy HCO_3^--rich mineral water may be effective.

After ingestion of a HCO_3^--rich mineral water (3388 mg HCO_3^-/l) under standardized diet urine pH-value increased significantly from 6.15 to 6.73. The citric acid excretion accordingly increased from 3.5 mmol/d to 4.9 mmol/d. In comparison with these results the ingestion of a HCO_3^--poor mineral water (345 mg HCO_3^-/l) had no influence on pH-value and citric acid excretion. Refered to these parameters the results with HCO_3^--rich mineral water differ significantly from the results with HCO_3^--poor mineral water. Both mineral waters have nearly the same calcium content (232 mg/l and 242 mg/l). In both cases the calcium excretion increased significantly from 5.49 mmol/d to 6.18 and from 5.79 mmol/d to 6.35 mmol/d respectively. These results indicate that a low calcium content of the mineral water really has to take into consideration.

We have to conclude that a Ca-poor and HCO_3^--rich mineral water can be effective as a support of the alkalinization therapy in case of urolithiasis. A futher positive effect of this measure is the simultaneous high fluid intake.

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A new treatment of enteric hyperoxaluria – experimental and clinical investigations with an organic marine hydrocollid Monica Lindsjö, Bengt Fellström, Sverker Ljunghall, Björn Wikström, Bo G Danielson, Dept of Internal Medicine, University Hospital, S-751 85 Uppsala, Sweden

Urinary excretion of oxalate seems to be the most important determinant of calcium oxalate stone formation in the urinary tract. Urinary excretion is mainly dependent upon endogenous formation of oxalate, but in association with intestinal disorders the gastrointestinal absorption may be increased and cause hyperoxaluria.

Patients and methods. In the present study a fibre-rich organic marine hydrocolloid (OMH) was investigated. OMHs are polymers of high molecular weight extracted from plants and seaweeds. This OMH ist specially processed and charged with calcium and zinc. The binding of oxalate to OMH *in vitro* was studied by incubation of OMH with sodium oxalate at pH 5,7 and 9. The binding was monitored by ^{14}C-oxalate activity on the supernatant following 3 h incubation at 37°C.

Patients with enteric hyperoxaluria due to jejunoileal bypass or Crohn's disease with previous intestinal resection were studied regarding the oxlate excretion, the effect on bowel function and in two cases the effect on stone formation while taking 3 tablets t.i.d. of OMH (OX-ABSORB®). A two-week pilot study was performed to measure the effect on oxalate excretion as well as a six-month long-term-study.

Results. Based upon the content of calcium in 1 g OMH the binding of oxalate to OMH could become saturated at an oxalate concentration of 100 mmol/ml.

In the two-week pilot study a significant reduction in the 24-hour urinary excretion of oxalate was found in patients on OMH treatment. During the long-term study the oxalate excretion was significantly reduced by the same amount as in the short-term study. The urinary excretions of calcium, magnesium, citrate, phosphate and urate did not change.

There was a dramatic effect on bowel function and frequences of diarrhoea in 7/10 patients during the six-month study.

Two patients with a serious disease were treated for three years and the frequency of stone formation became reduced from 10–50 stones/year to 2–5 stones yearly.

Conclusions

1. OMH has the capacity to bind oxalate *in vitro*.
2. Treatment of patients with enteric hyperoxaluria and renal stone formation with OX-ABSORB® causes a significant reduction in oxalate absorption and urinary excretion of oxalate.
3. Treatment causes substantial improvement in the frequency of diarrhoeas and bowel function and
4. seems to have a potential to cause a dramatic relief in the stone-forming habits in these patients.

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BILATERAL NEPHROLITHIASIS

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We studied retrospectively 25 patients with bilateral, multiple renal stones who were followed up more than 2 years, and it was concluded that medical treatments prevented new stone formation, stone growth and deteriolation of renal function. Of the 25 patients, 12 had hypercalciuria (4 renal, 6 absorptive, 2 undetermined), 4 had renal tubular acidosis, 3 had hyperuricosuric calcium oxalate stone, 3 had gout and 2 had medullary sponge kidney. One had a question of 1,25(OH)2D3 excess. We treated them with Fluitran for hypercalciuria, Zyloric for hyperuricemia or hyperuricosuria, and Uralyt U for hypocitraturia. We were able to reduce the recurrence rate of their stone disease more significantly than in unilateral, recurrent urolithiasis patients.

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The effects of oral pyridoxine upon plasma and 24 hour urinary oxalate levels in normal subjects and stone-formers with idiopathic hypercalciuria.

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We studied the influence of the administration of vitamin B6 (200 mg/day) on plasma and urinary oxalate levels in 10 normal subjects and 7 stone-formers with idiopathic hypercalciuria (IHC), both groups being on low oxalate diets.

After three weeks of supplementation, plasma oxalate concentration decreased from 2.3 $\pm$ 0.37 µmol/L to 1.9 $\pm$ 0.49 µmol/L in normal subjects ($p = 0.008$, paired t-test). The stone-formers showed no significant change (from 2.09 $\pm$ 0.23 to 2.16 $\pm$ 0.33). B6 administration did not lower urinary oxalate in IHC patients but a considerable rise was observed in the normal subjects' oxalate excretion when results were corrected for creatinine (from 0.18 $\pm$ 0.05 to 0.25 $\pm$ 0.05; $p = 0.027$). It is interesting that no significant change was noticeable in urinary glycollate excretion either in normal subjects or in patients. Both plasma 5-pyridoxal phosphate levels and the urinary 4-pyridoxic acid levels were measured by HPLC and there were no significant differences between the levels for IHC stone-formers and normal subjects either before or after administration of vitamin B6.

There are two conclusions. First, that vitamin B6 slightly increases both the oxalate production and renal clearance in normal subjects. Second, on the basis of these results vitamin B6 cannot be recommended for stone-formers with idiopathic hypercalciuria.

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Treatment of Calcium Oxalate Stone-Formation in Saudi Arabia with Citracal.

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A novel treatment was designed to prevent calcium oxalate and uric acid stone-formation in the Arabian Peninsula. In this region the main urinary risk factors are a low volume, low pH, extensive mild hyperoxaluria and hyperuricosuria. Urinary calcium and intestinal calcium absorption are generally low.

Citracal (an effervescent form of calcium citrate) was used to block oxalate absorption, to alkalinize urine, to increase citrate excretion, to potentiate inhibitors and to increase fluid intake. Twelve idiopathic calcium oxalate stone-formers were studied for two weeks on each of three regimes - a basal period, a period on one Citracal tablet dissolved in water twice daily with main meals, and a further period on double this dosage. The Citracal added 500 mg and 1000 mg extra calcium per day to the basal diet. Two 24-hour urines were collected from each patient during each period and analyzed for risk factors. Urinary volume and pH rose slightly but not significantly. The calcium/creatinine and magnesium/creatinine ratios increased on the high dose ($P < 0.05$ for both). The most marked effect was a highly significant decrease in the oxalate/creatinine ratio ($P < 0.001$) such that all oxalate excretions except one fell into the normal range. This markedly reduced the risk of calcium oxalate but not of uric acid stones. We anticipate that incorporation of more alkali into the tablet will enable us markedly to reduce the risk of both types of stones in the population.

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Prophylaxis of the recurrence of urinary calculi with FARNOLITH dietary fiber granulate -Results of a long-term study.

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The high protein consumption and the continually decreasing proportion of roughage in the diet are causal factors in the prevalence of urinary calculi in our time.

In a multicenter study patients suffering from frequently recurring urinary calculi received FARNOLITH dietary fiber granulate over a period of 12 months. Under this treatment the rate of recurrence of the stones decreased from 2.75 to 0.46 stones/patients/year. Out of 59 patients, 53 did not have a recurrence at all.

19 of these patients took FARNOLITH continually for 4 years. Only 1 patient relapsed during this period; he suffered 2 recurrences of stones.

Besides the good efficacy of FARNOLITH, its excellent tolerability and the high patient compliance merit special emphasis.

