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ABSTRACTS

6th Eurolithiasis (eULIS) Society Symposium

14th European Symposium on Urolithiasis

15-17 October 2009 - Como

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Archives of Italian Urology and Andrology

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ORAL PRESENTATIONS

EPIDEMIOLOGY & RADIOLOGY

1 – THE ROLE OF RACE IN DETERMINING 24-HOUR URINE COMPOSITION AMONG WHITE AND ASIAN/PACIFIC ISLANDER STONE-FORMERS

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Objectives: To examine the differences in 24-hour urine composition between white and Asian/Pacific Islander stone-formers.

Materials and Methods: A retrospective review of a database of 24-hour urinalyses from a metabolic stone clinic was performed. Patients who presented for their initial metabolic stone workup and who were > 18 years of age were identified and included in the study if their race was marked as either White or Asian/Pacific Islander (Asian/PI) in the electronic medical record. Univariate analysis was used to compare 24-hour urine-composition between white and Asian/PI stone formers. Multivariate linear regression adjusted for possible confounders including age, gender, BMI, hypertension, diabetes mellitus, thiazide use, potassium citrate use, and 24-hour urine chemistries (volume, pH, calcium, citrate, creatinine, oxalate, magnesium, phosphate, potassium, sodium, sulfate, and uric acid).

Results: Three-hundred seventy-one (371) white patients and 91 Asian/PI patients were included for analysis. On univariate analysis, compared with white patients, Asian/PI patients excreted a significantly greater amount of uric acid and a significantly lower amount of citrate, magnesium, phosphate, and creatinine than white patients. On multivariate analysis, compared with white patients, Asian/PI patients excreted a significantly greater amount of uric acid (0.11 g/day, 95% CI 0.07 to 0.15), and had significantly lower urine citrate (-119.0 mg/d, 95% CI -201.7 to -36.2), phosphate (-0.07 g/d, 95% CI -0.12 to -0.01), creatinine (-97.6 mg/d, 95% CI -158.3 to -137.0), and volume (-0.2 L/d, 95% CI -0.4 to -0.04).

Conclusions: Significant differences exist in 24-hour urine chemistries between white and Asian/PI stone formers. Knowledge of these differences will be useful in the evaluation and treatment of these patients and prevention of stone recurrence.

** Marshall Stoller is a consultant for PercSys. Brian Eisner is a speaker for Boston Scientific.*

2 – WHAT IS THE DIETARY HABIT OF WOMEN WITH IDIOPATHIC CALCIUM NEPHROLITHIASIS? AN ITALIAN STUDY BASED ON NATIONAL INSTITUTE OF RESEARCH FOR FOODS AND NUTRITION (INRAN) RECOMMENDATIONS

Nouvenne A.[1], Prati B.[1], Guerra A.[1], Allegri F.[1], Deregibus S.[1], Dogliotti E.[2], Cossovich A.[2], Aloia A.[2], Rainone F.[3], Terranegra A.[2], Arcidiacono T.[3], Vezzoli G.[3], Soldati L.[2], Borghi L.[1], Meschi T.[1]

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Objectives: To assess whether: 1) the usual diet profile of patients with idiopathic calcium nephrolithiasis (ICN) living in a city in the North of Italy (Parma) is different if compared to healthy controls, 2) the dietary habits differ from INRAN guidelines, 3) the diet is related to nephrolithiasis clinical course.

Materials and Methods: 143 ICN women (mean age 43 years ± 13 SD) with no morbidity or interfering medications and 170 healthy controls (mean age 40 years ± 11 SD) were enrolled. All subjects compiled a 3 days dietary diary which was analyzed with a dedicated software (Dietosystem, DS Medica, Milan). To 51 stone formers and 72 controls was also administered a food frequency questionnaire for the last 60 days (Food Frequency).

Results: We found that: a) compared with controls, a significantly higher percentage of stone formers showed an higher consumption of sausages, meats and desserts as regards INRAN Guidelines (43.1% vs 11.1%, 29.4% vs 13.9%, 66.7% vs 18.1%, $p < 0.001$, Chi2 test) b) a significantly higher percentage of SF women compared to control group has a consumption of fruit and vegetables below INRAN recommendations (35.3% vs 18.1%, $p < 0.001$) c) as regards micronutrient, 3-d dietary diary analysis showed an intake of calories, carbohydrates, lipids and non-discretionary sodium about 10% higher respect controls ($p < 0.001$) and a lower intake of water ($p = 0.0003$). Finally, dividing the population into 3 age groups (≤ 30 years, 31-40 years, > 40 years) we found that the differences described above are amplified in the class ≤ 30 years where nephrolithiasis presents a more serious history (reduced recurrence interval, greater stone rate).

Conclusions: The ICN stone formers diet is significantly different from non SF and in particular it is characterized by reduced intake of fluids, fruits and vegetables and by an higher consumption of simple sugars and foods with high protein and salt content. This dietary imbalance could play a

primary role in the pathogenesis of the disease especially in younger subjects.

** Granted by Ministry of University and Research as part of a larger project about the prevention of kidney stones (PRIN 2005063822).*

3 – DOES MILD CADMIUM EXPOSURE ASSOCIATE WITH RENAL STONES IN THE GENERAL POPULATION?

Ferraro P.M., Costanzi S., Sturniolo A., Passalacqua S., Fulignati P.L., Naticchia A., Aureli F., D'Alonzo S., Porri M.G., Bonello M., Gambaro G.

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Objectives: An association between kidney disease and Cadmium was first noted at the end of the 19th century. Kidney stones are common among Cadmium workers. In Cadmium unpolluted areas, habitual cigarette smoking may create a serious source of mild chronic exposure to Cadmium. To investigate whether kidney stones are associated with mild Cadmium exposure we investigated the issue in the general population.
Materials and Methods: We thus analyzed data from the NHANES III adult population, a representative sample of the general United States adult population. Subjects have been stratified in quartiles based upon urinary cadmium levels. A multivariate regression analysis was performed. A number of possible confounding factors have been considered.
Results: The overall analysis included 15016 subjects older than 20yrs. In our stepwise multivariate regression model, age (odd ratio OR 1.018; $p < 0.000$), male gender (OR 1.669; $p < 0.000$), high blood pressure (HBP) (OR 1.354; $p = 0.001$), history of gout (OR 1.463; $p = 0.021$) did associate with history of renal stone(s). On the contrary, being Black or Hispanic conferred a protective effect (OR 0.322; $p < 0.001$ and OR 0.499; $p < 0.001$, respectively). Urinary Cadmium was not associated with renal stone(s) after adjustment for age, gender, race, smoking habits (former, active), HBP, CV Disease, DM, serum lead levels, serum creatinine > 1.5 mg/dL, gout, use of diuretics. The same regression model applied to recurrent renal stones.
Conclusions: Mild Cadmium exposure as that observed in the general population is not associated with an increased risk of renal stone(s). Smoking habits too are not associated. The study confirms the association of the renal stone disease with age, male gender, Caucasian race, HBP and gout.

4 – FRAGILTY OF BRUSHITE STONES IN SHOCK WAVE LITHOTRIPSY CORRELATES POORLY WITH CT-VISIBLE STRUCTURE

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Objectives: Shock wave fragility of both calcium oxalate and cystine stones has been shown to correlate with internal stone structure visible by helical CT. This study looked at brushite stones, a type of kidney stone that is especially resistant to shock wave lithotripsy.
Materials and Methods: Fifty-two brushite stones, ranging in size from 5 to 23 mm, were collected from discarded specimens from a commercial stone lab. The stones were characterized by micro CT, weighed, hydrated, and placed within a saline radiological phantom containing 3% iodine to emulate body tissue. The stones were scanned using a Philips Brilliance128 CT System, and the images evaluated by a radiologist for visibility of internal structural features. The stones were then treated with a Dornier Doli-50 lithotripter, and the number of shock waves needed to break each stone to completion was recorded. Fragments were analyzed using IR spectroscopy.
Results: The number of shock waves to break each stone, normalized to stone weight, did not differ according to CT-visible structure ($p = 0.19$). However, fragility of these stones did correlate with brushite content of the stone ($p < 0.001$), with stones of nearly 100% brushite requiring the most shock waves to break.
Conclusions: Unlike stones made of cystine or calcium oxalate, which have been shown to be more fragile when stone structure can be seen by CT, brushite stones did not have fragility to shock waves that correlated with internal structure that can be discerned using helical CT. However, the fragility of these stones did correlate with increasing brushite mineral content, which is consistent with clinical experience with brushite stone patients. Thus, apart from clinical history, there does not appear to be a way to predict which brushite stones will break well using shock wave lithotripsy.

PATHOGENESIS & CRYSTALLIZATION

5 – A NEW METHOD TO ANALYZE URINARY CRYSTALS

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Objectives: The study of a method for evaluating qualitative and quantitative crystalline phases in urines.
Materials and Methods: We have collected 1.5 L of urine from 40 patient of Nephrology Department of Pellegrini Hospital (Napoli), for consecutive 12 h. Urines were immediately freezed at -4°C and transported to Laboratory of Environmental and Medical Geology (Tito Scalo, Basilicata). The urines were centrifuged and after rinsing by distilled water, the solid residuals were weighted and wetted. The residuals have been analyzed by X-ray micro-diffraction. X-ray microdiffraction data were collected using a Rigaku D-max Rapid micro-diffractometer, operated at 40 kV and 30 mA. This instrument is equipped with a CuKα source, curved-image-plate detector, flat graphite monochromator, a variety of beam collimators, motorized stage and microscope for accurate positioning of the sample. The motorized stage allows two angular movements (rotation φ and revolution ω). The data are collected as two-dimensional images and then converted into 2θ–I profiles using the Rigaku R-Axis Display software. In particular, this analysis has been carried out by a collimator diameter of 0.3 mm and 20 minutes of collection time.
Results: The solid residue obtained from 1.5L urine has always resulted > 70 mg. The specimen attachment for powders has a volume of about 30 mm^3, and fine data collections are allowed filling only a half of the whole volume: this feature highlights the suitability of this instrument to analyze

samples with little material. The quantitatively analysis can be carried out adding a weighted amount of an internal standard to the powder sample, and refining the converted profile by Rietveld method.
Conclusions: This procedure has highlighted the powerful to analyze both qualitatively and quantitatively the crystals in the urines, avoiding any ambiguity in the phases identification. It is highly replicable and reliable.

6 – SPECIFIC BINDING OF OSTEOPONTIN TO URINARY AND INORGANIC CALCIUM OXALATE MONO- AND DIHYDRATE CRYSTALS

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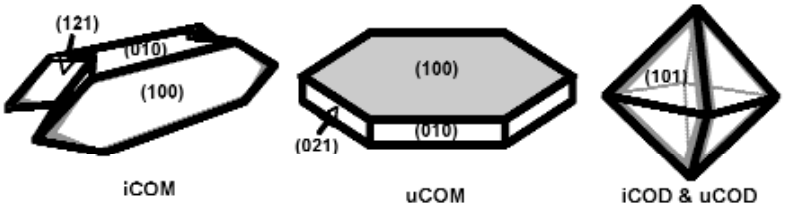
Objectives: To examine the attachment to, and incorporation of intact, fully phosphorylated osteopontin (pOPN) into inorganic and urinary calcium oxalate monohydrate (COM) and dihydrate (COD) crystals.
Materials and Methods: COM and COD crystals were precipitated from an inorganic solution and from ultrafiltered (UF) human urine containing pOPN purified from human milk and labelled with AlexaFluor 647. pOPN concentrations were 0.1-5.0 mg/L in urine, and 0.01-0.5mg/L in inorganic solution. Crystals were unwashed or rinsed with water or 0.1M NaOH to remove superficial OPN, and examined using fluorescent confocal microscopy and field emission scanning electron microscopy. Crystal protein content was analysed using SDS-PAGE and Western blotting: controls were COM and COD crystals precipitated from spun and filtered urine containing urinary OPN (uOPN).
Results: Shading depicts regions of the crystals to which pOPN bound.



Inorganic (iCOM) crystals: pOPN attached predominantly to the junction of the (100), (010) and (121) faces and to the edge between the (010) and (100) faces. It was removed by washing with water.
Urinary (uCOM) crystals: pOPN bound primarily to the (100) crystal faces and was not removed by washing.
Inorganic (iCOD) and urinary (uCOD) crystals: pOPN bound preferentially to the edges between adjacent (101) faces of both iCOD and uCOD crystals and was not removed by washing. SDS-PAGE and Western blotting confirmed that uOPN and pOPN were included in uCOD and iCOD crystals; pOPN, but not uOPN was incorporated into uCOM.
Conclusions: (i) pOPN binds to specific and different regions of inorganic and urinary COM and COD crystals; (ii) pOPN, but not uOPN, is incorporated into uCOM crystals: neither is included into iCOM crystals; (iii) Binding of OPN to urinary COM and COD crystals is dependent upon its degree of phosphorylation and is influenced by other urinary components.

7 – CRYSTALLURIC AND TUBULAR EPITHELIAL PARAMETERS DURING THE ONSET OF INTRATUBULAR NEPHROCALCINOSIS: ILLUSTRATION OF THE "FIXED PARTICLE" THEORY IN VIVO

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Objectives: The "fixed particle" theory states that, besides crystal formation in the tubular fluid, a phenotypically altered tubular epithelium with affinity for crystals is a prerequisite for the development of intratubular nephrocalcinosis. Whereas most evidence herto is provided by in vitro experiments, we set out to illustrate this theory in vivo.
Materials and Methods: We simultaneously investigated the temporal changes of nephrocalcinosis-associated parameters during and shortly after a 4 day ethylene glycol (EG)-administration period in rats. We measured oxaluria, crystal formation, crystalluria, apoptosis, epithelial injury/regeneration and luminal membrane expression of several crystal binding molecules hyaluronan (HA), osteopontin (OPN) and for the first time in vivo, annexin-2 (ANX2) and nucleolin-related-protein (NRP) and one of their receptors CD44 (HA/OPN-receptor). Clinically, renal biopsies of preterm infants, transplant patients and acute phosphate nephropathy patients were stained for ANX2, NRP, HA and OPN.
Results: In the presence of a rather constant and persistent intratubular crystal formation, crystal retention gradually increased during EG-administration and markedly increased after arrest thereof. All luminal membrane markers and a regenerating/dedifferentiated epithelium, unlike apoptosis, to various extents were upregulated and associated with crystal adhesion. Crystal containing tubules presented 40 ± 7%, 26 ± 11%, 33 ± 12%, 60 ± 12% and 44 ± 18% of ANX2-, NRP-, HA-, OPN- and CD44-expression, respectively. Additionally, both in humans and rats, expression of luminal molecules was not confined to crystal containing tubules.
Conclusions: The gradual increase in crystal retention indicates that the development of crystal adhesion requires more than just the mere presence of crystals in the tubular fluid. In addition, the fact that an altered epithelial phenotype was not confined to crystal containing tubules indicates that the expression of the crystal binding molecules under study is not specifically induced by intratubular crystal deposition. This is also supported by the partial expression of luminal markers in crystal containing tubules. Altogether, our observations corroborate that the currently investigated epithelial changes – known to be associated with crystal retention – are likely to precede crystal adhesion, and thereby support the "fixed particle" theory in vivo.

8 – ACTIVATION OF PI3-KINASE BY OXALATE MEDIATES MEMBRANE RECRUITMENT OF NADPH OXIDASE REGULATORY SUBUNITS AND REACTIVE OXYGEN SPECIES GENERATION IN RENAL EPITHELIAL CELLS

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Objectives: Hyperoxaluria is one of the major risk factors for urolithiasis. Oxalate-induced cellular injury plays a major role

in calcium oxalate crystal attachment and formation of kidney stones. Our earlier studies demonstrated that oxalate-induced NADPH oxidase (Nox) mediated reactive oxygen species play a significant role in the signal transduction leads to cell injury in renal epithelial cells. In this study we investigated the possibility that activation of PI 3-kinase by oxalate participates in the reactive oxygen species (ROS) generation via Nox subunits activation in renal epithelial cells.

Materials and Methods: Confluent monolayers of LLC-PK1 cells were pretreated with or without inhibitors (PI 3-kinase [LY292004; wortmannin] or Nox [DPI] or Rac1 [NSC23766]) were exposed to 0.5 to 1mM oxalate for different time periods. ROS (superoxide and hydrogen peroxide) production and cell injury (LDH release in media) were determined. Nox activity was determined by SOD-inhibitable cytochrome c reduction method. PI3-kinase activity was determined by ELISA. Nox subunits [Rac1, p67phox, and p47phox] membrane recruitment and p40phox (Thr 154) phosphorylation were determined by western analysis.

Results: Exposure to oxalate time and dose dependently increased ROS production and LDH release in LLC-PK1 cells. Pharmacological inhibition and enzyme activity assays revealed that Nox is one of the ROS inducing enzymic system involved in oxalate induced cell injury. Oxalate treatment rapidly induced the translocation of Rac1, p47phox, p67phox from cytosol to membrane and increased p40 phosphorylation. Inhibition of rac1 completely prevented the activation of oxalate-induced Nox activity and ROS generation. To evaluate the signaling pathways that mediate oxalate-induced activation of Nox, we studied the role of PI 3-kinase. Oxalate significantly increased PI 3-kinase activity in LLC-PK1 cells. Pretreatment with LY294002 or wortmannin significantly attenuated oxalate-induced Nox activity, ROS generation, cell injury, and prevented NOX regulatory subunit translocation.

Conclusions: Our data demonstrate that PI 3-kinase signaling pathway mediates oxalate-induced ROS generation by recruiting Nox regulatory subunits to the membrane thereby assembling the active Nox complex. Our data demonstrate that PI 3-kinase- dependent activation of NADPH oxidase might be one of the crucial mechanisms responsible for increased ROS generation in renal epithelial cells during oxalate toxicity and, therefore these pathways may represent a novel therapeutic target for patients with recurrent kidney stones.

Sources of Fund: NIH R01 DK 56249

9 – A COMPARISON OF THE INTRACRYSTALLINE PROTEINS OF URINARY CALCIUM OXALATE, HYDROXYAPATITE AND BRUSHITE CRYSTALS

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Objectives: To identify and compare the intracrystalline proteins of urinary calcium oxalate monohydrate (COM) and dihydrate (COD), hydroxyapatite (HA) and brushite (BR) crystals.

Materials and Methods: Crystals were precipitated from centrifuged and filtered healthy human urine. HA (pH 7.5, 20mM Ca) and BR (pH 6.0, 80mM PO_4) crystals were generated by incubation at 37°C for 6 hours. COM (pH 6.1, 2mM Ca) and COD (pH 6.1, 8mM Ca) crystals were precipitated by addition of oxalate and incubation at 37°C for 2 hours. Crystals were washed with water, examined using Fourier transform infrared spectroscopy and field emission scanning electron microscopy, and demineralised with 0.25M EDTA. Proteins in the resulting extract were identified by liquid chromatography mass spectrometry (LC-MS).