Metaphylaxis of cystin-, uric acid and infecteous stones

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A STUDY OF CYSTINE URINARY CALCULI

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Cystine calculi are commonly considered as being particularly pure in composition. Recently, however, the presence of calcium phosphates (apatite and brushite), calcium oxalates, struvite, sodium urate and uric acid has been reported.
In this study, 54 specimens of human (14) and canine (40) cystine urinary calculi have been examined by infrared spectroscopy, scanning electron microscopy (SEM) and electron dispersive X–ray analysis. Half of the specimens contained secondary components. The main associated compound was apatitic calcium phosphate, although brushite, struvite, calcium oxalate, urates and one drug (oxolinic acid) were also detected.
Under SEM examination, small spherules of calcium apatite were frequently seen over cystine crystals in the canine calculi. We also observed apatite spheroliths in some human cystine stones. In the infrared analysis, even small amounts of calcium apatite could be detected through the study of the spectra of the calcinated stones.
Calcium oxalates could be recognized in the infrared spectra of two canine samples and one human stone. The SEM micrographs showed well defined areas of this compound between areas of cystine.
Uric acid and sodium urate were not detected in the samples studied. However, we found ammonium urate, potassium urate and complex urates in two canine cystine calculi.
Finally, oxolinic acid was detected in one of the human cystine calculi.

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Cystinuria - investigations on the efficiency of ascorbic acid therapy.

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The high oral intake of ascorbic acid is a well known medical treatment of cystinuria. Ingesting up to 5 g per day, ascorbic acid should - as a reducing agent - change the redox-equilibrium of cystine and its monomer, cysteine, which has a much higher solubility. The concentration of cysteine should be increased while the cystine concentration should be decreased.

We have checked this therapy by a study with 7 healthy controls and 7 cystinuric patients. The study lasted nine days: during a first period all subjects collected 24 h-urines on three consecutive days. Starting with day N° 4 they were given 5 g ascorbic acid per day over a period of 6 days. The last three days they collected 24 h-urines. Quantitative amino acid determination was performed using a HPLC method described earlier.

During ingestion of ascorbic acid the mean excretion of cysteine of the control group increased from 134.1 µmol/d to 159.0 µmol/d while the excretion of cystine decreased from 107.1 µmol/d to 82.0 µmol/d. The corresponding values for the cystinuric patients increased from 352.4 µmol/d to 452.1 µmol/d for cysteine and decreased from 4131.6 µmol/d to 3663.2 µmol/d for cystine.

Thus, ascorbic acid seems to have only mild reducing properties in respect to cystine.

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HOW THE UREASE-INDUCED PH INCREASE VARIES BETWEEN DIFFERENT URINES

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The urease-induced crystallization in urine is related to the level of the urease-induced pH increase. It appears reasonable to assume that the rate of this pH increase is one of the factors which determine if crystallization will be initiated before urine is washed out from the kidney. This study has evaluated how the rate of the pH increase varies between different urines and how it is related to urine composition.

Method. Urine samples from 8 individuals were inocculated with the same amount of urease at 37°C. pH was then kept constant at 6 preset levels (between 6.4 and 7.4) using a pH-stat (VIT 90, Radiometer, Copenhagen, Denmark). The rate of the HCl addition necessary to keep pH stable at each preset level reflects urease enzymatic activity at that particular pH. The time it took for pH to reach each preset pH level was recorded and related to urine pH, phosphate and ammonium ion concentration.

Results. There was a pronounced intersample variation in time to the preset pH levels. The time to reach pH 7.4 thus varied from 7.5 to 25 minutes. The rate of the pH increase was only at pH levels below 7.0 related to the initial pH. It was negatively related to urine phosphate (especially at higher pH levels). It was less strongly related to urease enzymatic activity and the ammonium ion concentration.

Discussion. The factor of greatest importance for how fast a certain pH is reached appears to be urine phosphate. Phosphate exerts this effect by being the major urine buffer. The salts that precipitate secondary to urease activity in urine are phosphates but urine phosphate is always present in excess relative to the other components of these salts. A high urine phosphate appears thus more to protect against a massive urease-induced precipitation than to favour it.

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Morphologic aspects of 2,8 - dihydroxyadenine urolithiasis

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The rare 2,8-dihydroxyadenine (2,8-DHA) stone is misdiagnosed as uric acid if analyzed only by normal chemical methods. Therefore a detailed description is given of the urinary crystals and the stones of two patients.

Urinary crystals of 2,8-DHA have been investigated by light microscopy and SEM; two stones additionally by X-Ray diffraction and electron microprobe. The urinary crystals have been found to be brownish and of spherical shape with a size of 2 to 10 microns. By SEM bridging between crystals could be clearly seen, as well as the formation of bigger aggregates.

X-Ray diffraction of the two stones showed the typical pattern of 2,8-DHA, with the strongest reflections at 3.15 Å, 6.54Å and 10.68 Å. Electron microprobe investigation with energy-dispersive system in small areas of the stones (qualitative point-analysis of 1 micron in diameter), showed no further elements above atomic number Z = 10, which means that only organic substances were present. Macroscopically both stones had a size between 5 to 10 mm.

The colour was greyish-blue in one stone, the other showed a deep-brownish colour at the surface and a light-yellow one inside; in air the colours of the second stone changed into a brown-blueish colour within several days. Both stones were roundish and showed knobby protuberations on the surface. They were easy friable and had a rough appearance.

By light microscopy smaller spherical bodies were observed on the surface. The investigation of the stone fragments partially showed radial structures on the fracture zones and multiple cavities, sometimes bridged by thin organic membranes. By SEM very small platelets (below 1 micron) were discovered additionally on the surface; the fracture lines were mostly irregular, sometimes showing a radial structure; inside the stones amorpheous organic material was detected, besides spherical bodies of variable size. Residues of the organic membranes (partially destroyed by sample preparation for electron microscopy) still could be seen.

The description and investigation show that the insoluble 2,8-DHA forms typical urinary crystals, bigger aggregates (microlithes) and multiple formation centres within the stones. The outer appearance and high friability clearly differentiate them from other stones.

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Screening of Cystinuria using the UROCYSTIN-kit.

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Cystinuria is known as hereditary metabolic disease. Excessive urinary excretion of the relatively insoluble amino acid cystine (R-SS-R) results in recurrent urolithiasis.

The discovery of cystine crystalls in the urinary sediment is a usefull diagnostic test for cystinuria. After centrifugation the characteristic hexagonal crystalls can be seen using a microscope.

The use of a simple screening test named UROCYSTIN (Hoyer GmbH, Siemensstr. 14, D-4040 Neuss) is even less difficult. A color reaction with nickelsulfide after reduction of cystine by sodium hydrosulfite shows the presence of cystine.

Cystine concentrations of 50 µg/ml or more can be detected. The coloration of the kit is judged two minutes after adding the urine: dark brown, positive; light greenish blue, negative; light brown, suspicious.

In case of a positive or suspicious result a quantitative amino acid analysis of this urine sample should be made. The screening of the family of the positive patient has to follow.

ESWL/EPL

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LASERLITHOTRIPSY IN THE MANAGEMENT OF URETERIC CALCULI RESISTENT TO EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY.

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Extrcorporeal Shock Wave Lithotripsy (ESWL*) was started in June 1987 with the Siemens Lithostar°. Treatments are carried out anaesthesiafree and on an outpatient basis. Our experience after 5.000 treatments within 2 years, makes clear that stone composition and location rather than stone burden is the limiting factor : disintegration is apparent in calcium oxalate dihydrate, uric acid and struvite ; in the distal ureter, calcium oxalate monohydrate remains poorly fragmentable.

Pulsed dye laserlithotripsy has been performed in 50 patients with a mid or distal ureteric calculus, after a previous ESWL without disintegration. Failure of ESWL could be related either to the extreme oedematous ureteric portion at the calculus location, or to the stone composition (calcium monohydrate oxalate-COM). Initial experience with the 200µ laser fiber-60 mJ energy output divice revealed the need for higher energy output to disintegrate COM. Disintegration, or at least fragmentation into pieces of the COM calculi can be achieved with the 320µ -140 mJ device as depicted in a comparative study between the two devices.

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TREATMENT OF URETEROLITHS BY ESWL : IN SITU VERSUS PRIMARY STONE-RESETTING

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Within ESWL treatment of upper ureteroliths 33 stones were treated by push mash in the period from 12/87 to 2/89. As against that, 20 upper ureteroliths were treated in situ. While no significant differences were found as to the mean period of storage, tension and absence of stone, significant differences were seen as to the number of treatments per patient, the stone size and the number of shots. In primarily reset stones and with small number of shots (1 430 : 1 756) a small average number of treatments per stone is found. The primarily non-reset stones require a considerably greater number of endourologic measures (ureteric catheter application, double-J-insertion).
Recapitulating it becomes evident that the number of endourologic measures required after ESWL with ureteroliths can be reduced by pinpointed resetting of the stone in question before the first ESWL treatment; in this way the stress on the patient can be reduced as well (fewer shots, smaller number of treatments per stone).

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A RADIONUCLIDE METHOD FOR DIAGNOSTIC OF RENAL DAMAGE AFTER ESWL.

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The study concerns a new method for evaluation of the renal damage after ESWL. ^{125}J-fibrinogen is applicated IV before treatment. After lithotripsy, the accumulation of radionuclide in the area of renal damage is detected by means of gamma camera scintigraphy followed by computed substraction of the image. An additional test with ^{99}Tc DTPA can be applied for accurate localisation of the kidney.
It was established that parenchimal lesions caused by lithotripsy appear after 800-1000 shock waves (18 kV) and increase progressively with the number of shock waves.
The authors suggest, shock waves number to be limited and in cases of big stones the treatment to be done in two sessions with an interval of 20 days between them.

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Extracorporal Shock Wave Lithotripsy for stones in the lower third of the ureter. In situ or with a Loop catheter ? A randomized trial.

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The treatment of choice for stones in the lower third of the ureter is still to be demonstrated. Both in situ ESWL treatment (IS) and ESWL with a loop catheter (LC) around the stone are recommended.
We randomized patients with stones in the lower third of the ureter into these two treatment groups. 44 patients were evaluated. Both groups consisted of 22 patients.
In the IS group, 8 patients (36%) were stone-free after two weeks. Absence of impaction, resulting in hydronephrosis at the site of treatment seemed a prognostic factor for a high success-rate in this group.
In the LC group, all men needed epidural anesthesia during treatment. The positioning of the LC failed in 9 patients. In this group of 9 patients, 5 (56%) were stone-free after two weeks. The LC was successfully positionned in 13 patients. 9 of them (69%) were stone-free after two weeks.
The stonefree-rate for treatment of lower ureteral calculi is almost twice as high if they are treated with a LC compared to IS treatment. Although epidural anesthesia is mandatory in all men and LC positioning does not succeed in 41 % of the cases, we believe LC positioning is justified, especially in cases of impaction, proved by hydronephrosis. If dilatation is absent, the stone can be treated in situ.
If desintegration fails and hydronephrosis persists two weeks after treatment, ureterorenoscopy can be performed.

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URINARY STONE MANAGEMENT IN 1990, Nabil K. Bissada, M.D., Medical University of South Carolina Hospitals and the VA Medical Center, Charleston, South Carolina

Surgical and Medical management of urinary lithiasis is changing rapidly. Different ESWL machines, rigid and flexible ureterorenoscopy, perartaneous nephroscopy, laser, ultrasound and electrohydrolic lithotripsy are now available to most major urologic centers. Adjuvant medical, mechanical and chemical methods of treatment are also available. In this environment of a multitude of choices, clinical judgement becomes more crucial than ever before.

While we continue to utilize most of the available modalities at the Medical University of South Carolina, a rational approach to thrapeutic choice has evolved. Our approach will be illustrated and discussed.

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Flavoxat (Spasuret 200^{R}) versus Urol^{R} after shock wave lithotripsy

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Flavoxat has been shown to modulate the frequency and amplitude of ureteral contractions in the guinea pig, suggesting a spasmolytic effekt on human ureters, too.

In a prospective randomized trial in 1988 we studied the effect of Flavoxat (5x200 mg/d) versus Urol^{R} (5x2 Cps/d) in patients hospitalized after shock wave treatment of kidney and ureteral stones.

Both groups consisted of 100 patients and were quite similar in terms of age, diameter and location of stones an there was no difference in the time of stone passage.

Flavoxat treated patients needed less spasmolytic or analgetic drugs (about 10%) than patients treated with Urol. The drug showed no side effects and could be useful in the treatment of urolithiasis.
Another placebo-controlled study should answer this question.

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Therapy of kidney stones with Lithostar Plus - nuclear medical examinations and clinical results

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Since May 1987 we have performed more than 2500 shock wave therapies of stones in the kidney, ureter and the biliary tract with Lithostar.
Until now we have treated more than 100 patients with calculi in the kidney or the ureter by Lithostar Plus. In comparison with the Lithostar we found the following advantages: reduction of necessary X-Rays, less pain with the therapy, extension of the therapeutic possibilities by higher energy supply.
We have performed in prospective studies scintigraphic investigations before the therapy, on the first day, the fifth day and three months after the therapy. With it also patients who for different reason have been treated with higher energy levels (level 5-8) have been examined. The results were compared with scintigraphic studies after therapy with Lithostar.

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First Experience with the mobile Lithotryptor WOLF 2300.

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Since September 1988 the Dept. of Urology has the opportunity to use the mobile Lithotryptor WOLF 2300 one day per week.
Materials / Methods: 248 treatments have been performed on 152 patients (51 % men, 49 % women). In 11 patients it had to be done on both sides, therefore 163 renal units were treated. In 69 % treatment was carried out on hospitalized patients (average lengths of stay: 3 days) and in 31 % on out patients.
133 renal units had one stone, 26 had two and 4 cases had three or more calculus. The average size of the stones was 7.98 mm.
Results: The state of being free from stones or of desintegration with remaining remnants of tiny desintegrates that required no more treatment was achieved in 149 cases (92 %): with one treatment in 56 % and with multiple treatments in 44 %. In the remaining 14 cases (8 %) open stone-surgery had to be performed.
Before EPL, a push back with a double-J catheter had to be carried out, on account of a stone in the upper ureter, in 26 cases (17 %).
After EPL, percutaneous nephrostomy had to be performed due to a "Steinstrasse" in 7 cases, ureterenoscopy or Zeiss loop in 11 cases. Colic during treatment occured in 78 cases (31 %), but desintegration had to be interrupted in 10 cases (4 %). Emergency admission of out patients because of colic was necessary in 2 cases (2,6 %).
Summary: The main problem of lithotrypsy with a mobile device is the duration of multiple treatments which cannot be carried out within a short time. The remaining modalities of stone therapy with the mobile lithotryptor correspond with those of the stationary devices. The use of a mobile lithotryptor is a possibility to lower the expenses without reducing the medical convenience for the patients.

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First experience using a multifunctional overhead lithotripsy module to the Lithostar: Physical properties and clinical application.

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The successful treatment of more than 300,000 patients in over 200 centers world-wide has demonstrated the effectiveness of the Lithostar in urinary lithiasis. Biliary calculi, however, prove to be harder and non-radiopaque in many instances requiring higher shock wave energy and non x-ray dependent localization systems. In order to broaden the versatility of the Lithostar an overhead shock wave generator was added to the standard set-up allowing for a wide range of power settings (150 - 850 bar), a variable focus-length and an in-line ultrasound scanner for stone localization. The wide aperture guarantees pain-free treatment of urinary calculi. In vitro experiments have shown that even cystine calculi are effectively disintegrated thanks to the wide power range offered by this machine.
The focal zone was reduced to 12 x 4 mm rendering in-line monitoring of the treatment mandatory.
The Lithostar upgraded with the overhead lithotripsy module will cope with the demands of biliary and urinary lithotripsy even in calculi so far refractory to extracorporeal shock wave lithotripsy (cystine).
The combination of x-ray- and ultrasound-guided treatment together with the wide power range available should provide a solution to any "lithotripsy problem".

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AMBULATORY SHOCK WAVE LITHOTRIPSY USING EDAP LT-01

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EDAP LT-01 is a shock wave lithotripter which uses ultrasound for stone localization and piezo-electric elements for shock wave generation. EDAP LT-01 lithotripsy is said to be more or less painfree due to a small energy focus and a low energy intensity at skin level.