Results: Protein composition and abundance differed between urine samples. The table shows the top 10 proteins in each crystal type, based on their cross correlation value (Xc). The total number of proteins identified is shown in the last row.

COM	COD	HA[1,2]	BR[1]
keratin 1	keratin 1	albumin	keratin 1
calgranulin B	keratin 10	keratin 1	pro EGF
keratin 9	calgranulin B	uromodulin	osteopontin
keratin 10	hep S proteoglycan	keratin 9	ser protease inhib
prothrombin F1	α-1-μglobulin/bik	hep S proteoglycan	uromodulin
IgG κ var 1-5 chain	osteopontin	keratin 10	VIP36
syndecan-4	inter-α-inhibitor	calgranulin B	gelsolin
osteopontin	ser protease inhib	pro EGF	inter-α-inhibitor
calgranulin A	pro EGF	inter-α-inhibitor	collagen α-1(IV)
A-1-μglobulin/bik	ser prot inhib C1	keratin 2	hep S proteoglycan
Total 39 proteins	Total 47 proteins	Total 32 proteins	Total 62 proteins

Altogether, 180 distinct proteins were identified, only 9 of which were common to all four crystal types.

[1] Prothrombin fragment 1 detected in small amounts.

[2] Osteopontin (OPN) detected in small amounts.

Conclusions: (i) proteins bind differently and selectively to COM, COD, HA, and BR crystals formed in human urine; (ii) protein content does not reflect urinary abundance: albumin was present in COM and HA, but absent from COD and BR crystals; (iii) protein composition depended upon urinary pH and the thoroughness with which the crystals were washed, particularly for HA crystals, which were very small; (iv) differences in the binding preferences of urinary proteins for calcium oxalate and calcium phosphate crystals may influence their likelihood of intrarenal attachment and intracellular destruction, and thus, progression to stone formation.

PATHOGENESIS & TREATMENT

10 – RENAL PAPILLARY INJURY AND RANDALL'S PLAQUE

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Objectives: Results of histopathological studies indicate that idiopathic calcium oxalate (CaOx) kidney stones develop attached to renal papillary sub-epithelial deposits of calcium phosphate (CaP) called Randal's plaques. It has been indicated that these plaques are not associated with renal injury or inflammation (I&I), which is unusual because crystal deposition anywhere in the body generally provokes a cellular

response. In addition exposure of renal epithelial cells to both CaOx and CaP crystals in vitro also leads to cell injury. It is our hypothesis that the absence of injury and inflammation in association with interstitial crystal deposition in kidneys of stone patients indicates that they have become inactive and that the associated tissue injury has been resolved. We developed and tested our hypothesis in a rat model of renal crystal deposition.

Materials and Methods: Male Sprague-Dawley rats were given hydroxy-L-proline (HLP) mixed with chow. Rats in group 1 continued on hydroxy-L-proline for 63 days, while in group 2 rats stopped taking HLP after 42 days. Urine was collected and analyzed once a week for creatinine, calcium, oxalate, lactate dehydrogenase (LDH), 8-isoprostane (8-IP) and H2O2. Urinary pH and crystalluria were monitored. Rats were sacrificed on days 28, 42 and 63. Renal tissue was examined for crystal deposition and markers of inflammation osteopontin (OPN) and ED-1.

Results: All rats receiving HLP developed CaOx nephrolithiasis by day 42. Urinary excretion of LDH, 8-IP and H2O2, markers of stress and injury increased significantly. After HLP was discontinued there was significant decrease in urinary oxalate, 8-IP and H2O2 and half of the rats appeared crystal-free. There was significant staining for OPN in the epithelial cells lining crystal containing renal tubules 1. ED-1 positive cells were common in the interstitium. After discontinuation of HLP, there was a significant reduction in OPN staining and no ED-1 positive cells were seen.

Conclusions: Administration of hyperoxaluria lead to crystal deposition in the kidneys with the development of inflammation and associated degradation in renal biology. Discontinuation of HLP caused a decrease in urinary excretion of oxalate and reduced CaOx crystal deposition in the kidneys. As a result renal structure and function returned to normal with resolution of injury and inflammation. Results indicate that crystal deposition can be reversed, inflammation can be resolved and renal structure restored. Results also indicate that the absence of inflammation and injury at a specific time does not indicate its prior non-existence.

** Research Supported by NIH.*

11 – INCREASING WATER INTAKE BY 2 LITRES REDUCES CRYSTALLIZATION RISK INDEXES IN HEALTHY SUBJECTS

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Objectives: Urolithiasis occurrence has dramatically increased in the past decades in most western countries with a prevalence now reaching more than 10%. Whereas the benefit of increasing water intake has been proven in stone formers, its benefit on the urinary crystallization risk in healthy subjects exhibiting concentrated urines (i.e. at risk of urolithiasis), is unclear. The impact of drinking 2 additional liters of water per day on several risk factors for urolithiasis was studied in healthy subjects from two different countries.

Materials and Methods: Ninety-six healthy subjects (48 in Spain and 48 in Mexico) selected on the criteria of highly concentrated urine excretion, were randomly assigned (24 subjects in each group) either to consume 2L of FONTVELLA® water per day (Spain, group S1) or 2L of BONAFONT® water per day (Mexico, group S2) for 6 days in addition to their usual consumption of beverages or to keep their usual drinking habits (Spain: group T1; Mexico: group T2). At day 5, all micturitions were collected separately and the Tiselius ApCaOx index (Tis) was determined.

Results: Mean urine volume at baseline was 1.80 ± 0.56 and 2.18 ± 0.67 L/day for S1 and S2, respectively and was 1.98 ± 0.60 and 2.04 ± 0.69 L/day for T1 and T2. In first morning urine, mean Tis value was 2.00 ± 2.34 and 1.75 ± 3.71 for S1 and S2, respectively (NS) and was 1.89 ± 2.17 and 2.11 ± 3.51 for T1 and T2 (NS). On 24h urines, Tis was respectively 0.59 ± 0.74 and 0.16 ± 0.10 for S1 and S2 ($p < 0.01$, S1 vs S2) and 0.39 ± 0.25 and 0.19 ± 0.18 for T1 and T2 ($p < 0.01$, T1 vs T2). At day 5, mean urine volume was significantly increased: 3.20 ± 0.74 L/day in S1 ($p < 0.0001$ vs baseline), 3.31 ± 0.86 L/day in S2 ($p < 0.0001$ vs baseline) while urine volume was 2.05 ± 0.68 in T1 (NS vs baseline) and 2.12 ± 0.69 in T2 (NS vs baseline). Tis values in the first morning urine were 1.50 ± 1.67 and 1.36 ± 2.43 for S1 and S2, respectively and 4.24 ± 5.17 and 1.71 ± 2.40 for T1 and T2. Corresponding values in 24h urine were 0.14 ± 0.16 for S1 ($p < 0.001$ vs baseline), 0.08 ± 0.08 for S2 ($p < 0.01$ vs baseline), 0.66 ± 0.96 and 0.25 ± 0.25 for T1 and T2, respectively (NS vs baseline). Of note, mean Tis value in first morning urine of healthy subjects containing calcium oxalate crystals is 2.52 in our experience (n = 94, unpublished data).

Conclusions: Increasing diuresis by 1.1 to 1.4 litre in healthy subjects significantly improved the Tiselius Crystallization Risk Index evaluated in first morning urine and in 24h urine collections thus significantly decreasing the theoretical risk to develop urolithiasis.

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12 – OBESITY, METABOLIC SYNDROME COMPONENTS AND RISK OF KIDNEY STONES IN JAPANESE

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Objectives: Recent population-based studies conducted in the US, where obesity is very common, have shown a positive relationship between obesity, metabolic syndrome (MS) components and kidney stone formation. The aim of this study was to clarify associations between obesity, MS components and risk of kidney stones in Japanese population with low prevalence of obesity.

Materials and Methods: We analyzed total 1,112 people (566 men and 546 women) who visited Okazaki City Medical Association Public Health Center for comprehensive health examination from February 2006 to March 2008. Written informed consent was obtained from all participants.

Participants were measured height, weight, waist circumference and blood pressure. Self-reported history of kidney stones was examined, and fasting venous blood samples were drawn. Total cholesterol, triglyceride, high-density lipoprotein cholesterol, uric acid, fasting glucose, insulin and adiponectin levels were measured. Homeostasis model assessment ratio (HOMA-R) was also calculated to assess insulin resistance. Participants were diagnosed with MS defined by the Committee to Evaluate

Diagnostic Standards for Metabolic Syndrome in Japan. Multiple logistic regression analysis was used to estimate the odds ratio (OR) and 95% confidence intervals (CI) for self-reported history of kidney stones by sex.
Results: The mean ± standard deviation (SD) of age and BMI were 60.2 ± 10.3 years and 23.3 ± 3.0 kg/m^2, respectively in men and 56.1 ± 9.5 years and 22.2 ± 3.0 kg/m^2, respectively in women. Of the participants, 87 men (15.5%) and 37 women (6.8%) reported history of kidney stones. The MS was present in 96 (17.1%) of male and 27 (5.0%) of female subjects. For men, there were no significant associations between parameters and self-reported kidney stone disease. In contrast, BMI, waist circumference, systolic blood pressure and fasting insulin level were positively associated with self-reported kidney stones (OR (95% CI): 1.48 (1.10-2.00), 1.54 (1.11-2.13), 1.51 (1.07-2.13) and 1.34 (1.04-1.72), respectively) for women. HOMA-R and adiponectin levels showed no significant associations for self-reported kidney stones in total population.
Conclusions: Different from previous studies in the US, positive association between obesity and kidney stone disease was observed only in women, in the present study. It may be explained in part by the differences in the study subjects' ethnic backgrounds. For Japanese women, obesity was considered as an important risk factor for kidney stone disease.

13 – WITHDRAWAL OF SODIUM CHLORIDE AND SALT RICH FOOD FROM THE TABLE OF CALCIUM OXALATE STONE FORMERS WITH IDIOPATHIC HYPERCALCIURIA: A THREE-MONTH RANDOMIZED CONTROLLED TRIAL

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Objectives: To evaluate the effect of salt withdrawal for three months in patients with calcium nephrolithiasis and idiopathic hypercalciuria (ICN).
Materials and Methods: 210 calcium oxalate stone formers (150 M, 60 F) with idiopathic hypercalciuria (Ca > 300 mg/die in men and > 250 mg/day in women) were randomized to receive hydropinic therapy only (Fiuggi water) (group 1, n. 102, men 71, age 40 ± 10) or hydropinic therapy (Fiuggi water) and salt withdrawal (group 2, n. 108, 78 men, age 39 ± 9). All patients collected two 24h urine samples, one at baseline on usual free diet and one after three months of treatment, to determine urinary stone risk profile.
Results. No patient was lost to follow-up. Two patients assigned to hydropinic therapy only and 11 of salt withdrawal group left the study. Of these, 7 withdrew for treatment, in particular due to the salt removal: for taste intolerance (n. 4), dizziness and hypotension (n. 3). The good compliance to low salt diet was given by the difference in the two groups, after 3 month, in urinary sodium and chloride (Na: 68 ± 43 vs 200 ± 61, p < 0.001; Cl: 74 ± 62 vs 197 ± 70, p < 0.001). Moreover, group 2 compared to group 1 showed a significant reduction of the values of urinary calcium (271 ± 86 vs 361 ± 129, p < 0.001), oxalate (28 ± 8 vs 32 ± 10, p = 0.001), phosphorus (801 ± 237 vs 893 ± 245, p = 0,013), and urea (23 ± 8 vs 25 ± 6, p = 0,037). Furthermore a significant decrease of BMI was found (24 ± 3 vs 25 ± 3, p = 0,049).
Conclusions: Low sodium diet is highly effective in reducing urinary calcium excretion in patients with idiopathic hypercalciuria. Moreover, the salt reduction is accompanied by a significant decrease in other urinary stone promoters. Finally salt withdrawal is well tolerated and may help to achieve ideal values of BMI.

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14 – LONG TERM TREATMENT OF ADULT NEPHROLITHIASIS PATIENTS WITH HYPOCITRATURIA OR GOUTY DIATHESIS WITH POTASSIUM CITRATE

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Objectives: to evaluate the long term treatment with potassium citrate of patients with calcium oxalate o uric acid nephrolithiasis whose urine metabolic risk factors were hypocitraturia or gouty diathesis.:
Materials and Methods: We retrospectively reviewed the charts of 92 adult patients with recurrent renal stones whose urine metabolic risk factors were either hypocitraturia (HypoCit; n = 42) or gouty diathesis (GD; n = 50) who had been treated with potassium citrate 30 to 60 meq/d one or two times daily, for more than 3 months.
Results: Patients with HypoCit had a mean age of 44,1 ± 15,1 years, 22 males/20 females; patients with GD had a mean age of 49,4 ± 12,2 years, 33 males/17 females. Treatment median time was 8 months for patients with HypoCit and 11 months for patients with GD; mean dose of citrate was 47,1 ± 15,0 meq/day in HipoCit patients and 41,4 ± 14,7 meq/day in patients with GD. In HypoCit patients, potassium citrate therapy caused a sustained increase in urinary citrate (basal 237,7 ± 65,9 mg/24 hr to 449,7 ± 207,0 mg/24 hrs at last determination; p < 0,001) urine pH (Basal 5,73 ± 0,61to 5,92 ± 0,72 at last determination; p = 0,038) a decrease in urinary calcium (basal 166,8 ± 112,1 to 138,6 ± 68,4 at last determination; p = 0,048). Patients with GD had a significant increase in urine pH (basal 5,15 ± 0,19 to 5,57 ± 0,60 at last determination; p < 0,001), in urinary citrate (basal 668,7 ± 308,1 to 755,8 ± 372,1; p = 0,02) a decrease in urinary calcium (basal 198,3 ± 71,4 to 161,1 ± 72,3 at last determination; p < 0,001).
Conclusions: that potassium citrate effectively corrects metabolic derangements in patients with hypocitraturia and gouty diathesis with an associated decrease in urinary calcium and these effects were sustained in time.

STATISTICS, GENETICS & PAEDIATRICS

15 – PREDICTING FIVE-YEARS RECURRENCE RATE OF KIDNEY STONES: AN ARTIFICIAL NEURAL NETWORK MODEL

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Introduction: Tools for predicting the risk of stone formation have been searched by many authors, due to the high recurrence rates of urolithiasis. Artificial Neural Networks (ANNs) seem to fit well for this purpose. Our aim was to find a set of parameters able to predict the 5-years recurrence rate of stone formers.
Materials and Methods: Eighty idiopathic calcium stone formers, who had never followed any kind of therapy, were extracted from a database of 542 patients. Fifty-four were males (aged 46.37 ± 13.45 years) and 26 females (39.42 ± 13.00). Patients started a therapy including both general measures and personal therapy and they were recalled in the medical centre for periodical controls. After 5 years, patients were classified in two subsets: single stone formers (SSF) that were the 45 subjects (56.25%) without recurrence episodes and recurrent stone formers (RSF) that were the 35 subjects (43.75%) who presented, at least, a stone recurrence after baseline examination. Serum and urine lithogenic risk parameters were measured in all the patients at baseline.
Statistical Methods: Difference in baseline parameters between SSF and RSF have been evaluated by a traditional approach: a one way ANOVA was used and a P value lower than 0.05 was considered statistically significant. Afterwards three Discriminant Analysis (DAs) have been performed: standard, backward stepwise and forward stepwise. The standardized coefficients for canonical variables have been analyzed, in order to find the parameters in peculiar position. Logistic Regression (LR) accuracy, sensitivity and specificity were obtained for a comparison with ANNs results. Analysis have been performed using STATISTICA (STATISTICA, StatSoft Italia S.r.l., Italy).
Artificial Neural Network Methods: No commercial simulation software were used but an ad hoc simulation program was built up, starting from a general purpose computer language, C/C++ (C++ Builder Professional, Borland International, Inc., Scotts Valley, CA, USA). This way of work allows to interact and to trim ANNs in a deeper and more detailed manner. A Multilayer Perceptron (MLP) or best a Multilayer Feedforward Neural Network with Backpropagation algorithm was built up. The Delta Rule was used. The input layer was made up with serum and urine parameters. The output layer had a single neuron expressing the presence of recurrence of stone formation.
Results: Several ANNs have been built up, changing the input parameters, chosen among those suggested by conventional statistics. Best results have been obtained by using both plasma values of Na and K and urinary values of Na, P, Oxalate and AP (CaP) index. Once the optimal input parameters have been found, the best result were obtained by setting the Net with 4 hidden nodes. Both in training and testing sets ANN gave better results than LR. Accuracy increased of roughly 20% from LR (67,5%) to ANN (88,8%). While specificity did not change significantly, ANN almost doubled the sensitivity of LR (97,1 vs 51,4%).
Conclusions: ANNs cannot give any clear information about the biological role of the single parameters examined, as they are made to examine complex, non-linear problems. The ANN created to analyze our patients identified in serum Na and K as well as in urine Na, P, Oxalate and AP(CaP) index the parameters able to predict stone recurrence. Our ANN is a promising predicting algorithm and it suggests that a strong, non linear relationship, exists between analyzed parameters and stone recurrence episodes. Our ANN has been embedded in a software for Windows platform which that can be used to predict future risk of stone recurrences in a particular patient.

16 – CYSTINURIA IN EUROPE: FIRST RESULTS OF A NEWLY ESTABILISHED MULTICENTRE DATABASE

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Introduction: Cystinuria (CU) leads to recurrent urinary stone formation. Preventive measures rarely achieve long-term control. Aim of this study was to establish a European database that allows for analysis of current treatment modalities and to develop new therapies.
Materials and Methods: European Intra-Renal Surgery Society (EIRSS) members throughout Europe were asked to complete mailed questionnaires. All patients regularly seen were collected and recorded in a SQL database. Assessed parameters included: Age, family history, age at diagnosis, gene analysis, stone recurrences, history of interventional therapy, history and current medical/dietary stone prevention, functional data (blood and 24-hrs-urine lab, renal scintigraphy).
Results: 83 patients entered the database since October 2006. So far, 11 centres from six countries do participate (Germany, Austria, Italy, Great Britain, Sweden and The Netherlands). Mean age was 31.7 yrs. (6-72), gender ratio was 1.4:1 male/female. Only 6 patients had CU family history. Long-term f/u was available for most pat. with mean f/u of 22 yrs. (0-35). Stone formation rate is 0.58 stones/pat./year. First dx was made at mean age of 19 yrs. Current stone preventive measures were: none (2/83), diuresis only (3/83), alkalinization (44/83), ascorbic acid (12/83), tiopronin (32/83) and captopril (1/83).
Multiple procedures were performed in all pat. (mean/pat.): 7.2 SWL, 2.1 PNL, 2.6 URS, 0.7 open/lap. 2 patients underwent nephrectomy, 1 patient received a transplant kidney. Gene analysis was performed only in one patient.
Conclusions: This new multicentre database may contribute to a better understanding of pathophysiological mechanisms and to improve therapeutic approaches to optimize the management of cystinuria. The low number of cystinuria family history could indicate a high rate of spontaneous mutations. Gene analyses have to clarify this issue and could – after correlation with clinical data – be supportive in predicting the course of cystinuria. The common interventional therapies as well as the high rate of tiopronin and controversial drugs (e.g. ascorbic acid) underline the need for an optimization of treatment algorithms.