Material and method: From March 1988 until September 1989, 591 patients were treated. Available for a follow-up period of at least one month were 467 patients. Of these 87 had ureteric stones mostly located in the upper third of the ureter. Because of difficulties to localize ureteric stones with ultrasound, 88% of them were pushed back to the kidney before treatment. The mean stone size was 10 mm, range 4 - 30 mm. Patients with stones > 15 mm or multiple stones got a double-J ureteric stent inserted before treatment. The mean number of sessions per patient was 1.7 (range 1 - 7).

Results: Sixty-four per cent of the patients with renal stones were completely stone-free after ESWL monotherapy. Another 6% were stone-free after auxiliary procedures in the ureter, mostly ureteroscopy. Fifteen per cent of the patients had residual fragments < 5 mm. Of the patients with ureteric stones which were pushed back to the kidney 91% were stone-free after ESWL. The treatment was most successful in patients with single stones < 10 mm located in the pelvis, 94% being stone-free after ESWL monotherapy. Most patients experienced no or very little discomfort during the treatment and only 27% required analgesics. This allowed 98% of the patients with renal stones to be treated on an out-patient basis. Young female patients with pelvic stones were overrepresented in the patients who required analgesics during the treatment.

Conclusion: Lithotripsy with EDAP LT-01 resulted in a satisfactory stone fragmentation and was mainly painless. Thereby the vast majority of patients could be treated without hospitalization.

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THE INFLUENCE OF STONE LOCALIZATION, SIZE AND COMPOSITION ON STONE FREE RATE AFTER ESWL. G Haupt, B Liedl, D Jocham, Ch Lunz, Ch Chaussy. Ruhr-Universität Bochum, LM-Universität and Städt. Krankenhaus Harlaching München, FRG.

754 patients (810 renal units) underwent 932 ESWL treatments. Pretreatment stone localization and size, composition and the stone free rate (SFR) at discharge and after 6 months and 3.6 years were evaluated.

Stone localization (%)		Stone size (%)	
upper calix	10	< 1 cm	33
middle calix	6	< 2 cm	44
lower calix	16	< 3 cm	14
renal pelvis	56	> 3 cm	9
ureter	12		

Composition (%)	total	female	male
calcium-oxalate	77	55	88
calcium-phosphate	14	30	6
struvite	4	8	1
cystine	3	5	2
uric acid	2	1	3

SFR was 45% at discharge, 84% after 6 months and 78% after 3.6 years. After 6 months and 3.6 years most fragments were in the lower calix (60% respectively 68%). For kidney stones SFR after 6 months was 72-84%, ureteral stones had a higher success rate (94%) due to auxiliary procedures.

Larger stones had lower SFR:	<1cm	<2cm	<3cm	>3cm
SFR at discharge	57	44	28	18
SFR after 6 months	89	83	79	71

SFR for cystine stones was 80% at discharge and 100% after 6 months due to intensive treatment. All other stones had a SFR of 41-47% at discharge and 80-83% after 6 months except struvite, with a SFR of 60% after 6 months. Detailed evaluations of SFR after 3.6 years are in progress.

While stone localization in the kidney did not influence SFR, stone size correlated inversely to SFR. Residual struvite stones are more likely to grow than to pass spontaneously. A consequent treatment of UTI, especially urease forming bacteriae, seems mandatory.

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THE EFFECTS OF SEQUENTIAL ESWL ON THE STRUCTURE AND FUNCTION OF RABBIT KIDNEYS. G Haupt, JM Donovan, C Weber, O Seemann, M Chvapil, RB Nagle, GW Drach. Ruhr-Universität Bochum, FRG, and University of Arizona, Tucson, USA.

Extracorporeal shock wave lithotripsy (ESWL) is a safe and effective treatment of urolithiasis. Safety limits and optimal timing interval for sequential treatments have not been evaluated. In an animal model the effects of shock waves on renal physiology and structure were tested.

35 New Zealand white rabbits underwent unilateral left nephrectomy. After creatinine clearance (Ccr) stabilized, the right kidney of each animal was subjected to 2000 shock waves (SW) per treatment at 18 kilovolts in a Dornier experimental lithotripter XL1. Eight groups of rabbits were treated: Group 1 single treatment, groups 2-4 2 treatments within 2, 4 or 8 weeks, groups 5-7 3 treatments within 4, 8 or 12 weeks and group 8 4 treatments within 12 weeks. Hematuria and Ccr were measured before and 1, 7, 14 and 28 days after treatment; on these days after the last assigned treatment one animal per group was sacrificed for gross and histological evaluation.

75% of the rabbits had hematuria after treatment. Grossly, 60% of the kidneys had capsular hematomas, which usually had been replaced by capsular fibrosis after 28 days. Sequential ESWL had an additive effect on both of these findings. 32% had interstitial hemorrhage, 28% showed cortical-medullary fibrosis, both in correlation with the time interval between treatments. Ccr decreased in 57% of rabbits, which correlated with the amount of hematuria. Ccr returned to baseline by the 7th day post ESWL.

ESWL is associated with renal tissue damage (subcapsular and parenchymal bleeding, followed by fibrosis) and reversible diminished function. Changes correlate with number of treatments and inversely with the time interval between treatments.

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Management of Cystine Stones

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This report describes our experience with the management of cystine stones by ESWL and prophylaxis. Since Februar 1985 we have treated 15 patients, 13 with ESWL and 2 conservatively. 8 women and 7 men between the age of 20 - 68 years. 11 cases involved renal stones, 3 cases ureteralstones and 1 both. The analyses of the stones was in all cases 100 % cystine.
After ESWL, 9 of 13 patients were stone free. 4 patients had residual stones and two of them required addition of auxilliary techniques such as "Double J (Splint)" or "PCN" (Percutaneos nephrostomie) Our experience is that cystinstones are very hard and also difficult to locate. The success in ESWL depends on the size of the stone. For large stones, combination therapy with "PCLL" (Percutaneos Litholapaxie) or Ureterorenoskopie, is necessary.
Alkaline therapy or Vitamine C in addition to fluid intake and diät was used as further prophylaxis.
In nearly all cases urine cystine excreation was below 700 mg/l, therefor it was not necessary to use α-mercaptopropionyglycin or D-penicillinamin which has strong side effects.

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Expanding the indications for the MPL 9000 Lithotripter

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Abstract not submitted

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Antibiotic prophylaxis and ESWL treatment.

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250 patients (n=250) with stones were investigated to know if antibiotic prophylaxis is useful before ESWL. Patients were divided into 3 groups.

Group one (n=100): patients with sterile urine and no instrumentation.
Group two (n=100): patients with sterile urine and instrumentation.
Group three (n=50): patients with asymptomatic bacteriuria and no instrumentation.

All patients were randomized to a control group and to a group who received 1500 mg Cefuroxim immediately before ESWL. In all groups urine was controlled 6 and 24 hours after ESWL.

We concluded from this study the following points:

1. antibiotic prophylaxis is unnecessary, if urine culture is sterile and ureteral instrumentation is not required.
2. prophylaxes reduces incidence of bacteriuria after ureteral instrumentation and ESWL.
3. prophylaxis in cases, where urine culture is not available at the time of treatment, reduces incidence of both asymptomatic and symptomatic infections.
4. prophylaxis is recommended in cases with normal urine microscopy ("clinically sterile") with no urine culture available.
5. sensitivity spectrum of single blind shot prophylaxis should include Enterococcus and possibly Pseudomonas.

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DIFFERENTIATION BETWEEN PRE- AND POSTGLOMERULAR DETERIORATION BY PROTEIN EXCRETION AND RENAL FUNCTION BEFORE AND FOLLOWING ESWL.

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Extracorporal stone lithotripsy (ESWL) causes a hematuria and a proteinuria. From morphological investigations in small animal experiments (F.Recker et al., Urol. Res. 17: 229, 1989) it is known, that a rupture of the vv. arcuatae may be the cause of haemoglobin- and proteinuria. In our study we investigated the protein fractions and the electrolyte composition of the urine in patients, who were treated with ESWL. The aim was to get information on the degree and the localisation of the glomerular, tubular or vascular destruction caused by ESWL in man.