17 – CLINICAL COURSE OF PEDIATRIC UROLITHIASIS: FOLLOW-UP DATA IN A LONG-TERM BASIS

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Objectives: The clinical course as well as the natural history of stone disease in this children has not been well defined as it is in adults. In this present prospective study, natural course of stone disease from different perspectives including the spontaneous passage and stone recurrence rates were evaluated during long-term follow-up.

Materials and Methods: A total of 142 children were evaluated and followed in a long-term basis (> 5 years). In the beginning of the study, all children were divided into 2 groups with respect to the age (Group 1: 0 to 6 and Group 2: 6 to 15 years) and age at first presentation, stone localization and size, positive family history and the results of metabolic evaluation are all well recorded. Children were well followed with respect to spontaneous passage and recurrence rates, pyhsical growth rates and the size of affected and normal kidneys during long-term follow–up (> 5 years). Reasons and type of intervention during follow-up were also recorded. in an attempt to define well the above mentioned parameters.

Results: Metabolic risk factor data revealed either single or multiple abnormalities in 50% of the cases in Group 1 and in 38% of the cases in Group 2 patients. While stone recurrence has been noted in 44% of the cases in Group 1, this value was 31% in Group 2 and the obtained data did clearly demonstrate the profound effect of the presence of metabolic abnormality on this parameter where the average stone recurrence rate in children without any metabolic abnormality in the whole group was 14%, this rate approached 50% in children with an identifiable metabolic abnormality.While the spontaneous passage rate for renal calculi was 24% in group 1 and 50% in group 2; evaluation of the these rates for ureteral stones demonstrated higher stone free rates and the values were 63%, and 69% respectively in both groups.Of the stones that remained in situ (74.1% n: 23/31 in group 1, 50% n: 15/30 in Group 2) the overall stone re-growth rates in both groups was higher for renal calculi than ureteral ones as expected.A total of 58 children (46%) did require stone removal during follow-up period in both groups and Evaluation of the physical growth per centiles of the children in both groups did show a significant failure to thrive (< 3%) in the first group (11/48 children, 22.9%), this value was 11.5% (9/78) in the second group.

Conclusions: Stone recurrence in pediatric stones is an important consideration and the evaluation of metabolic risk factors is the basis of medical treatment aimed at preventing recurrent stone events and the growth of pre-existing calculi.

18 – RELAPSING CALCIUM LITHIASIS AND DENT'S DISEASE IN COMPARISON: A CLINICAL AND MOLECULAR STUDY OF A FOUR GENERATION FAMILY

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Introduction and aims: Relapsing calcium lithiasis is most frequent in males. Nephrolithiasis does not induce chronic renal failure with the exception of long term obstruction. Dent's disease is an X-linked recessive renal proximal tubular disorder. It is usually characterized by low-molecular-weight proteinuria, hypercalciuria, nephrolithiasis, nephrocalcinosis and progressive renal failure in males suffering from this disease. This pathology is associated with mutations in CLCN5 gene that encodes the renal chloride channel ClC-5 localized in the endosomes. Metabolic-instrumental study of nephrolithiasis was carried out in a family where some members had Dent's disease and others had microlithiasis in order to compare the two nephrolithiasic forms.

Materials and Methods: Twenty-six out of the 52 members belonging to 4 generations have been subjected to molecular analysis of CLCN5 gene. Metabolic study of the nephrolitiasis consisted in: evaluation of the creatinine, uric acid, Ca, P, Na, K, Cl, Mg both at the plasmatic and urinary level, pH haematic (venous); PTH, osteocalcina, vit. D3, bone ALP at the plasmatic level; in the 24-h urine excretion: α1 microglobuline, oxalate (Ox) and citrate. Instrumental survey involved renal ultrasonography and densitometry.

Results: Genetic analysis showed in 8 males out of 11 and in 11 females out of 15 a non conservative missense mutation Gly260Val. The metabolic study carried out on 9 subjects (3 mutated M, 3 heterozygote H, 3 not mutated NM) showed in 5 (3M, 1H and 1NM) hypercalciuria; in 6 (3M included) hyperphosphaturia, hypersodiuria and hyperuricuria; in the 3 patients with the mutation the hyperuricuria was associated with hyperuricemia; in 5 (2M, 2H, 1NM) hyperossaluria; in 2 (1M and 1H) hypocitraturia. None of the 9 patients showed hypomagnesiuria or hypomagnesiemia. All patients had a normal level of PTH, Osteocalcina, bone ALP, and Creatinine Clearance. Renal ultrasonograpghy revealed that all subjects had microlithiasis and in 8 of them it was bilateral. Densitometry showed moderate demineralization at the lumbar level which was not connected with the mutation. Some interesting correlations were found: inverse between TmPO4/VFG vs UPO4; direct between EFNa/ UNa; UNa/ UPO4, UCa vs UPO4; UNa vs UCa. The direct relations between UOx vs Ucitrate and UOx vs UMg were unexpected.

Conclusions: The presence of microlithiasis in M subjects is characteristic of Dent's disease in this family as shown from the results of the metabolic study (hypercalciuria, hyperuricuria, hyperphosphaturia, hyperossaluria); microlithiasis was unexpected in heterozygotes and in the non mutated subjects. Indeed, in mutated and not mutated subjects, the results from both metabolic and instrumental study were comparable.

These data demonstrate that in this family microlithiasis is not correlated to the mutation. In the second generation (average age 70), M patients had both nephrolithiasis and chronic renal failure as expected from the natural history of the disease. However, none of the members of the 3rd generation (average age 40) had renal failure including the 3 mutated patients. It is also significant to point out that hyperuricemia that was present in these patients associated with hyperuricuria, is not reported as a Dent's disease related characteristic. Furthermore, it cannot be considered a secondary effect since it was not accompanied by renal failure.

19 – GENETIC POLYMORPHISMS OF THE CITRATE CARRIERS ARE ASSOCIATED WITH CITRATE EXCRETION AND STONES

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Objectives: Citrate transport in proximal tubule is mediated by two carriers. NaDC1 is a low affinity carrier sited on the apical membrane and coded by SLC13A2 gene (17q11.2). NaDC3 is a high affinity carrier located on basolateral membrane and coded by SLC13A3 gene (20q12-13.1). Both carriers transport dicarboxylate acids within the cells coupled with 3 sodium ions. NaDC1 and NaDC3 gene polymorphisms are candidate for citraturia and calcium kidney stones.
Materials and Methods: Three SNPs on SLC13A2 (rs3764866, rs2191090, rs7503430) and six on SCL13A3 gene (rs6063003, rs761218, rs389905, rs847058, rs383551, rs2425883) were genotyped in 459 stone formers (F/M 185/274) and 405 controls (F/M 252/153).
Results: The analysis of allele frequency in all participants showed that the variant allele (defined as the rarer allele) at rs389905 (T > G) was significantly less frequent in stone patients than controls (31% vs 36%, chi square test, p = 0.031). The variant allele at rs383551 (G > T) was less frequent in hypocitraturic than normocitraturic subjects (both groups included patients without or with stones) (21.6 vs 30.2%, p = 0.02). Both SNPs were located on SCL13A2 gene. Citrate excretion was higher in homozygous subject for the variant allele at rs383551 (670 ± 47, n = 35) than heterozygous for the variant allele at rs383551 (585 ± 18.8 n = 190, ANOVA with Tukey test, p = 0.04) or homozygous for the common allele at the same SNP (535 ± 16.2 mg/24 h, n = 239, p = 0.005). The same trend was observed in stone patients (ANOVA, p = 0.049).
Conclusions: Our findings suggest that polymorphisms of SCL13A2 gene are associated with citrate excretion (rs383551) and calcium stones (rs389905). rs383551 is associated with increased citrate excretion and we speculate that it is a marker of low citrate reabsorption.

POSTER A

EPIDEMIOLOGY, WATER & DIET, URETERAL PHYSIOLOGY, CRYSTALLIZATION, STONE ANALYSIS

20 – RECURRENCE RATE AND PLACE OF DOMICILE IN STONE PROPHYLAXIS

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Objectives: Patients with stone disease after stone retrieval are usually sent home wth short term alkalinizing therapy. The recurrence rate in such situations appears to be very high. It is usually complained that the compliance rate is poor among patients with stone disease. WE had reported earlier that the incidence of stone disease is greater in Gulf returned Keralites compared to the local natives. The study was undertaken to find out the difference in recurrence rate of stone disease between the two groups.
Materials and Methods: 2000 randomly selected patients, who had attended the stone clinic for metabolic assessment and were given appropriate chemoprophylactic and dietetic advice and were followed up for a minimum period of 2 years were classified into Gulf returned and natives. At the latest visit, they were assessed for the presence of symptoms and recurrence of radiological/USS evidence of stone disease, urine deposits and 24 hour urine and blood metabolic risk status. Recurrence was considered when the patients were getting pain typical of stone disease, haematuria without other obvious causes, significant crystalluria on studying urinary deposits, presence of radiological stone or ultrasonically recognized stone > 5mm. Compliance was considered as totally compliant atleast for a minimum period of last two years, intermittent, when the patient stopped prophylaxis and restarted at the onset of symptoms, irregular, where the patient consumed medicines at random and non compliant, where the patient stopped drugs completely. The recurrence rate and degree of compliance were compared between the two groups using appropriate statistical tests.
Results: The period of follow up ranged from 2 to 8 years. 62% of the patients were domiciled in the Gulf countries and made visits to the clinic at intervals of 1 to 2 years. Among the Gulf patients, the compliance rate was 93.8% compared to 37.4% among the natives (P < 0.001). The recurrence of urinary symptoms in the Gulf patients was 13% as against 57% in the natives (P < 0.001), presence of significant urinary deposits 3% against 22% (P < 0.001), Radiological stones 2% against 8% (P < 0.001) and USS stones 4% against 13% (P < 0.001).
Conclusions: It is concluded for the study that the compliance rate was very high in the Gulf domiciled patients compared to the natives. Recurrent of symptoms and presence of urinary deposits were significantly higher in the natives. This was evident in the patients who were not compliant with the prophylactic advice. Proper prophylaxis against stone disease yields significantly good results in prevention of further stone formation.

21 – THE IMPACT OF POSITIVE FAMILY HISTORY ON THE AGE AT ONSET AND NATURAL COURSE OF STONE DISEASE

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Objectives: To evaluate the possible effect of positive family history on the age at the urinary stone disease onset and the frequency of symptom episodes related to stone disease.
Materials and Methods: Between March 2006 and April 2009; a total of 1595 patients with a previous diagnosis of stone disease were asked to fill an inquiry. Depending on the family history positivity patients were divided into two groups as follows; Group I included 437 (27.4%) urinary stone patients with positive family history and Group II included 1158 (62.6%) patients without a positive family history. A questionnaire is designed to obtain particular data regarding the age at the onset of stone disease, previous stone passage and interventions, time to first recurrence, number of total stone episodes, recurrence intervals, the number and

the type of the family members suffering from the same disease. Patients with one or more previous episodes of stone disease were defined as recurrent stone formers. The data were analyzed by using the SPSS 15.0. Statistical analysis were done by t-test and chi-square.
Results: Mean age in the whole group was 41.7 years (14-69 years). Male/female ratio was 1.38 (926/669). Of the 1595 patients referrred, 437 had a positive family history (27.4%). In Group I, 40.7% of the males (n: 178) and 59.3% of the females (n: 259) had positive family history. Female patients tended to have higher rate of family history positivity (F/M: 1.45). Patients with positive family history seemed to be affected by the disease at relatively younger ages (with a mean age of onset 24.8 ± 9.66 years in males and 26.1 ± 9.72 years in females) when compared with the patients without positive family history.
Patients in Group I had relatively more often stone episodes from the onset of the disease when compared with the patients in group II. In Group I, male patients seemed to have more stone episodes within the same period when compared with females. While the majority of the patients in Group II did have only one stone episode without any further recurrence; the percentage of patients having 2-5 recurrences as well as more than 5 recurrences were significantly higher in group I.Mean time interval between reccurrences has been noted to be significantly shorter in Group I (25.4 ± 9.66 months in males and 27.3 ± 9.72 in females) when compared with the patients in Group II (34.6 ± 12.3 months in males and 33.9 ± 11.4 months in females). There was no statistically significant difference between the chemical composition, location, size and the number of stones in both groups. The number of previous interventions were higher again in Group I patients (74.1% vs 59.1%) than the patients in Group II. Lastly; incidence of co-morbidities (hypertension, diabetes, hypercholesterolemia etc.) were higher in Group I (30.4% vs 18.2%) patients when compared with Group II patients.
Conclusions: Our data did show that urinary stone formation begins at relatively younger ages and frequency of symptom episodes is significantly higher in the patients with positive family history. We believe that the positive family history for urinary stone disease is strongly predictor for the age at the disease onset and frequency of symptom episodes and these patients should be followed more carefully to preserve renal function and to prevent stone recurrence both in pediatric and adult population.

22 – EPIDEMIOLOGIC SURVEY OF NEPHROLITHIASIS PREVALENCE: A MODEL OF STUDY IN THE FLORENCE AREA BY MEANS OF GENERAL PRACTITIONER'S INVOLVEMENT

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The epidemiological study of nephrolithiasis is particularly complex due to the difficulties connected to two sets of problems 1) the difficulty of collecting case histories, particularly if the collection is carried out by non specialized personnel or if the questionnaire is completed by the patient himself 2) the difficulty of identifying asymptomatic forms, which would make it necessary to investigate the population being studied with large-scale x-ray or ultrasound tests. Most of these difficulties could be overcome by involving the General Practitioner (GP) in this type of survey. The GP undoubtedly represents the best epidemiological look-out of this type of illness, which he cannot fail to become aware of either during diagnostic check-ups carried out for other purposes or in the patient's case history.
This study concerns a model of epidemiological survey currently being adopted in the Florence area. The data are obtained by a statistically sufficient number of GPs (GEA, Florence) by means of a specific questionnaire on a randomized sample of their patients. The main goal of the survey is the determination of the prevalence of nephrolithiasis in the population being studied. All the informations gathered with the questionnaire will subsequently make it possible to proceed, with a further processing of the data, for the purpose of observing any link between some of the features of the analized population and nephrolithiasis.

23 – FOOD QUALITY AND CO-MORBIDITY IN THE KIDNEY STONES: OBSERVATIONAL CASE-CONTROL STUDY

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Introduction: Kidney stones (KS) are a multifactorial disease and different causes contribute to the development of this disease.
Objectives: an observational case-control study on KS was performed, evaluating different risk factors and trying to find correlations to the development of the disease.
Materials and Methods: Databases of 10 General Practitioners were evaluated and cases of KS were recorded. Risk factors included: gender, age, Body Mass Index (BMI), food intake, familiarity, goiter, water type intake, and other co-morbidities. Height and weight were evaluated and BMI was calculated. Also water type and food intake were evaluated considering urate, oxalate and natrium intake.
Results: 513 cases are recorded: females 51.9% (266), males 48.1% (247), average age 59.1 years; control group includes 515 patients, 53% females (273) and 47% (242) males, with average age 58.6. There are not significant differences in the two groups as far as age and gender ($p > 0.005$). The 27.7% of cases and 10.9% of controls have positive familiarity for KS ($p < 0.001$); 13.5% of cases versus 4.5% of controls have goiter (risk factor, $p < 0,001$); there is no positive correlation with overweight and obesity; use of mineral water is a protective factor versus use of tap water ($p < 0.001$), while oligo-mineral water is a risk factor ($p < 0.001$). Vascular hypertension (VH) is correlated to KS ($p = 0.04$), to age ($p < 0.001$) and to co-morbidity ($p < 0.001$). The multivariate analysis shows that co-morbidity are still related to KS, while there is not significant correlation among KS and VH. The 73.1% (375) of patients versus 58.3% (300) of controls have at least another pathology: co-morbidity is a risk factor for KS ($p < 0.001$). Analysing co-morbidity: while there are no correlations between diabetes, cardiac diseases, arthrosis, digestive pathologies and KS; nephro-urinary pathologies, chronic obstructive lung disease and tumors are risk factors for KS. Urate-rich diet and some oxalate-rich foods appear protective factors.
Conclusions: co-morbidity is a risk factor for KS, while the correlation between KS and VH loses statistical significativity if age and co-morbidity-corrected. Data concerning water and food intake may be the consequence of KS as secondary preventive measure.

24 – ON THE RELATION BETWEEN DIET AND URINARY STONE RISK FACTORS IN RECURRENT CALCIUM OXALATE STONE FORMERS AND HEALTHY SUBJECTS

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Introduction: The exact role of the diet in the pathophysiology of calcium oxalate (CaOx) stone formation remains to be elucidated. The aim of the present study was to analyse cumulative frequency distribution curves of urinary stone risk factors and activity products of CaOx and calcium phosphate (CaP) in urines of recurrent male CaOx stone formers and healthy males while maintained on free-choice diet.
Materials and Methods: 118 recurrent male CaOx stone formers and 122 healthy males were included. The participants were asked to keep a 7-day food record. 24-h urines were sampled on a week-day without dietary restrictions. Urine was analysed and the risk of CaP and CaOx crystallisation was estimated by means of the AP(CaP)- and the AP(CaOx)-indices according to Tiselius. Data was analysed using cumulative frequency distribution curves and multivariate analysis.
Results: There were no differences in fluid intake and dietary intake of minerals and major nutrients between stone formers and healthy subjects. The cumulative frequency distribution curves of urinary calcium excretion and the AP(CaP)- and AP(CaOx)-indices were significantly displaced to the right in the stone formers compared to controls. The curve for urinary citrate excretion was significantly displaced to the left. Performing a multivariate analysis the characteristic of the male stone formers that most clearly distinguished them from the healthy men was a high level of urine calcium for any given level of citrate.
Conclusions: There seems to be no major differences in the dietary habits of male CaOx stone formers and healthy males. It may be considered, therefore, that a 'western' diet alone does not cause stone formation, and that the stone formers must have some metabolic abnormality to account for their susceptibility to form calculi. The differences between male stone formers and healthy males in the present study may be indicative of an altered metabolic response to protein catabolism.

25 – IMPACT OF DIETARY HABIT IN RECURRENT STONE FOMATION

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Objectives: To evaluate the dietary habits of patients with first time kidney stoneformers as well as the recurrent formers and to assess the impact of nutritional risk factors.
Materials and Methods: Sixty six stone formers were prospectively enrolled in this study. Of these cases, while 25 patients had recurrent kidney stone history (%38),41 were first time stone former (%62). All patients were well evaluated with questionaries inquiring medical history, sex, age at onset, body mass index and dietary consumptions.
Fluid, alcohol, salt, animal protein, oxalate rich food (cocoa, black tea, coffee, whole wheat bread, nuts, peanuts, pecans, nut oil) consumption along with the BMI and metabolic status is well recorded. Data recorded in two groups were comparatively evaluated.
Results: The mean age of whole patients was 42,77 ± 13.89 and there was no difference between reccurent stone formers and the their counterparts. Also no statistical significance was found between two groups regarding BMI and daily salt intake. But the patients with recurrent stone history had significnat lower water intake, higher daily alcohol consumption as well as higher animal protein intake.
Conclusions: Dietary factors may play an important role in stone formation especially in patients with recurrent stone formation. Strict dietary follow-up is mandatory for this group of patients in an attempt to limit possible stone recurrence.
However patient motivation and ompliance are also importatnt factors for a successful outcome

26 – UROLITHIASIS AND THE QUALITY OF WATER

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This research was carried out to evaluate ionic concentrations in the waters of rivers from the localities of Santa María de Cariaco, Cancamure, and Tataracual in the state of Sucre, Venezuela and in the blood samples of the inhabitants of those places. To achieve this goal twelve water samples were taken from different spots of the previously mentioned rivers. Furthermore, 100 blood samples taken from people living adjacent to those rivers were analyzed.
Water samples were kept in plastic material, cleansed with nitric acid at 10%, poured into polyethylene bottles and frozen (-20 ºC) until the moment of determining calcium, magnesium, iron and phosphorus ion concentrations. Blood samples of persons living adjacent to the rivers were taken by venous puncture and then placed in dry, sterile test-tubes which were left to stand and centrifugalized at 3,000 r p m for 10 minutes to obtain blood sera, in which calcium, magnesium, iron and phosphorus ion concentrations were determined. The quantification of phosphate ions was performed by the peroxidisulphate- boric acid system.
The calcium, magnesium, and iron ions were determined by atomic absorption spectrophotometry using no flame. Determinations of ionic concentrations in the blood of river inhabitants were performed in the following way: calcium by the o-cresolphthalein-complexone method without deproteinization, magnesium by the sulphonated magon method, iron by serum spectrophotometry and phosphate by the molybdate procedure.
The simple anova statistical analysis applied to the mean values of ion concentration measured in the water samples of the rivers mentioned previously show highly significant differences for calcium ($Fs = 63.92$; $P < 0.001$), magnesium ($Fs = 23.46$; $P < 0.001$), and phosphorus ($Fs = 30.23$; $P < 0.001$) ions, and significant differences for iron ions ($Fs = 4.59$; $P < 0.05$). In blood ions highly significant differences were found for calcium ion ($Fs = 9.34$; $P < 0.001$), very significant differences for iron ($Fs = 6.70$; $P < 0.01$) and phosphorus ($Fs = 6.58$; $P < 0.01$) ions, and significant differences for the magnesium ion ($Fs = 2.73$; $P < 0.05$).
It can be concluded then that the waters of the rivers from these localities are polluted by domestic and industrial wastes, sewage channels, fertilizers, pesticides and thus cannot be employed as drinking water since they are potentially lithogenous.

27 – APPLICATION OF SKIN ELECTRICAL CONDUCTANCE OF ACUPUNCTURE MERIDIANS FOR URETERAL CALCULUS: A CASE REPORT

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Objectives: Renal colic caused by ureteral stone is a common condition in the emergency department (ED). This study reported the possible application of skin electrical conductance of acupuncture meridians for patients with ureteral calculus.
Materials and Methods: We described a 30-year-old male with a left ureteral calculus who presented with frequency and normal-looking urine. He had ever visited the outpatient department, but in vain. Normal urinalysis and non-obstructive urogram were told at that time. Then, he went to ED due to abdominal pain of the left lower quadrant 2 days later. In the ED, urine analysis was rechecked again. Urinalysis did not detect red blood cells in the urine. The ultrasonography also did not found hydronephrosis.
Results: The meridian energy analysis device was used to get the patient's information. The meridian electrical conductance and index of sympatho-vagal balance were abnormal. Significant high ratio of left to right side bladder meridian was also found. The unenhanced helical computed tomography was arranged and left ureterovesical stone was found. Ureteroscopic intervention was smoothly practiced later, and the pain was relief. The follow up measurements showed the meridian parameters returned to normal one month after treatment.
Conclusions: The case suggests that the bladder meridian electrical conductance, especially the index of sympatho-vagal balance, may be used as valuable predictors of elective intervention in patients with ureteral calculus.

28 – ENDOLUMINAL ISOPROTERENOL IRRIGATION DECREASES RENAL PELVIC PRESSURE DURING FLEXIBLE URETERORENOSCOPY. A CLINICAL RANDOMIZED, CONTROLLED STUDY

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Objectives: Irrigation during ureterorenoscopic procedures causes increased pelvic pressure (PP) which may lead to intrarenal backflow with potential harmful consequences. This study aims to investigate PP response to intraluminal administration of isoproterenol (β-agonist; ISO) during flexible ureterorenoscopy.
Materials and Methods: Twelve patients admitted for Retrograde Intrarenal Stone Surgery (RIRS) were included. Patients were randomized to 1) irrigation with saline (n = 6) or 2) irrigation with ISO 0.1 μg/ml (n = 6). Irrigation rate was standardized to 8 ml/min. A ureteral catheter was retrogradely placed in the renal pelvis for PP measurements. PP, heart rate (HR) and mean arterial blood pressure (MAP) were measured.
Results: Baseline PP was 12.1 (± 4) mm Hg in the saline-group and 10.3 (± 4) mm Hg in the ISO-group (p = 0.44). In the saline-group PP increased to mean 33 (± 12) mm Hg during ureterorenoscopy. In the ISO-group PP was mean 19 (± 3) mm Hg (p = 0.029). During endoscopy PP peaks as high as 328 mm Hg were noted during saline irrigation. The number of pressure peaks above 50 mm Hg were minimized dramatically during ISO irrigation (p = 0.01). No systemic side effects to ISO irrigation were observed.
Conclusions: For the first time a randomized controlled human study demonstrates that pharmacological modulation of the ureter is possible during upper urinary tract endoscopy. Capability of relaxing ureteral tone during endoscopy may imply clinical advantages.

29 – THE APPLICATION OF MERIDIAN ELECTRICAL CONDUCTANCE FOR RENAL COLIC: A PROSPECTIVE STUDY

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Objectives: Renal colic caused by ureteral stone is a common condition in the emergency department (ED). This study was designed to measure the meridian electrical conductance of patients with ureteral stone in the emergency settings.
Materials and Methods: Consecutive cohorts of patients who had ureteral stone with acute, renal colicky pain and visited the ED were enrolled in this study. A device, the design of which is based on the Ryodoraku theory, was used to measure the meridian electrical conductance of patients in the ED. Sixty patients (aged 42.0 ± 12.6) who had a primary ED diagnosis of ureteral stone or renal colic were enrolled. On the other hand, 30 control volunteers (aged 40.8 ± 11.7) were recruited to serve as control group.
Results: Statistical analysis showed that (1) the average of the electrical conductance of the patients group was statistically decreased from that of control group ($P < 0.01$); (2) the average of index of sympatho-vagal balance of the patients group was statistically increased from that of control group ($P < 0.01$); (3) the average coefficient of variation of the electrical conductance and index of sympatho-vagal balance of the patients group was statistically different from that of control group ($P < 0.01$); (4) the patients who needed intervention had a higher imbalance of autonomic nerve than the patients who had spontaneous stone passage ($P < 0.01$).
Conclusions: Electrical conductance measures, especially the index of sympatho-vagal balance, may be used as valuable predictors of elective intervention in patients with acute renal colic.

30 – DISTAL URETER FUNCTION AND RENAL PELVIC PRESSURE IN PATIENTS WITH VARIOUS STONE LOCATION

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Objectives: The contractile function of ureter can play an important role to maintain adequate urine passage from renal pelvis towards the urinary bladder. The purpose of this study was to clarify the impact of functional ureteric characteristics on renal pelvis urodynamics.
Materials and Methods: Patients with renal (12), proximal (11), and distal (12) ureteral stones comprising, respectively, the groups 1, 2, and 3 were examined during ureteroscopy after lithotripsy procedures. The peristalsis amplitude,

ureteral wall tone, the contractile waveform, its direction and velocity were assessed in the distal ureter by multichannel impedance ureterography with the help of a special probe and an impedance converter RPKA2-01. Three patients were examined similarly during diagnostic ureteroscopy (control group). Renal pelvic pressure (RPP) was measured by electromanometer in the patients with nephrostomy tube indwelled.

Results: Peristaltic function of ureters without stones was characterized with a high-amplitude (2.1 ± 0.9 Ohm) rhythmic antegrade contractions (peristaltic rate 2.0 ± 0.7 min^{-1}, velocity of 1.83 ± 0.30 cm/sec) and ureteral wall tone 2.6 ± 0.8 Ohm^{-1}. These parameters differed significantly from those measured in patients with renal and ureteral stones. Compared to the control group, the patients with stones demonstrated smaller amplitudes of 52, 67, and 76% in the respective groups 1, 2, and 3. In contrast, the tone values were larger in these patients: 4.0 ± 0.6; 4.3 ± 0.3; 6.2 ± 0.6 Ohm^{-1}, correspondingly. The antegrade contractile waves were observed in 50% patients with renal stones, and only in 9-12% patients with stones in ureter. The peristalsis rate was faster by 35-45%, and velocity of contraction was quicker by 62-123% in patients with stones compared to the control group. The simultaneous contractions of the whole distal ureteral cystoid were observed in patients with uroliths (50-63%). The retrograde contractile waves in distal ureter were found in ureters of patients with renal and proximal ureteral stones (50-54%), while the aberrant peristalsis was often recorded in patients with ureteral stones (38-45%), in contrast to patients with renal stones (10%). Dilation of pelvicaliceal system obtained by US before stone treatment was registered in 80, 64, and 50% patients in the groups 1, 2, and 3, respectively, and elevated RPP was observed in 57, 83, and 71% patients. In the group 1, RPP was significantly elevated (> 20 cm H2O) at rest supine position in those patients, who demonstrated persistent retrograde and cystoid waves, but did not exceed 10 cm H2O in the patients with antegrade contractions in distal ureter. In the groups 2 and 3, an elevated RPP (> 10 cm H2O) was observed in the patients with weak chaotic peristalsis and enhanced ureteral wall tone. These patients as rule had pelvicaliceal dilation (range 1.4-5.5 cm).

Conclusions: Disorders in distal ureter peristalsis can affect renal pelvis urodynamics and induce elevation in RPP. The underlying mechanisms are different in the cases of renal and ureteral stone location. In patients with renal stones, evident retrograde and cystoid peristaltic waves are supposed to provoke refluxes and urine stagnation contributing to pressure elevation. In patients with ureteral stones, an aberrant peristalsis and increased ureteral wall tone correlated with pelvicaliceal dilation and elevated pressure in renal pelvis.

31 – DIAGNOSTIC OF ACUTE OBSTRUCTION OF UPPER URINARY TRACT FOR UROLITHIASIS

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Objectives: Diagnostics of acute obstruction of the upper urinary tract urolithiasis by means of ultrasound.

Materials and Methods: 62 patients (first group), with a "renal colic" attack and suspicion of obstruction of the urinary tract were surveyed (32 men, 30 women; age range from 22 up to 62 years). For comparison 20 healthy people (second group) without obstruction were surveyed (10 men and 10 women; age range from 20 up to 63 years. By means of the ultrasonic device "Logic-500" in a mode color Doppler chart-making (CDCH), and pulse dopplergrafici, the qualitative and quantitative estimation of parameters of emission of urine through the ureteral orifices was made for revealing the degree of obstruction of the upper urinary tract. The investigation necessarily requested an oral water loading at the rate of 10 ml/kg of body weight approximately 20 minutes before the study. Physiologically for an usual level of diuresis ureteral emissions are registered with a frequency of 1-2 in a minute. Technique of research: in a mode impulsive-wave doppler the control volume was established as much as possible close to a ureteral orifice. Estimated qualitative and quantitative parameters of streams: presence and quantity overshoot in a minute, form of curves, maximal speed of a stream, integrated speed, average speed, acceleration of a stream, time of acceleration of a stream, and also index of asymmetry (as the attitude dopplergrafici showing a healthy kidney and a kidney in presence of a stone in the ureter). The maximal values quantitative dopplergrafici parameters of spectra of speeds of ureteral streams emissions have been received at bladder filling from 150 up to 350 ml.

Results: 20 patients (32,3%)of the first group at CDCH showed a condition estimated as "full obstruction". Using spectral characteristics. two different degrees of incomplete obstruction were observed in patients of the first group. The first degree, observed in 24 (38,7%) patients, was characterized in the maximal speed of emission of 5-15 sm/with, time of emission of 10-20 seconds and 1-3 emissions in a minute. The second degree of incomplete obstruction, observed in 18 (29,0%) patients, was chracterized in the maximal speed of emission of 4-5 sm/with, time of emission of 20-30 seconds and from 1 up to 2 emissions in a minute. Thus, at incomplete obstruction the curve has been deprived of characteristic peaks and presented by low monophase amplitude in the form of a so-called venous spectrum with low acceleration of the stream, greater time of acceleration of the stream, greater time of the emission, expressed asymmetry of parameters of healthy and sick kidneys. The second group investigated (without obstruction) (20 subjects) was chracterized by maximal speed of emission of 20-30 sm/with, time of emission of 6-10 seconds and 4 up to 6 emissions in a minute.

Conclusions: For the purpose of the diagnosis of acute obstruction of the upper urinary tract by urolithiasis, the application of a technique of registration of ureteral emissions is useful allowing to define passableness of the stones.

32 – THE ROLE OF LONG-TERM LOADING OF CHOLESTEROL IN RENAL CRYSTAL FORMATION

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Recently, some researchers reported that cholesterol plays an important role in urolithiasis formation. In patients with urolithiasis, the mean daily intake of fat was significantly higher than that in controls. Meanwhile, in patients, it is reported that the daily intake of fat was higher in men than

women and the difference was statistically highly significant, which is one of the reasons that there is a significantly higher incidence of urolithiasis in men than that in women. Lipid and fatty acid-related hyperoxaluria and hypercalciuria have been also observed. Thus, a close relationship may exist between pathological renal calcifications and lipids. The aim of the present work was to test whether long-term exposure to a dietary excess of cholesterol and lipids results into urinary calcium stone formation.

Materials and Methods: We studied the effects of cholesterol load on urinary stone in rats receiving a standard diet or a high fat diet. Sixty male rats were randomized to two groups and were fed either a standard diet (SD group) or a high fat diet (HFD group) for 8 weeks. Then the two groups were further divided into four groups (SD group, HFD group, SD+EG group (with standard diet + ethylene glycol administration for two weeks), and HFD + EG group (with high fat diet + ethylene glycol administration)). The starting date of EG administration was considered to be week 0. Twenty-four-hour urine samples were collected in week 0, week 1, and week 2, and oxalate excretion and citrate excretion were measured by capillary electrophoresis analyzer. The excretion of phosphorus, magnesium, and creatinine for 24 hours was measured using an automated analyzer. Serum sodium, potassium, chlorine, calcium, phosphate, magnesium, creatinine, total cholesterol, triglycelide, HDL-cholesterol and glucose were determined using an automated analyzer. The kidney tissues were obtained to perform hematoxyline-eosine staining and Pizzolato's staining to detect calcium-containing crystals. Immnohistochemical staining of adiponectin was performed.

Results: The average body weight in the HFD and HFD+EG group in week 0 was significantly higher than that of the SD and SD+EG group. The calcium oxalate crystal deposition was not observed in all groups in week 0. The HFD+EG group in week 1 has sporadically calcium oxalate crystal deposition in renal distal tubular cells and tubular lumens. In week 2, the number of crystal deposition in the HFD+EG group was increased remarkably. The crystals were slightly observed in the SD+EG group in week 2. The excretion of urinary calcium and phosphate in the HFD and HFD+EG group was significantly higher than that of the SD and SD+EG group in week 0. The amount of urinary citrate excretion in the SD and SD+EG group showed a significantly higher value compared with that of the HFD and HFD+EG group in week 0. The level of serum total cholesterol in the HFD and HFD+EG group was higher compared to that in the SD and SD+EG group. The serum triglyceride level was no significant in four groups in week 0. Interestingly, the level of triglyceride of EG administration groups (SD+EG and HFD+EG group) was significantly higher than that in EG no-administration groups (SD and HFD group) in week 1 and week 2. The adiponectin staining was decreased in the HFD+EG group compared with the SD+EG group.

Conclusions: This result suggested that long-term loading of cholesterol could increase renal calcium stone formation. Renal stone formation is related to metabolism of lipid and adipocytokine.

33 – EVALUATION OF METHODS FOR URINE INHIBITORY POTENTIAL FOR PRECIPITATION OF CALCIUM OXALATE

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Renal lithiasis is a significant medical and social problem with still a high recurrence rate (3%-5%) worldwide. In Croatia urinary and/or renal stones are composed predominantly of calcium oxalate and phosphate stones (about 75%), uric acid (about 10%-12%) and sometimes so-called infection stones struvite (about 10%-15%). Major factors contributing to renal stone formation are urine supersaturation and various metabolic factors. However urine can contain various substances which by different mechanisms can inhibit the precipitation process.

The objective of this paper is to evaluate and compare several chemical methods for distinguishing between stone formers and non-stone formers. The examined methods are based on testing the inhibitory capacity of urine with respect to precipitation of calcium salts. The two methods in question are:

a) initiation of precipitation from whole urine by addition of calcium oxalate monohydrate seed crystals – this method monitors ionic calcium concentration with seed crystals of calcium oxalate monohydrate (COM) (initiated precipitation) and without (spontaneous precipitation) after 3h and 24h incubation at 37°C. Results are shown according to the following criteria:

$\Delta c\ (Ca) = c\ (Ca)_{spont.prec.} - c\ (Ca)_{init.prec.}$

b) testing the capacity of urine for calcium complexing by adding calcium solution to whole urine – urine samples (first morning urine) are titrated with calcium chloride solution ($c(CaCl_2) = 0.1\ moldm^{-3}$). The discriminating criteria for the results is the slope of the titration curve.

Preliminary research shows that these two methods have a great potential for discriminating between the stone formers and non-stone formers. The theoretical background experimental design and parameters for discrimination between urines of stone formers and non-stone formers are explained for both methods. The results for experimental groups (stone formers) and control group (non-stone formers) are compared and the advantages and disadvantages of each method are discussed.