34 stone patients were treated once or several times with ESWL. As parameters we used: total protein, albumin, immunglobulin G, N-acetyl-ß-D-glucosaminidase (ß-NAG), α-1-microglobulin, fractional excretion of Na^+ and apolipoprotein-A-1.

After ESWL treatment a proteinuria and albuminuria occurs. Our parameters show no deterioration of the glomerulum or the tubulus. But the increase of apolipoprotein-A-1, a postglomerular parameter, supports vascular destruction after ESWL, but this comes to a restitutio ad integrum within 2-3 days. Sometimes even an improvement of kidney function is gained, especially in obstructed kidneys.

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Clinical introduction of a new 3rd generation lithotripter: Modulith SL 10/20 - characterisation and clinical experience

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More than 20 2nd generation lithotripters have been introduced for ESWL. Despite great technical progress, each machine still has its specific shortcomings. In collaboration with the Department of Urology Mannheim, the Storz Company has developed a new lithotripter whose design is aimed at overcoming these drawbacks.

Energy source: Electromagnetic cylinder with paraboloid reflector (40 cm) for focussing, providing a wide range of pressure (300-2000 bar) and a focal zone of 28 x 6 mm. The focal depth is max. 15 cm.

Coupling and positioning: Water cushion with patient lying on a specially-designed "acoustic cradle" consisting of an impedance-adapted foil. This is integrated in either a manually or automatically-operated stretcher.

Localization: Coaxial ultrasound probe for real time scanning and integrated C-arm with pulsed fluoroscopy using a virtual focus (moved along x-axis) for stone localization.

In 1989, we commenced with the first treatment based on our own in vitro and in vivo studies to determine the range of energy required for safe clinical application. With the first 71 patients, we treated 116 stones (91 caliceal, 18 pelvic and 7 ureteral). The mean generator voltage was 16 kV (10-18 kV). Successful disintegration was achieved in 66 patients (93%) employing an average of 2326 impulses (1000-3500). 17% of the treatments were performed without any anesthesia on lower generator voltage (10-15 kV), whereas the majority of calculi were treated under i.v. analgesia. The 5 failure cases included 2 stones in a caliceal diverticulum. Based on our good experience, we recently started with the treatment of biliary calculi.

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Combined PCNL-ESWL therapy in renal stones bigger than 3 centimeters.

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In a ESWL era the treatment of renal lithiasis bigger than 3 cm is still a controversy.
The aim of this work has been to specify what a complex lithiasis is in relation to the procedures to solve it.
We report results achieved with debulking PCNL associated to ESWL (sandwich procedure), which, in our opinion, has been the most successful.
Our reported serie consists of 500 Pts. of whom 30 underwent PCNL plus ESWL. Stone average size was 4.8cm.
At a three month follow-up 70% of cases were stone-free, 23% of cases were fragments bigger than 0.5 cm.
ESWL treatment average was 1.75.
Furthermore we report problems related to this technique: the interval between the procedures, urinary drainage, and priority of technique. Other parameters influencing the choice of the most suitable procedure are considered.

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Our experience in the treatment of lumbar ureteral lithiasis with ultrasound guided lithotripter (Sonolith 3000).

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The efficacy of ESWL in lumbar ureteral stones has been demonstrated since a long time. Ultrasound localization of ureteral calculi is more difficult than the radiologic one but with the latter Pts. and operators undergo a relevant Xray exposure. The aim of this study has been to evaluate the efficacy of an ultrasound guided lithotripter in lumbar ureteral lithiasis. 50 Pts. were treated. Ultrasound localization was feasible in 90% of cases and in situ ESWL achieved fragmentation in 33 out of 45 (73%) localized stones. Calculi larger than 1,5cm (3 cases) were by-passed with an ureteral catheter prior to be treated. Of those 17 Pts. for whom an in situ fragmentation was not achieved, 14 underwent a push-up procedure with 7 success (50%) 1 with ureteroscopy. Three Pts. went lost in the follow-up. The successful push-ups were stone-free after three months. In general ESWL was efficacious in 76% of cases. In 31 cases fragments were completely eliminated within 3 months, but 4 stones needed more than one session. When fragmentation was not sufficient or unsuccessful 3 Pts. underwent ureteroscopy and 7 a surgical procedure.In conclusion a lower localization (90% vs 100%) and a lower fragmentation rate (73% vs 98,5%) were achieved with ESWL treatment for ureteral stones compared to renal stones but the efficacy is comparable (75% vs 80%). This is probably due to a smaller size of ureteral stones and to an easier passage even of bigger fragments. Concerning the lower ureteral stones, the URS, achieving an higher percentage of success even with a slightly higher invasivity, is in our opinion more indicated.

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The Storz Modulith SL 20 - First Results of a third generation lithotripter

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The new developed Modulith incorporates a cylindrical acoustic source based on electro-magnetic principles combined with a parabolic reflector system with an aperture angle of 83°. The focal dimensions of lateral 6 mm and axial 30 mm combined with a pressure wave of 0 MPa up to 900 MPa seems to be perfect for the stone desintegration.
Since end of october 1989 there is a Modulith installed at the Urological Dept.of the University of Frankfurt. We started with only ultrasound guided localisation system but at the end of the year the machine will be upgraded with a x-ray system.
The ultrasound localisation system is incorporated in the shock wave source. For the x-ray localisation of ureter stones it is necessary to move the patient away from the shock wave source and after visualizing the stone, the patient is replaced to the focal point guided by a computerised system. This mode allows a good localisation of the stone combined with a high efficient shock wave.
We report on our experiences of about 100 patients with kindney and ureter stones according to the number of treatments, the desintegration rate and the crossover rate to our upgraded Dornier HM3.

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IN SITU ESWL - THE CHOICE OF TREATMENT FOR URETERIC STONES ?

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Currently there are several options available for the treatment of ureteric stones. These include Push Back and ESWL or antegrade ureteroscopy for upper ureteric stones and transurethral ureteroscopy for stones in the middle and lower ureter. A much less invasive technique is fragmentation of the stone by in situ ESWL and this paper describes the experience in one institution.

649 ureteric stones were treated by primary in situ ESWL using Siemens "Lithostar" lithotriptor which uses biplanar x-ray to locate the stone. Shockwaves are produced by electro-magnetic induction. All the treatments were given under local cutaneous anaesthesia. Stones in the upper and lower ureter were treated with the patient in the supine position. Stones in the middle ureter (i.e. medial border of L5 vertebra to below the sacro-iliac joint) were treated in the prone position. If there was no radiological change at all after the first treatment or if the fragmentation was less than 25% after the second treatment, alternate forms of treatment, described above were used.

78% of the stones could be successfully fragmented and the fragments passed with in situ ESWL alone. In 22% alternate methods had to be used either to remove unpassed fragments or unfragmented stone.

It is concluded that in situ ESWL is effective in the treatment of ureteric stones and should form the first line of management for ureteric stones.

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INTRARENAL PARENCHYMA LESION FOLLOWING ESWL- ITS PATHOMECHANISM AND DEPENDENCE ON APPLICATION FORM

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Investigations were performed to judge the questions: 1. What is the most vulnerable intrarenal structure and the pathomechanism following ESWL. 2. Does the extent of parenchyma lesions depend on the kind of shock wave (SW) application (single shot/double shot) and dosage of SW.
Material: In a first series, 54 Wistar rats were randomized into 3 groups which received 500,1000 or 2000 single SW with the DORNIER HM3 at 15 KV. A third a each group was sacrificed 24h, 7day or 35 days after ESWL. Immediately after ESWL and prior to necropsy, magnetic resonance imaging (MRI) was performed to jugde the course of intrarenal lesions. Histologic and scanning electron microscopic examination (SEM) followed. - In a second series 40 rats received the number of 600 or 1200 SW as single shot (SS) or double shot (DS). They were sacrificed 24h or 35 days later. The lesions were determined by the extent of intrarenal hematoma (24h group) or fibrosis (35 days group). In urine the functional renal tubular marker N acetyl-glucosaminidase (NAG) was determined in the different groups.
Results: The following pathomechanism is responsibe for longterm lesions: Ruptures of the Vv. arcuatae (documented by SEM) led to hematomas in the region of cortico medullary junction. This and its subsequent development of segmental fibrotic shrinking was detected by MRI. Interstitial fibrosis followed, which compressed the vessels, diminished the blood supply and leading to destruction of tubuli and glomeruli. - Results of the second series: Double shot is more vulnerable than single shot. The extent of intrarenal hematomas (25h) and fibrosis (35 days) enhanced ($p<0.02$) under double shot. Functional parameter NAG increased in DS compared to SS ($p<0.04$).
Clinically it is necessary to define high risk patients for intrarenal lesions. NAG seems to be recommendable for a course marker in ESWL.