34 – EVALUATION AND CLINICAL APPLICATION OF THE UROLIZER®-DEVICE FOR DETERMINATION OF THE BONN-RISK-INDEX OF CALCIUM OXALATE STONE FORMATION

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Objectives: The BONN Risk Index (BRI) successfully determines the calcium oxalate (CaOx) crystallization risk from urine samples. The BRI is based on a standardized crystallization test performed on native urine. A BRI measuring device, the "Urolizer®", was developed, operating automatically and requiring only a minimum of preparative efforts. In this study, the Urolizer® was 1) tested in respect to its precision, and 2) evaluated regarding its analytical and diagnostic practicability for metaphylaxis control in the framework of the daily routine of a stone surgery. Furthermore, the influ-

ence of urine storage at moderate temperatures on BRI was investigated.

Materials and Methods: 24h-urines from recurrent CaOx stone-formers (SF) were collected and routine urinalyses performed. 37 urine samples were used for the investigation of Urolizer® precision by performing six independent BRI determinations in series. From 51 SF, 24h-urines were collected at the beginning and after 3 months of metaphylaxis. With the results obtained from the first urinalysis, 27 patients were indicated to suffer from mild hypercalciuria (Ca: 5-8mmol/d), low urinary pH or hypocitraturia, and 24 patients from hypercalciuria (Ca: > 8mmol/d). The former were treated with alkaline citrate (AC), and the latter with hydrochlorothiazide (HCT). Analyses of urines collected before and during treatment, BRI using the Urolizer®, and urinalysis-based risk indices were evaluated. 30 samples were taken for investigation of urine storability and were measured thrice: directly after collection, after 24h storage at T = 21°C, and after 24h cooling at T = 8°C. Outcomes were statistically tested for identity with regard to the immediately obtained results.

Results: Repeat measurements for evaluation of Urolizer® precision revealed statistical identity of data ($p < 0.05$, VC = 10.1%, Passing-Bablock). In both patient groups, BRI decreased significantly during metaphylaxis ($p < 0.001$, Wilcoxon-Test). In the AC-group BRI decreased from 1.08 (± 0.58) to 0.56(± 0.39)L^{-1} and in the HCT-group from 3.30 (± 1.15) to 1.60(± 0.52)L^{-1}. In most patients, urinary parameters changed as desired and related risk indices (e.g. AP(CaOx)) decreased appropriately. 24h storage of urine at both tested temperatures did not significantly affect BRI ($p < 0.05$, Bland-Altmann, Passing-Bablock).

Conclusions: The pilot-run Urolizer® shows high analytical reliability, the clinical utility of Urolizer®-based BRI is demonstrated. By quantifying the "overall" therapy effect within 15 minutes, the analysis device may be especially suited for urologists specializing in urolithiasis treatment. The possibility for urine storage at moderate temperatures without loss of analysis quality further demonstrates the applicability of the BRI method.

35 – VARIABILITY IN LABORATORY ANALYSIS OF URINARY STONES

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Objectives: Testing of the accuracy of urinary stone analysis by commercial laboratories has been done primarily through the use of artificial mineral samples, as that has been the only way to ensure known compositions of the specimens submitted to the laboratories. However, this means that laboratories are not scrutinized for accuracy on the basis of their ability to analyze actual stone specimens. We used micro computed tomographic imaging (micro CT) to non-destructively assess the compositions of pure and mixed stone specimens, and prepared identical specimens to send to commercial laboratories to assess the accuracy of identification on real stone specimens.

Materials and Methods: Stone specimens were taken from a stone library and cleaved into six pieces. Uniformity of the specimens was assessed using micro CT (on a SkyScan 1172 system, with typical settings of 59 kV, 167 mA, and isotropic voxel size of 7 um). Specimens judged to be uniform in composition were sent to five commercial laboratories, with one fragment retained for analysis in-house.

Results: Of 46 stones cleaved into fragments, only 26 stones yielded fragments that appeared to be identical in composition by micro CT. Of these, 4 pure stones (2 uric acid [UA] and 2 cystine) were correctly identified by all 5 laboratories; 2 stones containing majority brushite were also correctly identified by all labs. For 2 stones composed of UA and calcium oxalate (CaOx) monohydrate--which are easily identified by micro CT--1 lab missed the CaOxcomponent. For 9 CaOx stones, in which apatite (AP) is easily seen by micro CT, the AP was missed by 1 or more labs in 4 stones. For 8 infection stones, labs missed struvite on 3, and descriptions of AP content differed among labs, with 1 never listing carbapatite (CA) but only hydroxyapatite and another listing CA as AP plus calcium carbonate. Finally, no lab correctly analyzed a stone containing atazanavir mixed with CaOx and AP.

Conclusions: Micro CT provides an excellent, non-destructive method for identifying several components commonly found in urinary stones; the most clinically significant exception to this is struvite, which is difficult to visualize by micro CT in mixed stones. When analyzing identical fragments from the same stones, commercial laboratories reliably recognized pure calculi; however, there was substantial variability in reporting compositions of mixed calculi, errors which likely related to sampling choices made during analysis. There was also a lack of standardization of nomenclature used by laboratories. We conclude that micro CT assessment of stone composition is quite powerful for the most common components, and that it provides improved detection of components that can be missed by traditional methods.

36 – CAN INFRARED SPECTROSCOPY BE USED FOR RAPID IDENTIFICATION OF MELAMINE-CONTAINING NEPHROLITHIASIS?

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Melamine-contaminated milk formula caused infant nephrolithiasis in some areas of China. Its combination with cyanuric acid causes crystallisation in renal tubules. Following renal damage and even renal failure that require long-term hemodialysis has been reported. Therefore, correct and timely diagnosis these complex diseases are critical. Melamine containing stone was a combination of equal molar of common stone compositions that has been reported from previous animal study. We have previously identified the compositions of urinary tract stones with IR spectroscopy. We wonder if the absorbance of wavelength of IR can identify melamine in the presence of mixing human stone compositions. In the present study, we made an artificial stone composition and examine under IR absorbance by mixing equal volume of melamine and different types of human urinary stones, and firstly established a reference of IR analysis for the identification of melamine-containing

human urinary tract stones. Knowledge of the precise stone composition allowed institution of appropriate prophylactic dietary and medical therapy and this may help in the prevention of urinary stone recurrence. The results are promising that melamine and cyanuric acid can be identified clearly in a very low percentile (1%) of stone mixture pellet. Therefore, IR seems to be an ideal tool for the identification of melamine-containing stone.

37 – MUTATION SCREENING AND NUCLEOTIDE SEQUENCE ANALYSIS OF OSTEOPONTIN (OPN) GENE IN PATIENTS WITH KIDNEY STONE

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Objectives: Urolithiasis also known as kidney stone formation, is a discomforting prevalent disease in the southeastern region of Turkey. kidney stone formation is a complex process including crystal nucleation, growth, aggregation and retention within the renal tubules. The osteopontin (OPN) gene product exist in stone matrix as the stone formation modulators and potent inhibitor of Caox stone formation and have aspartic acid rich residues. OPN gene is located on chromosome 4q21-25 and consists of 7 exons and a large promoter region.

Patients and Methods: In this study, three families having familial transmission (n = 21), and sporadic urolithiasis patients (n = 100), and control cases (n = 100) were included for OPN gene analysis by PCR-SSCP and DNA sequencing methods, respectively.

Results: Ttwo SNP's in exon 7 (C-6983A, T-8274C) and three SNP's in promoter (G-1748A, A-592T, G-155T) were found as reported earlier. Among the polymorphic sites, G-155T and G-1748A double mutations were found only in 12 familial transmission patients in three families and were frequent stone formers. A-592T mutation in promoter region were also frequent among the familial transmission patients; 32 versus to 16 sporadic and 12 controls. The exon 7 mutations namely C-6983A mutation was more common in sporadic patients then the familial transition patients and the control group (16 versus to 4 and 4, respectively). The T-8274C mutation was found equally between the sporadic patients and the control group. In exon 7, C→A missense mutation at position 6983 nucleotide caused His^{287}→Arg and T→C mutation at nucleotide 8274 caused Cys^{430}→Arg changes, respectively. T→C mutation was found only in one patient in familial transition patient while sporadic patients and the control group had equal distribution (1 versus to 16 and 16, respectively).

Conclusions: Entire OPN gene analysis revealed that it is highly conserved gene and three mutaions in the promoter region are peculiar in terms of their effect on the expression of this gene among the stone former patients awaits further studies.

38 – CANEPHRON N AS INHIBITOR OF URINE PATHOLOGICAL CRYSTALLIZATION

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Objectives: The aim of our research is to detect ability of Canefron N to inhibit the pathologic crystallization of urine in patients with urolithiasis.

Materials and Methods: It were investigated urine samples of 42 patients in vivo and 4 samples in vitro by method V-shaped dehydrotation adding albumine. Canephron N was prescribed 50 drops 3 times a day for 14 days.

Results: We revealed ability of Canephron N to inhibit pathological urine crystallization in 37 cases (86%) ($p < 0,05$). Results were confirmed by experiment in vitro. We added in urine samples of patients with nephrolithiasis albumine and Canephron N.

Conclusions: Canephron N as plants extract efficiently inhibits pathological urine crystallization in patients with urolithiasis despite kind of urolithiasis makes no matter.

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39 – URINE BIOCHEMISTRY VS ELECTRICAL CONDUCTIVITY AND TOTAL DISSOLVED SOLIDS

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Objectives: Various urinary biochemical abnormalities are reported in stone disease. The study is aimed to correlate the 24 hour urine biochemistry including urinary oxalate, calcium, uric acid, magnesium and citrate with the other urinary parameters, namely electrical conductivity (EC) and total dissolved solids (TDS).

Materials and Methods: 279 proved urinary stone patients including radiological proved stones patients, stone passers, colic patients and crystalluria patients. 24 hr urine biochemistry was performed in the initial sitting. The other urinary parameters namely EC and TDS were assessed and correlated with the biochemical parameters using Pearson's correlation coefficient test.

Results: Significant variation was recognized between the various urinary biochemical values and EC and TDS. Urinary calcium was found to be inversely proportional to the EC (-0.247 at P = 0.000) and TDS (-0.238 at P = 0.000). Urinary magnesium was also found to be inversely proportional to the EC (-0.164 at P = 0.006) and TDS (-0.158 at P = 0.008). Urinary oxalate showed a similar inverse relation with both EC (-0.324 at P = 0.000) and TDS (-0.303 at P = 0.000). Same pattern was noted in the correlation of citric acid also to EC (-0.184 at P = 0.002) and TDS (-0.158 at P = 0.008). There was no correlation between the EC and TDS and urine uric acid. Since inverse relationship in noted between both promoter and inhibitor parameters in the urine and EC and TDS, their role may not be directly related to the biochemical parameters. Further studies are needed to identify the actual mechanism of involvement in calculogenesis.

Conclusions: It is concluded that the 24 hour urinary biochemical parameters are inversely correlated with EC and TDS except uric acid. Further studies are needed to identify their role in calculogensis.

40 – TYPES OF CRYSTALLURIA IN PATIENTS WITH URINARY STONES OF DIFFERENT CHEMICAL COMPOSITION

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Introduction: Crystalluria is one of the most important and informative values reflecting features of metabolism in patients with urolithiasis. The presence of certain features in

metabolism disorders in patients with different urinary calculi suggests specificity of crystalluria.
Objectives: To define the type of crystalluria in patients with uric acid, calcium oxalate, calcium phosphate and magnesium-ammonia-phosphate urinary stones.
Materials and Methods: We have investigated 193 patients (101 women and 92 men), aged from 27 to 58 years old. Among them 93 patients with different urinary stones were regularly followed up for 4 years. In 49 patients we diagnosed uric acid stones, in 88 patients – calcium oxalate or mixed stones (with calcium oxalate prevailing), in 45 – magnesium-ammonia-phosphate and in 9 patients – calcium phosphate stones. Chemical composition of the stones was detected using infrared spectrophotometry and X-ray difraction. The sediment of the morning portion of urine was analysed by means of microscopy – once in 100 patients and several times in 93 patients.
Results: It has been shown that in patients with uric acid lithiasis crystals of uric acid and sodium urate are found in 69% of cases. In 24% of patients of the same group urine contained not only crystals of uric acid and urates but also crystals of calcium oxalate. For 7% of patients crystalluria of calcium oxalate was a characteristic feature. In 74% of patients with calcium oxalate urinary calculi we detected crystalluria of oxalates. 23% of patients were shown to have crystalluria of oxalates in combination with crystalluria of urates. In 2% of cases, apart from crystalluria of oxalates, we have found crystalluria of calcium phosphate. Patients with magnesium-ammonia-phosphate stones in 100% of cases demonstrated crystalluria of the same chemical composition and sometimes in combination with calcium phosphates. Patients with different calcium phosphate stones were shown to have phosphates in urine (crystals of calcium phosphate) in 89% of cases, in one case we detected phosphates in urine along with crystals of calcium oxalate.
Conclusions: Given results suggest that the type of crystalluria does not always correspond with the chemical type of the stones. The presence of crystals of the type other than that, forming the calculus, might be a prognostic criterion of urolithiasis development.

41 – DOES THE SYMPTOM OF THE PATIENT CORRELATE WITH THE EXTENT OF CRYSTALLURIA?

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Objectives: Patients with urinary stone disease are usually administered various chemotherapeutic regimes and advised to return for review. The percentage of patients coming back for review is very small. Most of the patients come back only when they have recurrent symptoms. Very few patients return to the stone clinic even wile they are not having symptoms. In this study, an attempt has been made to correlate the extent of crystalluria and the extent of urinary symptoms during the subsequent visits.
Materials and Methods: 300 patients attending the stone clinic for review after administration of different categories of chemoprophylactic and chemotherapeutic regimes were assessed for their urinary crystal pattern and the other deposits. Patients were classified as having nil, mild, moderate, severe or excruciating symptoms. All the patients had early morning urine and random sample analysed. The differences in extent of crystalluria and size, presence of RBCs, pus cells, crystal aggregation and clumping were assessed between the patients in different groups. Statistical tests were conducted to identify variation in the pattern of urinary deposits in the groups.
Results: It was observed that 22% of the patients did not have any symptoms whereas 78% had symptoms like Pain (61%), haematuria (7%), Burning micturition (1%), dysuria (4%) and combination (27%). 87% of the patients with urinary symptoms had significant urine deposits (2+ or more) whereas the others did not have. Of the 22% patients with out symptoms, 68% had significant urinary deposits. It was seen that 27% of patients with significant urinary deposits did not have any symptoms at the time of their presentation. Similarly patients with significant symptoms did not have crystals. RBCs and pus cells in the urine were more in the patients with higher grade of symptoms, though not to statistically significant levels. When the stone symptoms were factorised, the group with combination of symptoms had the largest number of COM and COD crystals. It is obvious from the findings that patients without symptoms may still have active stone disease. The presence of blood cells in the absence of crystals may be due to the urothelial injury produced by a moving stone.
Conclusions: It is concluded that the extent of urinary deposits does not correlate with the clinical symptoms presented by the patient at the time of urine collection. Hence it is suggested that decision regarding starting of drugs or altering the dose of drugs administered should not be based on symptoms of the patient alone but also on the status of urinary deposits.

42 – TEMPORARY CLINICAL RISK INDEX VS URINARY RISK INDEX

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Objectives: Various risk indices are mentioned in literature for the identification of possible causes for stone activity. In this paper and attempt was made to study the temporary clinical risk index of the stone patient attending the stone clinic and assessing the severity of the urinary deposits in the patient on the day of the presentation.
Materials and Methods: The patients who attended the stone clinic were interviewed to assess the clinical symptoms. Temporary clinical risk index took into consideration, symptoms like pain, haematuria, burning sensation, dysuria, ultrasound stone, back pressure, stone passage and radiological stone. The urinary risks considered included pH below 6, specific gravity above 1020, redox potential < 100 mV, electrical conductivity < 20mS, total dissolved solids < 11K ppm, cystine, red blood cells, pus cells, whewellite, weddellite, phosphate, uric acid / ammonium urate, crystal clumping, crystal aggregation and stone passage. were assessed and the total value was taken as percentage.
Results: It was seen that the clinical risk index values did not correspond totally with the urinary risk index values. Many of the patients with severe urinary symptoms did not have significant urinary deposits. Many other patients with out any urinary symptoms and without radiological and ultrasound recognized stones did have significant crystals.
Conclusions: It is concluded from the study that the clinical risk index considers the clinical features of the patient alone. This will not assess the stone activity completely. Crystalluria may be the cause of pain but it is not always so. Presence of crystalluria may indicate stone activity but pain may indicate

in the stone passage without evidence of actual stone activity. RBCs and puscells may be produced by trauma of stones or crystals. Presence of puscells alone in the urinary stone disease may not indicate urinary tract infection as 80% of the patients with significant puscells alone without any RBC's did not have positive urine culture. They did not required urinary antibiotics and the puscells disappeared after appropriate chemotherapy and the metabolic abnormalities.

43 – DOES URINARY DEPOSIT VARY WITH TYPE OF STONE?

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Objectives: Several patients with urinary stone diseases attend the urinary stone clinic with symptoms of pain, dysuria or haematuria and end up in retrieval of stones by stone passage, uretro-renoscopy, PCNL, ESWL or open surgery. Literature dose not provided records of studies were the urinary deposits have been assessed depending on the type of stone former. The objective of this paper is to analyse the urinary deposits of different categories of stones formed in the urinary tract and identify the difference.
Materials and Methods: 141 stone patients who had stones retrieved from their urinary system had their urinary deposits done and the findings were compared between the six groups namely predominantly Calcium Oxalate Monohydrate (COM), predominantly Calcium Oxalate Dihydrate (COD), Predominantly Uric acid/Ammonium urate (UA), Combination of COM and COD, combination of Oxalate and Uric acid, other combination of mixed stones like calcium, phosphorus and uric acid.
Results: Analysis of variance showed that there was no statistically significance variation in the type of crystals that were encountered in the different groups of stone formers – Pus Cells (PC) P = 0.404, Red Blood Celles (RBC) P = 0.718), COM – P + 0.540, COD P = 0.334, UA P = 0.117, Phophate P = 0.080 and Ammonium Urate P = 0.327. However, PCs were seen most in the COM + COD stones forming patients and the least in the UA group (P = 0.053). RBCs were maximum seen in the COM + COD group and the least in the Oxalate + UA group (P = 0.178). COM crystals were maximum in COM stones and least in COD stone group (P = 0.300). COD crystals were maximum in COD stone group and least in UA stone group (P = 0.080). UA crystals were maximum in the UA stone group and were absent in the COM + COD group (P = 0.059). Phosphate crystals were maximum in the COM stone group and least in the COD group (P = 0.087). Ammonium urate crystals were maximum in COM and were absent in COD and COM + COD stone groups (P = 0.175).
Conclusions: It is concluded that the urinary deposits vary the type of stone which is the formed by the patient. But the absence of statistical significance in these findings indicates that there may be combination effects of different crystals in the all types of stones formed, thereby indicating that treatment should be centred on the possible types of crystals formed in these patients.

44 – NEED FOR TOTAL METABOLIC STUDY IN FIRST EPISODE OF STONE FORMATION

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Objectives: It is generally believed that when a patient is presenting with symptoms of urinary stone for the first time, it is not necessary to perform a complete metabolic study. It is believed that total metabolic study needs to be performed only for recurrent stone disease. This paper is presented with the intention of assessing the need for a total metabolic study even at the first episode of stone disease.
Materials and Methods: 500 patients presenting the stone clinic for a first time episode of stone formation (Primary Stone Former – PSF) were assessed. In contrast, 300 patients who presented with the stone disease but who had been suffering with stone disease earlier for a minimum of three years (Recurrent Stone Former – RSF) were also assessed. It was presumed that the patients who had stone disease during the previous three years were not metabolically investigated and not scientifically treated. All the patients were studied by standard protocol including the family history, personal history, dietetic history, clinical examination, radiological examination, urinary deposit assessment and metabolic studies. The PSFs and RSFs were followed up for a minimum period of three years to look for recurrence. The stone episode rates of the three groups PSF prospective, RSF retrospective and RSF prospective were calculated. The differences were statistically evaluated.
Results: Among the PSFs, 318 patients (64%) continued to have active stone disease with a recurrence rate of 7%. Among the 300 patients with recurrent stone disease followed up for period of 3 years, 245 continued to be on follow up at three years with a recurrence rate of 11.2%. The retrospective recurrence rate of RSFs was 30 % in the last three years prior to first attendance. The stone episode rate calculated in the retrospective three years was 2.9 per patient year compared to the prospective rate of 0.89 per patient year. The PSFs had a stone episode rate of 0.89% in the prospective study. The metabolic investigations proved that there was no statistically significant difference in the urine and serum parameters beween the PSF and the RSF.
Conclusions: The findings show that patients with first time stone episode were not different metabolically from the recurrent stone formers. The retrospective stone episode rate in the recurrent group of patients was significantly higher than the rate of the same patients in the prospective metabolically corrected follow up period thus indicating need for routine metabolic investigation in every stone patient presenting with first episode of stone. Appropriate chemoprophylactic advice and dietetic prophylaxis should be administered to all the patients till such time the urinary deposits are cleared and the patient is not having any symptoms for at least 6 months. The reduction in dose of the drugs followed by dietetic prophylaxis should be the scheme of management in this patients.

45 – DOES URINE AND BLOOD BIOCHEMISTRY DIFFER WITH STONE TYPE?

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Objectives: Prevention of stone formation is primarily centered on correction of metabolic abnormalities and type of stone. The objective of this paper is to correlate the type of stone retrieved form the patient with the urine and blood biochemistry.
Materials and Methods: 137 patients from whom stones

were retrieved and analysed using infra red spectroscopy and scanning electron microscopy were classified into 6 groups, COM, COD, uric acid, mixture of COM and COD, mixed oxalates and uric acid and other mixed stones. The 24 hr. urine calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium and serum calcium, phosphorus, uric acid, creatinine and magnesium were analysed in all the patients. Duncan's multiple range test was done to compare means.

Results: Analysis of variance showed no statistically significant variation in any of the above mention biochemical parameters. On performing range test, urine volume was highest in the COM group (3401.96) and lowest in the COD group (2875.00) P = 0.559. The urine calcium was highest in the mixed oxalate stone group (259.00) and least in the mixed stone group (218.16) P = 0.319. The urinary phosphate was highest in the COD group (937.71) and lowest in the mixed oxalate group (731.93) P = 0.254. Urine uric acid was highest in the COD group (589.00) and lowest in the mixed stone group (472.68) P = 0.126. The urinary magnesium was lowest in the COD group (6.39) and highest in the oxalate + uric acid group (8.64) P = 0.335. The urine creatinine was highest in the uric acid group (2.270) and lowest in the mixed stone group (1.548) P = 0.053. The urine oxalate was highest in the oxalate + uric acid group (112.71) and lowest in the mixed oxalate group (85.71) P = 0.310. Urinary citrate was lowest in the mixed oxalate group (279.07) and highest in the oxalate + uric acid group (561.71) P = 0.121. Urinary sodium was highest in the COD group (392.63) and lowest in oxalate + uric acid group (177.79) P = 0.061. Urinary potassium was lowest in the mixed oxalate group (44.36) and highest in the COD group (57.13) P = 0.371. Serum calcium was highest in the COM group (9.64) and lowest in the mixed stone group (9.22) P = 0.485. Serum phosphorus was highest in the mixed stone group (3.532) and lowest in the COD group (2.625) P = 0.066. The serum uric acid was highest in the uric acid stone group (7.05) and lowest in the uric acid + oxalate group (5.66) P = 0.146. Serum magnesium was lowest in the COM group (1.93) and highest in the mixed stone group (2.07) P = 0.151. Serum creatinine was highest in the COM group (1.390) and lowest in the mixed stone group (1.029) P = 0.419. From these observations, it is seen that abnormalities were more in the COD stone group.

Conclusions: It is concluded that the different types of stone formers are not significantly different biochemically, but have minimal role in altering the pattern of stone growth. Pure COD stones may be more amenable to biochemical correction. Disclosure: No significant financial interest or other affiliations with a funding organization or with a commercial supporter of the session and/or provider of commercial services exists.

46 – HOW TO ASSESS THE SEVERITY OF UROLITHIASIS?

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Objectives: We have reported earlier the utilization of a risk index for assessing severity of stone disease in patients. Most of the risk indices currently utilized are not feasible in a clinical setting. Even if they are performed, they do not represent the patient's stone forming propensity as a whole in terms of clinical severity of Urolithiasis. The present study was done to assess the severity of Urolithiasis by total assessment based on the symptoms of the patients, duration of the pathology, the extent of crystalluria and the presence of metabolic abnormalities.

Materials and Methods: The severity assessment regime consisted of 5 aspects permanent risk index, metabolic risk index, the risk ratio in Urolithiasis, temporary clinical risk index and the temporary urinary risk index. 200 patients with stone disease were assessed by using the five indices. Permanent indices included age, sex, family history, domicile, occupation, recurrent or primary, bilateral/ unilateral, stone passer, multiple organs, number of stones, incomplete removal and stone composition. Temporary clinical risk index took into consideration symptoms like pain, haematuria, burning sensation, dysuria, ultrasound stone, back pressure, stone passage and radiological stones. The urinary risks considered included pH below 6, specific gravity above 1020, redox potential < 100 mV, electrical conductivity < 20mS, total dissolved solids < 11K ppm, cystine, red blood cells, pus cells, whewellite, weddellite, phosphate, uric acid/ammonium urate, crystal clumping, crystal aggregation and stone passage. Biochemical risks and risk rations were also included. The correlation between the different indices was assessed.

Results: It was seen that the assessment of the permanent risk index alone did not significantly help in deciding the prophylactic regime for the patients. Stone disease appeared to the significantly variable in terms of severity and the frequency of recurrence. Among 200 with recurrent episodes of Urolithiasis for more than 5 occasions, 22% had a history of over 20 yrs., 18% had a history of 15 to 20 yrs and the next had shorter durations. Among patients with long duration, the stones incident rate was significantly low in 50% of the patients. The correlation between permanent risk index and temporary clinical risk index were not statistically significant (P = 0.232). Temporary clinical risk index did not correlate significantly with the Urine deposit index (P = 0.365). It is presumed that the duration of symptoms or size or number of stones alone will not predict severity of stone disease. Proper follow up of the clinical status, examination of the urine deposits, metabolic status and radiological growth of stone are needed to assess actual stone forming propensity.

Conclusions: It is concluded that in order to decide a proper treatment for the stone patient, all aspects of the stone disease have to be considered in assessing the severity of Urolithiasis.

47 – MONITORING FOR STONE

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Objectives: Various patients with urinary stone disease are monitor regularly. The different modalities of monitoring are seen to be unscientifically done in many situations. Ultrasonographic examination has become the standard protocol for assessing the extent of stone disease. Plain X ray KUB and CT scan are unusual investigations. The present study was undertaken to find out the status of patient monitoring investigations in 500 patients presenting with urinary stone disease for more than one year.

Materials and Methods: The patients who attended the stone clinic after having been followed up else where for more than one year were interviewed. The details of investigations done to identify or monitor presence and growth of stones were analysed.

Results: All the patients involved in the study had had an

ultrasound scan done during the previews one year. The number of occasions of scanning done ranged from 1 to 8 during one year. 30% of the patients reported to have ultrasound detected renal stone of > 5 mm in size. 37% patients had stones reported to be between 3 to 5 mm in size. 7% of the patients had reported stones less than 3 mm and size. 12% of patients had reports of stones multiple stones in multiple sites. 17% of the stones reported by the ultrasound were in the ureter and 16% had back pressure effects. The patients with renal stones had various treatments and the subsequent ultrasound scans showed disappearance of stones in 87%. In 53 patients, were more than three ultrasound since had been performed. Among these 17 reported stones which were not reported in the earlier ultrasound scans. The variations were more when the ultrasound scan was performed in different centers. X ray examination of the KUB region was performed in 33% of the patients. It was done in more than 3 occasions in 7.70% of the X rays taken were poorly prepared and did not show any significant findings. Properly prepared KUB x-rays did show movement of stones. Non contrast CT scan was performed in 5 patients only and 3 of the patient had recorded stones. None of them passed the stones subsequently and the two patients who did not show the radio opaque shadow in the CT scan passed stones spontaneously during the period of one year.
Conclusions: It is concluded form the study that monitoring stone presence and movement should be done according the rigid guidelines. Ultrasonography should be done once in order to assess the obstructive features and presence of radiolucent stones, rather than for assessment of the size of the stones. Plain x-ray KUB region should not be repeated frequently. CT scan is not cost effective and it is associated with negative findings.

POSTER B

SWL & URS

48 – WHICH ANALGESIA TYPE IS MORE COMFORTABLE FOR PATIENTS UNDERGOING ESWL TREATMENT?

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Objectives and Introduction: ESWL (extracorporeal shock wave lithotripsy) is one of the most effective treatment of urinary stones. But pain during the procedure limits the efficacy of the procedure. Some studies showed that pain during the procedure is related with the shock power. In this study we compared the efficacy of single agent narchotic analgesic and combination sedoanalgesia.
Patients and Methods: 46 patients included in the study. All patients underwent ESWL treatment for the first time. 21 patients (age: 21-64) received 50 mg. meperidine i.m. 15 minutes before the ESWL procedure. 25 patients (age: 26-62) received 2 mg. midazolam (Dormicum) i.v. and 50 mg. fentanyl i.v. All patients answered the VAS(visual analog scala). All patients numerated according to VAS after two hours from the procedure.
Results: The mean VAS score for meperidine group and dormicum-fentanyl group were 6.32, 4.58, respectively. The difference between two groups was not statistically significant. But 80% of the patients who received only meperidine before procedure mentioned that they do not want to undergo second procedure with the same analgesia method. Controversely, 88% of the patients those received dormicum and fentanyl pointed that they did not remember the procedure because of the amnesia effect. Therefore they mentioned second procedure of ESWL would not be a problem. The mean shock power for the meperidine group was 13.7, and for dormicum-fentanyl group was 18.2 ($p = 0.002$).
Conclusions: Although the difference between the VAS scores was not statistically significant, the elevated shock power when using dormicum-fentanyl analgesia may be useful for efficacy of ESWL.

49 – THE EFFICACY, SAFETY AND PATIENT SATISFACTION WITH SERIAL INPATIENT EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY (ESWL) IN A TERTIARY REFERRAL STONE CENTRE

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Objectives: Some patients requiring ESWL have complex stone burdens and others find the procedure painful or require stopping anticoagulation for their treatment. In such patients outpatient treatment may not be suitable or logistically too difficult to arrange to the patients satisfaction. We carry out serial inpatient ESWL (at least three sessions over a 5-day period) in such patients at our unit. We try to evaluate the efficacy, safety and patient satisfaction with serial ESWL for these stones and stratify the efficacy by stone burden and location.
Materials and Methods: Thirty six patients (15 males, 21 females) with a mean age of 51 years (range 28 to 85 years) had at least 3 inpatient ESWL sessions in 5 days. Of these, 10 patients with low pain tolerance who could not tolerate outpatient ESWL pain protocols received an intravenous pain protocol with opioid based analgesia, 9 had to stop anticoagulant therapy prior to ESWL, 14 had emergency ESWL for ureteric stones and 3 patients were treated for residual stones after percutaneous renal surgery. Stone burden and location were analysed for all patients. The stone burden or surface area was calculated by using the formula: SA = length x width x Π x 0.25 in mm^2. Our lithotripter (Lithostar multiline, Siemens) delivered 120 shockwaves per minute. 4000 impulses at a maximum power of 4 were given for renal calyceal stones, 4000 impulses at a maximum power of 5 for renal pelvic and pelvi-ureteric junction (PUJ) stones and 5000 impulses at a maximum power of 12 were delivered for ureteric stones. Stone free status was determined by a plain X-ray or CT KUB depending on case complexity and was defined as the absence of stones or residual fragments < 2 mm.
Results: 36 patients had a total of 93 calculi treated with serial inpatient ESWL. The mean stone burden per patient was 121 mm^2 (renal calyceal stones: 115mm^2, renal pelvic stones/PUJ stones: 213mm^2, ureteric stones: 92mm^2). The overall mean number of ESWL sessions per patient was 3.34. The mean number of ESWL sessions for patients' with a renal stone burden of less than 70mm^2 was 3.2 whilst in those with a renal stone burden greater than 70mm^2 it was 4.7. The mean number of ESWL sessions in patients with ureteric stone burden less and greater than 50 mm^2 was 3.0 and 3.2 respectively. The stone-free rate for patients with a kidney

stone burden less and greater than 70mm² was 87% and 67% respectively. For a ureteric stone burden less and greater than 50 mm², the stone free rate was 93% and 85% respectively. Four patients (11%) needed an auxiliary procedure (3 ureteroscopy and 1 PCNL). Only 2 patients (5.6%) had transient minor complications (1 urinary tract infection and 1 haematuria). No procedures were abandoned due to pain.
Discussion: Our experience with serial ESWL shows it to be a safe and effective procedure. Although there are no strict guidelines as to the frequency of giving serial ESWL, many clinicians feel that there ought to be at least a 48-hour gap between treatments. This stems from a feeling that this allows oedema especially in the ureter to resolve and hence aid stone passage. We found that even for ureteric stones our protocol produces acceptable rates of stone clearance. Patients found treatment safe, convenient and acceptable. Serial inpatient ESWL represents a valid treatment for patients with large stone burdens, those with low pain thresholds and in those who have to stop anticoagulation. It is also an acceptable cost effective treatment with good efficacy in patients presenting with ureteric colic requiring intervention.

50 – PRELIMINARY ANALYSIS OF 2-YEAR EXPERIENCE WITH DORNIER LITHOTRIPTER EMSE 220 XXP

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Objectives: Extracorporeal shock wave lithotripsy (ESWL) represents the non invasive treatment for urolithiasis: the Doli S EMSE 220 is a third generation electromagnetic shock wave emitter, with proven characteristics in terms of efficacy and safety. The modified Doli S EMSE 220 XXP represents an innovative improvement among other devices, with an increased acoustic output of the shock wave source and a consequent increased effective energy. We present our preliminary series with the Doli S EMSE 220 XXP in the treatment of renal and ureteral stones.
Materials and Methods: We performed 1014 ESWL sessions during 22 months with Doli S EMSE 220 XXP. 622 patients were admitted for renal stones (144 multiple caliceal stone disease) and 187 for ureteral stones. Mean stone size was 9.5 and 12.1 mm for caliceal and pielic site, respectively; mean stone size for ureteral stones was set at 9.1 mm. Stone focusing was obtained by means of both fluoroscopic and ultrasound monitoring; a total of 2800 and 3200 pulses were used for renal and ureteral location respectively. Follow up was performed by means of KUB rays and US or helical CT, at 1 and 2 months for renal stone location; the same exams were used at 3 and 6 weeks after ESWL of ureteral stones. Global stone free rate, number of treatment required (per stone), and side effects were recorded into a proper data base and reviewed.
Results: A complete stone free condition was evident in 542 patients (87.1%) with renal stones and in 167 patients (89.3%) with ureteral stones, respectively. Mean number of treatments per patient was 1.3 and 1.1 for kidney and ureteral localion, respectively. Analgesia requirement, that was easily achieved with ketorolac or tramadol, was more frequent for ureeral stones (48.1%) than for renal stones (19.2%). Global side effects consisted of 28 (2.7%) cases of Steinstraße requiring endourological approach and 3 subcapsular haematomas (0.4%).
Conclusions: The new Doli S EMSE 220 XXP can be considered an innovative improvement among previous lithotriptors: its disintegration capacity (Dc) is almost twice higher than the Doli S EMSE, thus providing better outcomes in terms of stone fragmentation. Our series provides satisfactory outcomes in terms of stone free and re-treatment rate. Slow SW rate, slowly increasing of energy level, ultrasound monitoring are simple recommendation that can provide safety and lack of major side effects even with this upgraded device.

51 – DETERMINATION OF SERUM AND URINARY CYSTATIN C (CYSC) MAY BE USEFUL IN RENAL FUNCTION MONITORING AFTER ESWL

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Objectives: As cystatin C (CysC) has been proposed as an earlier and more reliable indicator of renal function than creatinine (Cr), and ESWL causes kidney injury our objective was to determine whether serum or urinary CysC could identify alterations in renal function earlier than Cr after a unique treatment of kidney stones with ESWL.
Materials and Methods: Prior sample size calculation we prospectively included 33 patients with kidney stones eligible for ESWL. The treatment was performed on a regular basis with a Dornier Lithotripter S XP. We collected data on the ESWL and CysC and Cr were determined in serum and urine just before the ESWL, and 1 hour, 2, 4 and 7 days later. Statistical analysis with SPSS 13.0. $p < 0.05$*.
Results: Average age: 49 years [24-75]. 57% men. The average serum CysC and Cr values remained within normal ranges but showed significant differences between the 2 first and 3 subsequent measurements. Both of them showed a slight improvement 1 hour after the treatment, probably due to local hypervascularization, worsening afterwards and not gaining baseline values at the end of the study (7 days after treatment). Urinary Cr showed a chaotic pattern, and urinary CysC significantly raised immediately post-lithotripsy, returning to normality at day 2 after ESWL, suggesting that in addition to glomerular injury, there could be a damage in the proximal tubule requiring a shorter recovery time. No correlation was found between number or power of shockwaves and timed levels of serum or urinary CysC and Cr.
Conclusions: Attending to the results, although more comfortable than serum CysC, urinary CysC wouldn't be enough to repetitive ESWL planning as it normalizes two days after treatment (tubule recovery), while renal function worsening (glomerular damage) seems to persists at least one week.