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ESWL OF STONES IN THE MID URETER

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Although the initial experience with ureteral stones was less successful than with stones in the kidney, subsequent experience has shown that ESWL is a suitable and convenient method even for stones in the proximal and distal ureter. The major remaining problem, therefore, has been associated with stones in the mid ureter overlying the pelvic bone. The standard procedure to date has been push back or bypass. In case of failure an endoscopic procedure is required. Patients and Methods. Since 6.1987 1010 pts. have been treated with the Lithostar at our service, among these 220 pts. had a ureteral stone, which was located in the mid position in 61 pts. All treatments were done with sedoanalgesia only. Positioning was either supine or prone according visualisation. If the stone lodged in the mid ureter was unvisible in two projections contrast material was injected iv. The shock wave energy index was calculated. Results. In 80 % stone clearance achieved with in a few days. In 5 pts. disintegration was incomplete and additional endourologic manouvers were necessary. In the remaining pts. a second in situ-ESWL was done. In essence, this technique of primary ESWL for ureteral stones increates its applicability. It is of note, that the external treatment was done without regional or general anesthesia.

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COST-REDUCING IN ESWL TREATMENT BY USING REFURBISHED ELECTRODES

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At the department of Urology at Hannover Medical School we performed up to now more than 7000 treatment with a Dornier HM-3.The overall costs for original electrodes in 6819 treatments were appoximatly 2.5 millions DM.
In accordance to an new refurbishment process we compared refurbished and original electrodes. The in vitro experiments showed identical performance concerning stone disintegration in comparison with original electrodes using a standardizised test stone model. The usable life cycle and the pressure profiles in the second focus were also found similar to original electrodes.
In a randomized, prospective, doubleblind study we compared refurbished and original electrodes in patients-treatment.
The post-treatment follow up showed similar results in stone disintegration.Calculating the costs for refurbished electrodes and comparing them to original electrodes a cost reduction of 30 - 40 % can be reached without impaired quality of treatment.

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HISTOPATHOLOGICAL CHANGES IN RENAL AND PARARENAL TISSUE AFTER ESWL - A COMPARISON BETWEEN MODULITH AND HM-3

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At the department of urology at Hannover Medical School two generations of extracorporeal lithotrypters are in clinical use, the MODULITH (Storz Medical) and the Dornier HM-3. They differ in the production of shock-waves and in the principal of the focussing systems.
This study was set up to test wether the MODULITH because of its increase variability in shock-wave energie causes less trauma to the tissue.
Two comparable groups of rabbits underwent a standardized shock wave application with the MODULITH or the HM-3. The animals will be nephrectomized and parenchyma, capsula and pararenal tissue were investigated histological. Possible changes were recorded and judged as to their types and graduation.

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CLINICAL EXPERIENCE WITH THE DORNIER MULTIPURPOSE LITHOTRIPTER MPL 9000

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From March 1988 until May 1989 500 patients with 603 stones were treated with the Dornier multipurpose lithotripter MPL 9000. 61 % of the stones were situated in the calyx, 30 % in the renal pelvis, 1,3 % in the upper and 1 % in the distal ureter. 18,4 % of the stones were radiolucent. Multiple MPL treatments were performed in 8,6 %. In 6,2 % fragments post ESWL treatment were larger than 5 mm. In 93,8 % of the cases complete desintegration was achieved. 63,5 % of the treatments were performed without using analgesia or anesthesia. Intravenous anesthesia was used in 29 %. Analgesia and sedation in 13,6 %, general anesthesia in 1,7 % and epidural anesthesia in 1,1 %. After 3 months follow up 74,3 % were stonefree. Residual fragments were found in the upper calyx in 1 %, in the middle calyx in 5 %, in the lower calyx in 13 %, in the renal pelvis in 5,6 % and in the ureter in 1 %.
The MPL 9000 has been proven to be similar effective for the treatment of renal stones, while difficulties in localizing ureteral stones were noted. The major number of treatment was performed without any analgesia or anesthesia. No major complications were encounted. Due to the small focal area and the ultrasound location system. Special advantages were found for the therapy of children.

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ESWL-treatment of urinary stones in children

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Since 1984, 32 children (15 girls and 17 boys, age range 1 1/2 - 14 years, mean age 10 years) were treated by ESWL in a Dornier HM3 Lithotripter.
Two of the patients had cystine stones. Bilateral stones were treated in 4 cases. 27 children had renal pelvic and caliceal stones, 2 upper ureter and 3 lower ureter stones. In 6 children auxiliary measures were necessary. 10 children were stone free at the time of hospital discharge. Three months after ESWL, 90 % of the children were stone free. The pre- and posttherapeutic management required no other adaptions than to children's size.
There were no complications of treatment encountered. ESWL treatment of urinary stones is applicable to children and has proved to be safe and effective.

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ESWL-TREATMENT OF PEDIATRIC PATIENTS WITH THE DORNIER MPL 9000

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With the Dornier MPL 9000 in 1988 14 children, aged from 3 years to 12 years (X=8,6 years) were treated. Single stones were found in 11 cases and multiple stones in 3 cases. Three patients have had partial staghorn stones, the other concrements were located in the pelvic and caliceal regions of the kidney. General anesthesia was necessary in all patients (10 pat. with intubation and 4 under ketamine anesthesia). The mean treatment time was 45 min. (range from 14 - 17 kV) and the number of shockwaves 1800 (1400 - 2100). Multiple sessions (max. 3) were performed in 4 patients and single sessions in 10 patients. Antibiotic drugs were given intravenously due to fever post ESWL in 80 % of the patients. Nephrostomies for delayed passage of fragments and septicemia had to be placed in 3 patients. No endoscopic manipulations were necessary post ESWL. All patients were stonefree after three months follow up.
Prevention of damage to pulmonary tissue due to ultrasound "real-time-monitoring" and lack of x-ray exposure makes MPL 9000 the ideal choice for stone treatment in pediatric patients.

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EVALUATION OF PAIN IN PATIENTS TREATED FOR KIDNEY STONE DISEASE WITH LITHOTRIPTORS OF THE SECOND GENERATION.

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New second generation lithotriptors are available aiming at a painless treatment of stone patients without any anesthesia.
We have evaluated the physical discomfort of our patients treated without analgesics on two machines of the 2nd generation: Piezolith 2300 and Lithostar Plus.
We only evaluated first treatments of uncomplicated caliceal or pyelon stones. The total stone volume was < 1.5 cc in all patients. We registered the intensity of the patient's discomfort or pain at intervals throughout the treatment on a scale from 0 (= no pain) up to 20 (= unbearable). Informed consent was obtained from all patients prior to treatment.
49 first treatments of kidneys in 46 patients were carried out on the Piezolith 2300, none had to be discontinued. 4/17 treatments (16 patients) carried out on the Lithostar Plus had to be discontinued due to severe pain. In patients with completed treatment, the pain was described with both lithotriptors as moderate. The fragmentation rate in these patients was comparable. For uncomplicated, small renal stones, extracorporeal lithotripsy without any analgesics is possible, but moderate discomfort was observed in most patients.