52 – COMPARISON OF URETEROSCOPY AND SWL IN TREATMENT OF LOWER URETERAL CALCULI

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Objectives: To compare the success and complications of ureteroscopy (URS) and shock wave lithotripsy (SWL) for the treatment of lower ureteric calculi.
Materials and Methods: A total of 92 patients with lower

ureteral calculi treated between January 2004 and April 2008 included study. Of them, 52 patients underwent URS and 40 SWL for the treatment. SWL was performed with Stonelith V5 lithotripter (PCK, Turkey) under intravenous sedation. URS was performed with 9.5 F rigid ureteroscope under general anesthesia or sedoanalgesia. Pneumatic lithotripsy and/or forceps were used during URS. Medical records of patients were reviewed.

Results: The mean stone size in URS group was 8.4 mm and in SWL group 9.2 mm. Success rate in URS was 92.3%. Minor complication of URS (mucosal avulsion and bleeding) was seen in five patients (9.6%), ureteral perforation and stricture in one patient (1.9%). Of the 40 patients treated by SWL, 27 patients (67.5%) became stone free in a month. There were no significant complications related to SWL.

Ureteroscopy was needed for twelve patients (30%) where SWL failed. SWL had a re-treatment rate of 30% vs. 5% in the URS group. ESWL was administered on outpatient basis, while patients needed hospitalization and anesthesia for ureteroscopy.

Conclusions: URS is more successful than SWL for the treatment of lower ureteric calculi. However SWL can be the primary treatment option as it is minimally invasive and safe and ureteroscopy can be offered to patients who demand immediate relief or when SWL fails.

53 – EMERGENCY INPATIENT EXTRA-CORPOREAL SHOCKWAVE LITHOTRIPSY (ESWL) IMPROVES STONE CLEARANCE RATES AND ENHANCES PATIENTS' TREATMENT PATHWAY

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Background and objectives: Traditionally in the UK, patients presenting with ureteric stones who are clinically well are discharged home on medical expulsive therapy to await outpatient ESWL treatment. Our unit has an onsite lithotripter (Siemens Lithostar Multiline, 120 shocks per minute), operational from 8am to 9pm daily, five days a week and manned by experienced medical staff. We offer same day inpatient ESWL or treatment the day after admission to most of our patients presenting with ureteric calculi. No patients wait longer than 72 hours for initial ESWL as we have 3 vacant slots daily reserved for emergency ESWL treatment.

We assess whether this practice improves patients' stone free rate and time and reduces the need for operative intervention. If stone clearance rates are improved by this treatment, this translates to better patient care, quicker return to work and activities of daily living and hence significant cost saving to employers.

Patients and Methods: We retrospectively analysed the data of patients over a 12-month period, who presented with ureteric colic and had been treated with inpatient ESWL within 72-hours of presentation. We looked at the size and site of stones, and the number of treatments required to achieve stone free status and what proportion of these patients required ureteroscopy. Over the same period we looked at patients who underwent routine outpatient ESWL for ureteric stones and compared the outcome in terms of number of treatments required to achieve stone free status and the need for ureteroscopy. Only radio-opaque stones were included for ease of follow-up with plain KUB x-ray.

Results: 59 patients with a mean age of 41 years (43 males and 13 females) underwent inpatient ESWL for ureteric stones causing acute renal colic within 72 hours of their presentation. 12 % had pelviureteric junction (PUJ) stones, 19% had proximal third ureteric stones, 25% middle third stones, and 44% had distal ureteric stones. The mean stone size was 7.1mm. Patients underwent a mean of 1.8 ESWL sessions with the first treatment within 72 hours of their presentation and they stayed in the hospital for a mean of 3 days. 3 out of the 59 (5%) patients required ureteroscopy later to clear the stones. In the control group 38 patients' records were analysed. The mean age was 42 years with a 3: 1 male to female distribution. The location of the stones was similar in both groups. The mean stone size was 8.1 mm. Patients underwent a mean of 2.5 ESWL treatments with ureteroscopy required to clear the stones in 11% of patients. The power settings used during ESWL to the treat the ureteric stones were similar in both groups.

Discussion: We have shown that patients with ureteric calculi who get immediate ESWL (within 72 hours of admission: 43% had ESWL within 24 hours, 70% within 48 hours) need fewer ESWL sessions to clear their stones and have a significantly lower requirement for operative intervention. This is likely to be due to these patients having less ureteric oedema and stone impaction than those waiting longer for outpatient ESWL.

As patients are stone free quicker, they suffer less morbidity and can return to their activities of daily living quicker, with less time off work which has a significant cost implication for healthcare providers as well as employers. In order to achieve these goals a state of the art lithotripsy unit, offering daily slots for emergency inpatient treatment, run by well-trained medical staff is essential.

54 – EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY IN ELDERLY PATIENTS

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Introduction: Aim of the study was to assess effectiveness and complications of extracorporeal shockwave lithotripsy (SWL) in a population over 70 years of age.

Materials and Methods: A retrospective study was carried out on patients over 70 (age at treatment) who underwent SWL at our Division from January 1996 to April 2005, with a Storz Modulith SLX electromagnetic shockwave lithotripter.

One hundred and fifteen patients (73 males, 42 females) out of a total of 1,595 (7.2%) were studied. Mean age was 73.6 years (range 70-82). Patients were defined as stone free when no stone fragments could be found on ultrasound and x-ray. All patients underwent unenhanced abdominal x-ray and an ultrasound of the urinary tract 3 days and 1-3 months after treatment. A medium/long-term follow-up was also performed (mean length of follow-up was 59.2 months per patient).

During follow-up, we observed whether any of the following complications arose: arrhythmias and premature ventricular contractions, vasovagal syncope, steinstrasse, hyperpyrexia, arterial hypertension, formation of perirenal haematomas.

Results: Mean shock wave (SW) number was 2,850 per patient (range 1,800-4,500) with average power setting of 18 KV (range 16-20).

At short-term follow-up after each treatment or cycle of treatments (1-3 months from treatment) we observed 72.1% (83/115) stone free patients, 20% (23/115) of patients with residual stone fragments that could be passed (< 4 mm), 3.5% (4/115) of patients with residual stone fragments > 4 mm, 4.3% (5/115) of patients showing no change.
With respect to complications, arrhythmias/PVCs occurred in 7.8% of cases (9/115), nausea and/or vomit in 3.5% (4/115), hypertension episodes in 3.5% (4/115), hyperpyrexia with TA > 38°C in 4.4% (5/115), steinstrasse in 2.6% (3/115), a single case of subcapsular renal haematoma which did not require surgery but was simply monitored by ultrasound over time. In patients suffering from caliceal stones, 52.1% (25/48) were symptomatic and 47.9% (23/48) were asymptomatic prior to treatment. Medium and long-term follow-up of the latter patients (average 59.2 months per patient), showed 56.5% stone free patients (13/23), while new stone formation and recurrence were observed in 17.4% of cases each (4/23); furthermore, one patient who was asymptomatic prior to treatment became symptomatic after SWL.
Conclusions: Lithotripsy appears to be an effective first-line treatment for urinary stones in elderly patients, showing good results and no significant increase in complications. However, in elderly patients with asymptomatic caliceal stones which are not causing kidney pain, extracorporeal lithotripsy can provide more disadvantages than benefits.

55 – EFFECT OF ALKALINE CITRATE ON STONE RECURRENCE AND REGROWTH AFTER SHOCK WAVE LITHOTRIPSY AND PERCUTANEOUS NEPHROLITHOTOMY IN CALCIUM UROLITHIASIS: A RANDOMIZED CONTROLLED TRIAL

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Objectives: To evaluate the preventive effects of potassium sodium citrate on stone recurrence as well as stone growth post ESWL or PCNL in patients with calcium-containing stone.
Patients and Methods: Total 76 patients with calcium calculi who were stone free or had residual stones less than 4 mm following ESWL and PCNL were enrolled . All patients were independently randomized into two groups. Group I (N = 39) was given oral potassium-sodium citrate 81 mEq per day (27 mEq three time a day) and group II (N = 37) was untreated, served as controls. Blood, twenty-four urine evaluation and plain KUB were measured and compared at the baseline and 12 month.
Results: Hypocitraturia (urine citrate level less than 320 mg per day) was found in 44 of total 76 patients, which was 57.9% (18 patients in control group and 26 in treated group). Low urine output (urine volume less than 1,500 ml/d) was secondary common found which was 41.8% in all patients. The stone activity at 12 months follow up; of stone free group, 92.3% of treated group and 57.7% of control group was still stone free. The increase of stone size was found in 7.7% and 42.3% of treated and control group, respectively. Of residual stone group, stone free was found in 30.8% and 9.1 % of treated and control group, respectively Fifty percent of patients of treated group showed the same stone size. The increasing of stone size found in 7.7% and 54.5% of treated and controlled group, respectively.
Conclusions: Hypocitrauria is the most common metabolic disorder in calcium stone patients. Sodium-potassium citrate provides positive effects on stone-forming activities, in a 12 months follow up, in calcium stone patients. We therefore recommend administration of alkali citrates, in patients suffering from urolithiasis, following treatment with ESWL and PCNL procedures, for effective prevention of stone recurrence and stone growth.

56 – USE OF AN ALPHA-BLOCKER AFTER EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY

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Objectives: Estimation of the efficiency of Doxazosin (Cardura) after extracorporeal shock wave lithotripsy (SWL) in patients with a "stone path" in the lower third of the ureter.
Materials and Methods: 40 men with diagnosis of nephrolitiasis were investigated. The patients were subdivided in two groups of 20 patients each (treated and controls). Age of patients ranged from 45 to 70 years. Stones were fragmented by ESWL Fragments after ESWL formed a "stone path" in the lower ureter. The size and location of fragments were comparable in both groups. All patients accepted medicamentous therapy for improvement of passage of fragments after ESWL. Patients of control group accepted antispasmodic No-Spa on 1 tab. (80 mg) x 3 times a day, analgesic Ketanov on 1 tab. (150 mg) x 3 times a day, mineral water up to 2 liter in day and physiotherapy (sine wave modulation currents in a combination with inductiothérme). In the treatment group in addition patients accepted the alpha – blacker Doxazosin (Cardura) at a dosage of 1 tab. (2 mg) x 2 times day. Efficiency of treatment was estimated 3 weeks after the end of treatment by the following criteria: absence of fragments of stones in the lower third of the ureter, degree of painful symptoms and tolerability.
Results: No side effect of Cardura was registered. Patients of both group positively responded to treatment, but results of patients of the treatment group were significantly ($p < 0.05$) better than controls. The "stone path" after ESWL was passed out in 19 (95%) patients of the treatment group and in 11 (55%) patients of the control group. In one patient (5%) of the first group and in 4 (20%) patients of the second group was performed an ureteroscopy with the purpose of extracting stone fragments. In 5 (25%) patients of the second group contact lithotripsy was performed. The painful syndrome during the passage of stone fragments was noted in 4 (20%) patients of the treatment group and 14 (70%) patients of the second group. The positive results of patients of the first group suggests inclusion of the preparation Cardura in the complex lithokinetic therapies. The preparation selectively and competitively blocks postsynaptic and α1A- adrenoreceptor, mainly located in the smooth muscles of prostate, bladder, prostatic part of the urethra, and also α1D- adrenoreceptor, mainly located in the detrusor It leads

to decrease in the tension of the smooth muscles of the bladder neck and prostatic part of the urethra and to improvement of detrusorial function, that finally promotes stone passage.
Conclusions: The esults allow to estimate a positive action of the preparation Cardura on acceleration of the process of fragments passage through the lower ureter after ESWL.

57 – CLINICAL DIFFICULTIES OF ESWL TREATMENT IN CHILDREN WITH UROLITHIASIS – OWN EXPERIENCES

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Objectives: Urolithiasis is frequent, recurrent and familial disease. Actually it is rarely treated surgically, there are less invasive treatment methods: ESWL (extracorporeal shock wave lithotripsy), PCNL (percoutaneous nephrolithotripsy) and URSL (ureteroscopic lithotripsy). The aim of the study is presentation of variable clinical problems that may occur in patients treated by lithotripsy.
Materials and Methods: We present nine cases of patients with complications in the course of urolithiasis treatment. Case 1 describes 13y. old boy treated with ESWL. After second procedure a fragment of crushed stone blocked distant part of urethra and endoscopic procedure was necessary to remove it. Case 2: 2y. old boy with bilateral cast nephrolithiasis after five courses of ESWL, treated successfully but constantly forming new stones. Case 3 and 4: children with nephrolithiasis and encephalocele with paraplegia. ESWL successfully crushed stones, but it was impossible to excrete them from urinary tract. In case 5 we describe 15y. old boy with agenesis of left kidney and right kidney localized in the pelvis. He was successfully treated with ESWL. Case 6: 12y. old girl treated with success with ESWL after failure of URSL. Case 7: 11y. old girl after failure of removing stones crushed by ESWL, treated with success by URSL. Case 8: 12 y. old girl with stricture of ureteropelvical junction and nephrolithiasis. In this case the stone was removed by ESWL after surgical correction of anatomical anomaly. In case 9: (10 y. old boy) ESWL done 4 times was unsuccessfull because of ingrowing of the stone in ureteral mucous membrane. The patient was treated surgically.
Conclusions: Effectiveness of ESWL in children with urolithiasis depends mostly on careful selection of patients to lithotripsy. Good cooperation between nephrologist and urologist is necessary to use combination of variable treatment methods and determines effectiveness and safety of therapy. Clinical complications are possible on every stage of urolithiasis treatment, so individual control during whole therapeutic process is recommended.

58 – URETEROLITHIASIS IN CHILDREN

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Objectives: Urolithiasis is a process during which stones from different urine components are formed in the urinary tract. It is estimated that 5-10% of European population has lithiasis of the urinary tract. In developed countries 1-3% of children have urolithiasis. In Warsaw's Hospital for Children we have been treating children with urolithiasis for many years. Since 2007 we have performed endoscopic procedures such as URSL and PCNL in children with weight over 10 kilograms.
Materials and Methods: 37 children were operated on. Our youngest patient was 13 months. Patients with urinary retention, in ureters, after extracorporeal crushing of stones by ESWL or patients after stone crushing with ultrasound waves, with urinary blockade (stain strasse) were qualified for these procedures. We used ultrasound and pneumatic lithotripters 4.5 Ch. and 6 Ch. for this procedure. Stones were eliminated completely or they were crushed to little pieces achieving spontaneous evacuation.
Results: We had complications in three children. First case – probability of injury to one ureter- a pig tail catheter was installed – no post operative problems were observed. Second case – a small amount of irrigation fluid was observed around kidney capsule after the procedure (ultrasound on the second day has shown no fluid around the capsule). Third case – a stricture of the ureter after the procedure – a stone was lodged in the ureter for about a year before the procedure and it caused a big decubitus ulcer of the ureter.
Conclusions: Presented endoscopic procedure is a safe way to treat pediatric patients with urolithiasis; it is an alternative to surgery.

59 – HOW DID MEDICAL EXPULSIVE TREATMENT CHANGE OUR STRATEGIES IN URETERAL STONE MANAGEMENT?

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Objectives: To evaluate the impact of alpha blocker therapy on the management of the upper and lower ureteral calculi.
Materials and Methods: A total of 196 patients with a single radiopaque ureteral stone smaller than 10 mm (detected either with KUB or non-contrast spiral CT) were included into the study. The patients were randomized into two different groups. The patients in Group 1 (43 patients had upper 48 patients had distal ureteral calculi, n: 91) received (N-hycosyl bromur) medication and tamsulosin 0.4 mg/day for 3 weeks, Group 2 patients (n: 105) received only spasmolytic medication. Stone passage rate, pain, change in colic attacks and subsequent stone removal procedures were compared. Pain descriptions were measured by using the visual analog scale (VAS). Statistical analyses were performed with t test and chi-square tests.
Results: Totally, 92 upper and 104 distal ureteral stones were evaluated. The mean age of the patients were 31.5 ± 4.6 (19 to 51 years). No statistically significant difference was found among the four groups in patient age, sex, stone size or location. Of the 92 upper ureteral calculi, higher stone expulsion rates were noted in patients recieving alpha blockers (16/43; 37.2% vs 14/49; 28.5%) ($p < 0.01$). The similar effect has also been observed in distal ureteral calculi (35/48; 72.9% vs 29/56; 51.7%) ($p < 0.001$). While 27.9% (12/43) of the upper ureteral stones under specific medication did not change its position; one significant change in these calculi was relocation of the calculi to the distal part of the ureter in a meaningful percent of the cases 15/43 (34.8%). Of the 49 upper calculi under conservative follow-up, while in 14 cases (28.5%) spontaneous passage did occur, 11 stones moved to the distal part of the ureter (22.4%).

In proximal ureteral stone, the patients accepting alpha blocker had decreased renal colic episodes during follow-up period were compared to counterparts (34.9% vs 63.3%, p<0.001). The same situation again was valid for distal ureteral calculi with percentages of 29.2% and 67.9% respectively. Evaluation of the analgesic requirement as well as the mean visual analog scale score values during these pain episodes did show statistically significant difference (p < 0.001) in both groups. While of the 49 patients with upper ureteral calculi treated with specific medication needed a total of 27 procedures (20 ureteroscopies and 7 ESWL), this number was 38 in patients followed under conservative approach (28 ureteroscopies and 10 SWL). The total number of procedures were 13 (10 ureteroscopies and 3 SWL) and 29 (24 ureteroscopies and 5 SWL) respectively in subgroups of patients with distal ureteral calculi.

Conclusions: Patients treated with alpha blockers had a greater likelihood of spontaneous ureteral stone passage than the patients followed under conservative approach. Evident improvement in social life of the affected patient is also another reason to add these drugs to the existing medical therapy options. Low risk-profile of these drugs with wide therapeutic window; our results point out a new algorithm for ureteral stone management the treatment begins with a course of medical therapy, unless medically contraindicated.

60 – RESULTS OF RIGID RENOSCOPY AND PNEUMATIC LITHOTRIPSY IN PATIENTS WITH URETERAL STONES

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Objectives: To determine the efficiency of rigid renoscopy and pneumatic lithotripsy treatment in patients with ureteral stones.

Materials and Methods: We retrospectively evaluated 290 patients (296 renal units) with ureteral stones treated by rigid renoscopy with pneumatic lithotripsy. Results were evaluated 3 months after treatment, using excretory urography and/or ultrasonography. Complications and treatment success according to stone localization were compared.

Results: The mean age of the patients was 43.52 (17-80). Ureteral stone was found on the right in 149 (49%) and on the left side in 142 (49%) patients; Stones were bilateral in 6 (2%) patients. 99 (34.1%) patients were female and 191 (65.9%) were male. Most stones (80.1%) were localized to lower ureter, compared to middle (11.8%) and upper (8.1%) ureter. The mean stone diameter was 13.21 mm (range 5-30 mm). The mean stone free rate was 92.6%: Stone free rate was 79.2% in upper ureter, 91.4% in middle ureter and 93.2% in lower ureter (p = 0.067).