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Shockwave treatment of ureteric stones with an electromagnetic lithotriptor

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During a 2 years period we have treated 426 patients out of 475 patients presenting with symptomatic ureteric stones with an electromagnetic lithotriptor. Anxiety and discomfort were relieved with diazepam and pethidin chloride only. Ureteral stenting was used in 8.1% of upper, 36.4% of mid- and 6.0% of lower stones. The retreatment rate was 12% for upper, 21.3% for mid- and 18% for lower stones but no patients had more than 3 sessions. The success rate of the treatment at three months was 88% for upper, 65% for mid- and 84% for lower stones. It appears that "push and smash" procedure would increase the stone free rate of patients with midureteric stones. Open surgery had to be performed in 5 cases and ureteroscopies in 10 cases.

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THE MOBILE LITHOTRIPTOR ONCE A WEEK

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Since September 1988 more than 200 treatments in case of uni- or bilateral nephrolithiasis were carried out by extracorporeal piezoelectric lithotripsy (EPL) at our departement. The treatment was done by a WOLF PIEZOLITH 2300-Lithotriptor, which had been placed at our disposal regularly once per week by a outstanding private enterprise.
Almost 15 % of the patients were treated ambulant the remaining 85 % had a short hospital stay within 2-3 days. All stones lying in the renal collecting system or in the pelvis renalis were treated by EPL, except staghorn calculi. In case of multiple calculi or a diameter 2cm we used a preoperative JJ-stenting. The lithotripsy was done without anaesthesia or infusions, we simply used to apply always a antiphlogistic perorally, no antibiotics were used regularly. 5000-7000 shock-waves were applied per session, sometimes even bilateral. Furthermore we report about our experiences with regard to the side-effects under treatment, the complications such as urosepsis, the number of treatments and the interval until free of stone, the frequency of residual fragments and the costs of treatment. We finally belive that the rotation system of placing a appropiated lithotriptor at one's disposal has been approved. In such a way even middle or small hospital units are able to realize a efficent and costeffective lithotripsy in nephrolithiasis, whereat ambulant treatment will become more frequent in the near future.

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Shockwave monotherapy of staghorn calculi

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From June 1987 to October 1989 40 staghorn calculi were treated by extracorporeal shockwave lithotripsy with the Lithostar R Siemens and evaluable. Multiple sessions (1 to 13) were necessary according to the stone burden and kidney function. The mean hospital stay for complete treatment was 8 days. Double J stenting was used in 45% of calculi of less than 40 mm and in 95% of calculi of more than 40 mm. After 3 months 63% of patients with calculi of less than 40 mm were free of stones and 39% with calculi greater than 40 mm. After 12 months the stone free rate raised to 78%. In the two groups five severe complications were observed : two acute infected hydronephrosis with sepsis and three perirenal haematoma. Extracorporeal shockwave lithotripsy monotherapy of staghorn calculi is possible in multiple sessions treatment. Double J stenting is mandatory in most of the cases but even in this condition intravenous sedation only is sufficient in 96% of patients.

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Extracorporal shock wave lithotrypsy with the LITHOSTAR plus. Clinical experience with a combined fluoroscopic and ultrasound guided stone localization.

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Since introducing the extracorporal shock wave lithotripsy for non-invasive treatment of renal and ureteral stones lithotripter units provided either fluoroscopic or ultrasound stone localization. While ultrasound stone localization reduces x-ray exposure and facilitates treatment of radiolucent renal stones fluoroscopic stone localization is superior in the treatment of ureteral stones.

Since April 1989 we are using the Siemens LITHOSTAR plus, a new lithotripter system, which provides both biplanar fluoroscopic and ultrasound stone localization using a separate electromagnetic shock wave generator for each localization system. From April 1989 to July 1989 108 patients were treated with the LITHOSTAR plus using ultrasound alone or ultrasound in combination with x-ray for stone localization 38 patients.

Thereby 1 of 2 staghorn calculi, 11 of 16 renal pelvic stones (68 %), all 10 stones in renal calyces (100 %) and 5 of 6 ureteral stones (83 %) were be desintegrated sufficiently.

These data show an equal desintegration ratio by LITHOSTAR plus as by other 2end generation lithotripter units. On the other hand the advantages of ultrasonic and fluoroscopic stone localization can be alternatively used depending on stone localization and stone formation. Therefore we believe that both localization systems should be present in optimal future lithotripter units.

Endourology

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8,5 F. FLEXIBLE URETERO-RENOSCOPY AND PULSOLITH LASER (TECHNOMED) LITHOTRIPSY IN URINARY STONES.

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The Pulsolith laser (Technomed) is a new flash lamp pumped tunable dye laser for urinary stone fracturization. For a 320μm fiber, the maximum possible out put energy is 160 millijoules with a pulse repetition frequency ranges from 1 Hz up to 10 Hz. The 320μm fiber's small diameter and flexibility allow the use of a small flexible uretero-renoscope like the 8.5 F Circom-Acmi endoscope. The combination of these two devices presents three major advantages :
- easy and quick ureteric dilatation,
- treatment of any stone laying in the entire course of the ureter event in the renal cavities,
- safety procedure without risk of ureteral distension and no effects on ureteral mucosa surrounding the stone.
The authors analyze the results of their first 50 consecutive patients. Despite of the learning curve, the results are good. In 80 % the flexible ureteroscope was reached in front of the stone and the location in the ureter does not influence the success. In 50 % the only laser application was enough to cure. In the other half, auxilliary procedures (dormia, pushback + pyeloelectric extracorporeal litho-tripsy) were necessary.

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Follow up of uretero-renoscopic stone treatment.

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From 1984 until March 1989 1375 patients were treated for ureteral stones, 50 % by ESWL, 7 % by open surgery, 28 % by sling basket and 15 % (n=202) by ureterorenoscopy. In 202 patients 224 ureterorenoscopic procedures were performed, in 30 % of these are primary treatment and in 70 % as salvage procedures after failed other forms of treatment, mostly ESWL. Age of the patients ranged from 5 - 88 years (mean 53 years). 54 % were males and 46 % were females. Insertion of the ureterorenoscope required ureteral dilatation in 31 % and no dilatation in 69 %. For stone treatment intraureteral ultrasonic lithotripsy was used in 15 %, electrohydraulic lithotripsy in 5 %, stone extraction without lithotripsy either for primary stones or for Steinstrasse in 50 % and stone push-back for subsequent ESWL in 30 %. Succes rate of the procedure was 86 %. Technical failure like inability to engage the ureter or to visulize the stone or unsuccessful stone manipulation were encountered in 7 % and acute complications like extravasation in 7 %. Pyelonephritis developed in 15 % and subsequent open surgery was required in 8.5 %. Ureteral stents were used in 84 % and left for 1-28 days. At discharge from the hospital 64 % of patients were stone free and 27 % still had fragments mostly after ESWL therapy. Follow up radiographic and ultrasonographic studies were performed in 138 patients after 6-60 months (mean 36 months). 73 % of the patients were stone free and 23 % had UTI. 82 % had normal upper tracts, 14 % had grade I-II hydronephrosis, 4 % had grade III-IV hydronephrosis and 7 % required subsequent treatment. In 1.5 % of voiding cystograms asymptomatic grade I reflux was detected, which did not require treatment in any case.
In conclusion, ureterorenoscopy has a higher complication rate than reported from ESWL and open surgical treatment of ureteral stones and should be reserved for salvage treatment of failed ESWL cases if open surgery is to be avoided.

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Distal ureteric stricture as a complication of ureterorenoscopic stone removal (URS) - results of a long-term study.

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Our results should be presented, since, so far, there has been only little information about the incidence, the causes and the consequence of ureteric stricture related to URS.
Patients, methods: Between 1986 - 1988, 66 ureteric stones in 64 patients had been completely removed. The stone sizes varied between 2 x 2 and 15 x 10 mm on the plane x-ray film. The mean operation time was 85 (15 - 180) min. 20 times (30,3 %) the distal ureter had to be dilated. In 64 of 66 URS urinary drainage was secured either by temporary percutaneous nephrostomies which were inserted preoperatively (20 %), by ureteric splints (41 %) or both (35 %).
Perforation of the ureter or ureteric disrupture did not occur.
The postoperative follow-up period was 1 to 3,5 years.
Results:
Incidence: 11 out of 66 URS (16,7 %) resulted in post-operative ureteric stricture which was always located in the prevesical-intramural section of the ureter no matter whether the removed stone was primarily located in the upper, the middle or the lover third of the ureter.
Causes: The most common factors causing postoperative ureteric stricture apeared to be preoperative dilatation of the distal ureter (63,7 %), a stone size larger than 10 x 7 mm (45,4 %), an operation time longer than 115 min. (45,4 %) and repeated operations (18,2 %).
Sequelae: 10 out of 11 strictures were completely healed by ureteric splinting for additional 4 - 6 weeks with or without antibiotics or cortisone. 1 stricture had to be incised endoscopically.
No stricture persisted or recurred.

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Late Results and Present Indications in Ureterorenoscopy

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Until September 1989 we performed 128 URS with the following indications:

62 pat. primary stone management
28 pat. "Steinstrasse" after ESWL
18 pat. unsuccessful loop
15 pat. urothelium tumors
3 pat. stenosis of the ureter
2 pat. dislocated stents

We use the 11.5 F rigid ureteroscope and try to avoid the dilatation of the ureter with bougies or balloon-catheters. Normally we place a double-j-stent for two weeks.
In two patients the ureter was perforated causing an open operation with new implatation of the ureter into the bladder.
Meanwhile we have a follow up of 50 patients up to 4 years after URS with i.v.P. and laboratory-datas. There is no evidence for ureteral strictures as the feared complication.
We see the main indication for ureterorenoscopy in the auxiliary management of urinary calculi after shock wave therapy and in diagnosis and treatment of urothelium tumors or ureteral strictures as well.
In the age of shock wave therapy we perform URS primary to remove ureteral calculi only in special cases.

Laserlithotripsy

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APPLICATION DEVICES FOR THE INTRACORPORAL LASER-INDUCED SHOCK WAVE LITHOTRIPSY USING A ND:YAG Q-SWITCH LASER

F Frank

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For the laser-induced shock wave lithotripsy the electromagnetic energy of a laser light pulse is converted intracorporally into the acoustic energy of a shock wave. The lithotriptor is based on a specially developed, Q-switched Nd:YAG laser whose high power light pulses (70 mJ, 25 ns) are coupled into a flexible quartz fiber with a core diameter of 600 um.

Using focusing elements energy densities higher than $6 \cdot 10^5$ J m^{-2} can be achieved resulting in an optical breakdown in water followed by a shock wave.

As a result of different absorption mechanisms the breakdown threshold can be decreased by placing a metallic target into the laser beam. The different shock wave formations of such opto-mechanical transducers have been measured. First clinical applications have been performed.

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EXPERIMENTAL AND CLINICAL EXPERIENCE WITH THE NEW 590 NANOMETER LASERLITHOTRIPTOR

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Recent clinical trials demonstrate the potential of pulsed dye laser lithotriptors to break ureteral stones.

In vitro experiments have shown the efficacy of our new 590 nanometer pulsed dye laser in stone disintegration. Immediate and late examination of mongol dog's ureters confirmed the absence of deleterious side effects.

Our experimental and our first clinical experiences will be summarized.

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Clinical experiences in dye laser lithotripsy.

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We report on the first clinical experiences in the treatment of patients with ureteral calculi by laser lithotripsy using a new developed dye laser system with integrated optical stone detection and feedback mechanism ("Triptognost", Telemit Electronic GmbH, Munich, FRG). This system is apt to detect stone contact and to release full energy for plasma and shock wave generation at stone contact, but not at tissue contact of the distal fiber tip to prevent trauma of the ureteral wall. The laser generates pulses of 540 nm of 30 to 90 mJ pulse energy at the distal fiber tip, the pulse duration is 1 to 3 μs. Indication for treatment were all uretral stones requiring endourological management not apt for ESWL in situ. Laserlithotripsy was performed either under visual control by uretroscopy or under fluoroscopic control only. Laser energy was transmitted through 200 μm "bare" quartz glass fibers introduced to the ureter via a 5 Fr. ureteral catheter with open tip. 53 patients were treated, 50% with calculi of the lower, 40% of the middle and 10% of the upper third of the ureter. Laserlithotripsy could be done in 42 patients, in 9 cases calculi were accidentally pushed back to the kidney by the guide wire or the ureteroscope before the lithotripsy started. We observed 2 technical failures of the laser system. 35 treatments were performed under visual control, 7 under fluoroscopic control. 26 calculi showed complete and 12 partial fragmentation and could be marked as treatment success. In 4 cases no fragmentation was seen.

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Experience with laser lithotripsy

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In our stone center laser lithotripsy of ureteral stones represents about 10% of the cases which are not able to be treated by shockwave lithotripsy.
We had the opportunity to use and compare three different lasers : Calculas (Storz) - Candela (Candela) - Pulsolith (Technomed). We will discuss the advantages and inconveniences of each device separately and give a theoretical outline of the ideal laser machine for treating ureteral stone which is not yet available.

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THE Q-SWITCHED AND PULSED ALEXANDRITE-LASER LITHOTRIPTOR - IN VITRO AND IN VIVO EXPERIMENTAL RESULTS

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The use of Laser-lithotripsy in association with small-diameter fiberscopes offers a promising alternative to ultrasonic lithotripsy with relatively large sized, rigid ureteroscopes. The pulsed, flashlamp-pumped and Q-switched Alexandrite Laser (Dornier Medical Systems, Munich, FRG) was investigated for its lithotriptic potential as well as for its effects on biological tissue in the porcine urinary tract. It emits a wavelength of 750 nm, with a pulse energy between 20 and 80 mJ/pulse. In association with a pulse duration in the hundred nanosecond range this system allows the use of 200 mcm fibers. The time, required to brake a stone into fragments smaller than 2 mm can be used as a measure for the efficacy of a lithotripsy system. Human stone material gained during percutaneous or open surgery was put into a rigid net with a pore size of 2 mm and was kept in normal saline for Laser-lithotripsy: Four Ca-oxalate-monohydrate stones (obtained from four different patients, two of which having undergone unsuccessful ESWL), two Cystine stones and two Ca-phosphate/struvite stones were tested. Stone size ranged from 7 - 20 mm (measured at largest diameter). Successful stone desintegration was encountered in all but one of the Ca-oxalate monohydrate stones (large stone with smooth surface). The time, required for stone-fragmentation ranged from 5 - 12 minutes (depending on the stone size and composition), with a 10 Hz repetition rate of the laser.

In 7 pigs laparotomy and cystoscopic Laser-exposition of the bladder and ureteric wall were performed under general anesthesia. 100 and 200 pulses of 25 and 40 mJ were applied in two identical sets both to the bladder and ureteric wall, with one set of specimens to be taken out at the time of operation and one set after 18.8 days (2-5 weeks) when the animal was sacrificed. Macroscopically, we observed a high degree of intramural bleeding connected with plasma-formations, increasing with energy and number of pulses applied. Even perforation occured combined with one or more plasma-incidents. Histologically, the primary changes consisted of hemorrhage, edema, capillary dilatation and some inflamation. The extend of changes was depending on the applied energy. Maximal changes were found in the muscular layer. Late changes were hemosiderin-deposits and capillary-proliferation as a result of tissue reparation. Only one animal developed some mild to moderate fibrosis in almost all specimens. Macroscopically there were no severe changes in the secondary specimens whatsoever and in particular no stricture-formation in the ureter.

In conclusion, the Alexandrite-Laser holds promise as an alternative for the treatment of ureteric and kidney stones not accessible to ESWL.

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Experience with a pulsed Nd: Yag Laser in the treatment of ureteral stones: application, effectiveness, side effects.

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After a successful in vitro-evaluation of the LASAG-prototype LASOLIT (Nd: Yag-Laser, 1064 mm) and a 300 µ-fibre-system, we treat most of the lower and even some upper ureteral stones by laser-lithotripsy (20+xcases). We use a normal flexible 10.5 fr. ureteroscope or an usual 11.5 fr. rigid ureteroscope with a specially developed guiding tube for the fibre and the irrigation. There were nearly no problems to smash the stones in a tolerable time. Stone propulsion into the renal pelvis was prevented by low laser-energies and by the simultaneous suction. We had no complications. On the contrary we observed extremely poor damage of the epithelium. X-rays 6 months later will demonstrate a free ureteral passage.