Total complication rate was 13.2%: 11.8% in lower ureter, 14.3% in middle ureter and 25% in upper ureter (p = 0.174). Most common peroperative complications of the procedure were infection (3.7%), conversion to open surgery (2.7%), ureteral perforation (2.3%) and mucosal laceration (0.6%). The most common late postoperative complication was ureteral stricture (1.3%). Stone free rate was lower and complication rate was higher in upper ureteral stones, even though not significant.

Conclusions: Ureteroscopic treatment of ureteral stones provides higher success rates, quick stone clearance, short hospital stay and low complication rates for middle and lower ureter stones. Stone free rate was lower and complication rate was higher in upper ureteral stones, when treated with rigid renoscopy with pneumatic lithotripsy. Advanced flexible ureteroscopy systems may improve outcomes of treatment of ureter stones at this location.

61 – A COMPARATIVE STUDY OF THE REQUIREMENT OF INTRODUCER SHEATHS FOR URETERIC ACCESS BETWEEN AN OLD-GENERATION FIBRE-OPTIC FLEXIBLE URETEROSCOPE AND A NEW "CHIP ON THE TIP" DIGITAL FLEXIBLE URETEROSCOPE

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Background and objectives: Although the new generation "chip on the tip" digital flexible ureteroscopes provide significantly superior views during stone interventions and are likely to be more durable than the old generation fibre-optic flexible ureteroscopes, one area of concern might be their larger distal tip diameter as it houses the digital chip. This larger diameter might necessitate more frequent use of an introducer sheath to gain entry into the ureter. This of course may increase the risk of ureteric injury, the need for placing a JJ stent and has cost implications. We compare the need to use introducer sheaths to gain ureteric access for fibre-optic (FO) and liquid crystal display (LCD) digital flexible ureteroscopies (f-URS). We also looked to see whether there was a difference in the rate of post-operative stenting and complications in the two groups as a result of using the access sheath

Materials and Methods: We only looked at the need for a sheath in order to gain access to the ureter in all patients undergoing flexible uretero-renoscopy over a 30 month period between June 2006 and January 2009. Patients were scoped with either an old generation fibre optic flexible ureteroscope (DUR-8, Elite, ACMI; Working Length = 65cm; Distal Tip Diameter = 8.5F) or a new generation "chip on the tip" digital LCD flexible ureteroscope (Invisio D-URD flexible ureteroscope; Working Length = 65 cm; Distal Tip Diameter = 8.7F).

The need to use a sheath to gain access was recorded for both groups. All patients had a general anaesthetic and received 20milligrams of buscopan intravenously per-operatively to paralyse and relax the ureter to reduce the chances of using a sheath. The age and sex of the patients and indications for f-URS were noted and compared between the two groups. Any patients who had a pre-operative JJ stent in place were excluded from the study.

Results: FO and LCD flexible ureteroscopies were performed in 157 cases over the time frame. Sheaths were used for access more frequently in LCD f-URS cases; 19 out of 77 LCD f-URS cases required a sheath for access (25%), compared to 6 out of 80 FO f-URS cases (7.5%). Student's t-test produced a significant difference between the two groups (p value 0.00174). The two groups were well matched in terms of age and sex as well as indications for f-URS (85% for upper ureteric and renal calculi, 10% diagnostic and 5% for renal pelvic transitional cell carcinoma fulgaration). The vast majority of f-URS were carried out for stone disease and the

groups were well matched in terms of stone location and stone burden.
Post-operative JJ stenting was required in 35 of the 77 patients in the digital f-URS group and in 31 out of 80 in the fibre-optic f-URS group. This was not significantly different and may due to reduced operating time as a result of the superior image quality.
In 2 patients in the digital f-URS group, the procedure was abandoned due to ureteric perforation from the introducer sheath. There were no ureteric perforations in the fibre-optic f-URS group
Conclusions: A statistically significant increase in sheath use was observed in the new generation digital f-URS group despite an increase in the tip diameter of only 0.2F (8.7F VS 8.5F). This is likely to be due to the increase in distal tip diameter of these scopes. Despite the obvious improvement in the images obtained and the likely better durability, the increased use of ureteric access sheaths may increase morbidity and expense. Clinicians need to be aware of these drawbacks.

62 – STENTING AFTER URETEROSCOPY FOR URETERAL LITHIASIS: RESULTS OF A RETROSPECTIVE STUDY

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Introduction: Routine stenting following ureteroscopy is common, particularly after ureteroscopic lithotripsy. However ureteral stents negatively impact quality of life and can cause significant morbidity. This retrospective analysis was carried out to report our experience.
Materials and Methods: Between June 1999 and December 2008 529 patients underwent ureteroscopy with Lithoclast or Holmiun Laser 20 W intracorporeal lithotripsy for the treatment of ureteral stones. In 436 pts (82%) stenting was placed, in 281 double J stent (removed within 2-4 weeks) and in 155 mono J stent (removed within 24 h.). Ninety-three did not receive stenting.
The two stented groups were comparable with respect to the diameter, stone location and mean stone size. At 24 h the outcomes measured were post operative pain, fever and hematuria, at 4 weeks the need for hospital care (readmission or visit in the clinic) for LUTS (dysuria, urinary tract infection, frequency/urgency), hematuria, fever or pain were evaluated. KUB and renal sonogram were performed 3 months after the ureteroscopy. Excretory urography and CT were performed only in selected cases.
Results: No significant difference was observed between two groups regarding the complications at 24 h. after the treatment (hematuria p = 0.8, fever p = 0.7, pain p = 0.6). At 4 weeks after the ureteroscopy the incidence of LUTS, hematuria, pain and or fever requiring the need for hospital care (readmission or visit in the clinic) was higher in the group with double J stent respect to the group with mono J stent ($p < 0.05$). At 3 months follow-up no difference was observed between the two groups regarding stone-free rate (97% and 96%) and incidence of ureteral stricutre formation (0.6% and 0.7% respectively).
Conclusions: In this retrospective analysis routine stenting is necessary after ureteroscopy for ureteral lithiasis to prevent pain and fever without difference in stone free and incidence of stricture formation rate between the two groups. LUTS, hematuria, fever and/or pain needing for hospital care were more frequent in the group with Double J stent in spite of high stone free rate and low incidence of stricture formation. Further prospective randomized studies are needed to assess the role of use of "short" and "long" stenting after ureteroscopy lithotripsy, considering that intraoperative decision actually depends on the surgeon.

63 – COST ANALYSIS OF FLEXIBLE URETERORENOSCOPY AFTER 630 INTERVENTIONS

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Introduction: Flexible ureterorenoscopy plays an important role in the treatment of upper urinary tract diseases. Due to the use and technical wear of flexible scopes every procedure causes additional costs. Frequency and costs of repair were analysed.
Materials and Methods: 630 consecutive flexible ureterorenoscopic procedures were evaluated. In all cases an ureteral access sheath was used. In 514 cases renal pelvic or calyceal stones were treated. In 275 cases holmium laser-lithotrypsy (230 µm fibre) was used. In total the procedures were performed by 12 flexible ureteroscopes (Viper, Richard Wolf Company, Knittlingen, Germany).
Results: In total 29 repairs were necessary in 12 instruments. Total costs of repair were Euro 96.037,51. The mean costs per procedure were Euro 152,44. The average durability of each instrument was 21.9 procedures. Repair of flexible scopes was necessary due to alteration of the working channel, the wires for deflection, alteration of the scope´s surface and break of optical fibres. Damages were caused by use of holmium laser during operation, sterilisation process and transportation.
Conclusions: Flexible ureterorenoscopy is associated with additional costs due to the fragility of instruments. These costs of repair are acceptable as they only account for a minor part of the reimbursement. Because of the shorter treatment time, lower retreatment rate and higher stone free rate than shockwave lithotripsy it is cost-effective to use flexible ureterorenoscopy in endourological stone treatment.

64 – CAN FLEXIBLE URETERORENOSCOPY (FURS) BE RECOMMENDED IN THE TREATMENT OF STONE MASSES GREATER THAN 100MM² IN THE UPPER URINARY TRACT?

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Introduction: Since new flexible ureterorenoscopes have been invented, flexible ureterorenoscopy is more frequently used for the treatment of calyceal stones in combination or alternatively to extracorporal shockwave lithotripsy (SWL). For a reasonable procedure the diameter of the ureteral access seems to limit the maximal stonesize to 100mm³. With enhanced surgical ability the treatment of higher stone masses is possible.
Materials and Methods: A prospective study of 630 consecutive flexible URS-procedures for stone treatment, diagnostic purpose or laser surgery of calyceal stenosis was conducted. We compared a subgroup A (148 procedures on 107 patients with stonemasses > 100 mm³) with a subgroup B (482 procedures on 434 patients). Endoscopic procedures were done by

means of 270°-deflectable or double-bending ureterorenoscopes using an ureteral access sheath of 14 or 16 F. Lithotripsy was done by means of a holmium-laser. Data for stonefree rate, operating time, hospital stay length, complication rate, stone analysis, stone localisation and auxiliary procedures was collected.

Results: In group A in all cases urinary tract stones were detected and treated, in Group B in 354 cases (73.4%) stones were found in the calyceal system. Stonefree rates were 86.9% (A) and 94.8% (B). Mean operating time was 67.2 min (A) and 50.8 min (B). Reoperating rate was 32.7% in group A and 9.1% in group B. Complication rate was 14.9% (A) versus 6.6% (B) for pyelonephritis and 2.8% (A) versus 2.2% (B) for ureteral perforation. Mean hospitalisation time after the last procedure was 5.0 days (A) versus 3.2 days (B).

Conclusions: Flexible ureterorenoscopy is a reliable and effective diagnostic and treatment modality for stones of the upper urinary tract. With acceptance of a slightly higher complication rate and length of hospitalisation stones of more than 100mm^2 can be treated successfully. Until today SWL is the guideline recommended therapy for stones between 1 and 2 cm diameter. Randomized studies are needed to determine the significance of flexible ureterorenoscopy in the treatment of stones > 100mm^2 in the upper urinary tract.

65 – THE NEW GENERATION INVISIO® DUR-D URETEROSCOPES – EVALUATION OF CHANGES IN PHYSICAL PROPERTIES OVER TIME

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Background and Purpose: Flexible ureteroscopes have become an essential tool in endourological practice. Recently, a new generation of digital flexible ureteroscopes has been marketed (Invisio® DUR-D, ACMI, USA) with which a new optical technology was introduced. The tip houses dual Light Emitting Diodes (LED) driven light carriers. A 1mm digital camera at the tip eliminates the need for fragile low-resolution fibre-optics and provides superior resolution. In addition, the image quality is digitally enhanced. It was claimed that not only should this markedly increase the image quality, but also make the instrument more durable in the whole. We have therefore compared both, light intensity and deflection angles with and without indwelling instruments between identical scopes after different number of uses.

Materials and Methods: On three identical Invisio® DUR-D digital flexible ureteroscopes of different usages we measured and compared the light intensity at a given setting of the light source using an Ocean Optics optical spectrometer at 20mm distance from the tip. Measurements were taken three times each with the ureteroscopes in straight position and upwards/ downwards deflection, respectively. The first scope was brand new; the second had been used 30 times while the third had been used 44 times. We also measured and compared the deflection angles without and with instruments – a 0.035" Cook guidewire, a 200 µm laser fibre and a 3F zero-tip nitinol basket – inside the working channel in four identical scopes after 0, 10, 30, and 44 uses, respectively.

Results: Light intensity for each scope showed slight differences in relation to deflection angles, which is within the experimental error and did not significantly differ. Light output remained stable after many uses (Table 1).

Table 1.
Light intensity in different deflection (unit: Lux x 10^3)

	Straight	upwards	Downwards
0 uses	5.5	4.36	4.84
30 uses	6.19	6.30	6.25
44 uses	5.05	5.25	5.15

In contrast, the deflection angle is shown to deteriorate with instruments inside the working channel. This is relatively independent of the type of micro-instrument used, but the decrease is directly proportional with advanced age of the scope (Table 2).

Table 2.
Deflection angles with different instruments

	No instrum.	.035" guidewire	200 µm laser fibre	3F nitinol basket
0 uses upwards	218°	196°	205°	204°
10 uses upwards	216°	194°	203°	203°
30 uses upwards	197	173°	174°	174°
44 uses upwards	163°	148°	155°	152°
0 uses downwards	216°	194°	209°	191°
10 uses downwards	199°	191°	192°	190°
30 uses downwards	230°	139°	151°	147°
44 uses downwards	170°	123°	141°	158°

Conclusions: As an advantage over earlier generation scopes, light output remains constant due to the avoidance of the fragile low-resolution fibre-optics, further helped by digital enhancement. Similarly to the earlier generation scopes, there remains a decrease in deflection capability over time with the new Invisio® DUR-D digital flexible ureteroscopes.

66 – PROSPECTIVE STUDY OF 630 CONSECUTIVE FLEXIBLE URETERORENOSCOPIES (FURS) OF THE UPPER URINARY TRACT

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Introduction: Since new flexible ureterorenoscopes have been invented, flexible endoscopy of the upper urinary tract became easier and its significance has to be determined.

Pathologies of the upper urinary tract, such as calyceal and renal pelvic stones, calyceal diverticulum stones, morphological obstructions and tumors, can be treated under direct endoscopic vision. Especially in cases with lower pole stones flexible ureterorenoscopy shows more favourable results than extracorporal shockwave lithotripsy (SWL).

Materials and Methods: A prospective study of 630 consecutive flexible URS-procedures for stone treatment, diagnosis or laser surgery of calyceal stenosis was conducted. Endoscopic procedures were done by means of 270°-deflec-

table or double-bending ureteroreno-scopes using an ureteral access sheath of 14 or 16 F. Lithotripsy or incision was done by means of a holmium-laser. Data for stonefree rate, operating time, hospital stay length, complication rate, stone analysis, localisation of the stone and auxiliary procedures was collected in 630 procedures.
Results: Mean operating time was 55.6 min. In 514 cases urinary tract stones were detected and treated. Mean stone size was 72.1 mm^3. In 50.1% Holmium-laserlithotripsy was performed. 32.8% of the patients had been pretreated by SWL and flexible uretero-renoscopy was used to remove residual fragments.
Complication rate was 7.3% for pyelonephritis and 1.9% for ureteral perforation. Overall stonefree rate was 87.3%.
Conclusions: Flexible ureterorenoscopy is a reliable and effective diagnostic and treatment moda-lity for different pathologies of the upper urinary tract. Main advantage in comparison to SWL is an increased stone-free rate and a reduced treatment time. Anatomical abnormalities, e.g. calyceal stenosis, can be treated simultaneously with stone therapy.
Since now flexible ureterorenoscopy of the upper urinary tract is not recommended as a first line therapy by international guidelines. Based on the presented results randomized studies are needed to determine the significance of flexible ureteroreno-scopy in the upper urinary tract.

67 – RIRS – RETROGRADE INTRA RENAL SURGERY – SIMULTANEOUS TREATMENT OF RENAL AND URETERAL STONES WITH SEVERE STONE BURDEN

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Objectives: Laser retrograde intrarenal surgery (RIRS) allows the treatment of renal stones, especially lower caliceal location, with definite advantages in terms of reduced morbidity. We report a case of simultaneous treatment of reno-ureteral stones with RIRS approach.
Materials and Methods: A 39 years-old man was admitted to our Department for relapsing renal colic due to a staghorn pielic stone (30 mm) detected with helical CT scan. Stone radiodensity was HU 300-500, with associated hydronephrosis. Renal function (recorded as creatinine value) was within the range; however, the serum exam revealed a severe hyperuricemia.
A medical therapy with allopurinolo and urine alkalinization was promptly recommended; however, the patient refused any minimally invasive approach, such as percutaneous lithotripsy (PCNL) or RIRS. Thus, we decided to manage the patient with one session of extracorporeal shock wave lithotripsy (ESWL).
After a few days, a nephrostomic tube was positioned for the onset of steinstrasse with hydronephrosis and urosepsis. A retrograde approach was finally performed: firstly, a rigid ureteroscopy with ballistic lithotripsy and retrieval of fragments by means of a basket; afterward, the treatment was completed with flexible ureteroscopy and Holmium laser lithotripsy of residual caliceal stones. A double J ureteral stent was finally positioned with removal of the nephrostomic tube.
Results: The patient was discharged 2 days after the endoscopic procedure and ureteral stent was successfully removed 20 days later. Physical examination of the stone revealed a main uric acid composition, with associated calcium oxalate. A minor caliceal fragment 6 mm in size was detected at the follow up ultrasound, and successfully treated with ESWL.
Conclusions: The widespread introduction of upgraded flexible ureteroscopes, laser energies and baskets, allows the treatment of stones everywhere located along the excretory way. RIRS has been recently introduced as an alternative to PCNL, with less invasiveness, better esthetical result and faster discharge; our clinical case confirms its emerging role for the simultaneous treatment of renal (caliceal) and ureteral stones.

68 – TRANSURETHRAL ENDOSCOPIC CONTACT URETEROLITHOTRIPSY

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Objectives: The retrospective analysis and estimation of efficiency of contact ureterolithotripsy for ureteral lithiasis.
Materials and Methods: During the past 3 years at our faculty clinic 320 endoscopic contact ureterolithotripsies have been performed. Age of the patients ranged from 23 to 78 years, 197 men and 123 women. Out of them 281 (87,8%) presented as emergency indications. Stones (size range from 0,6 to 1,5 mm) were located in the upper or mid ureter in 189 patients and in the lower ureter in 131. For contact ureterolithotripsy the ultrasonic Storz device and the pneumatic lithotripter "Lithoclast" EMS were used. Contact ureterolithotripsy was performed after administration of wide spectrum antibacterial therapy under intravenous neuroleptanalgesia.
Results: Duration of operation varied from 10 to 50 minutes depending on the complexity of a case. In 279 (87,1%) patients complete stone fragmentation was obtained and in 41 (12,9%) partial fragmentation with upward migration of fragments to the calyces – pelvis system and subsequent successful extracorporeal lithotripsy.
Conclusions: Ureteral lithiasis is the most common reason of obstruction of the ureters. Today endoscopic methods of removal of ureteral stones are the most widespread and effective. Contact ureterolithotripsy is an effective and less invasive method of treatment for ureterolithiasis.

POSTER C

METABOLISM, TREATMENT

69 – COMPARATIVE VARIATIONS IN WHOLE BODY ELECTROLYTE FREE WATER CLEARANCE (WB-EFWC) IN PATIENTS WITH TWO LEVELS OF HYPERCALCIURIA IN CALCIUM NEPHROLITHIASIS

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Objectives: The increase in urinary volume is a mainstay of the "stone clinic". However, urinary volume is the end-result of a complex equilibrium between water intake and renal han-

dling. The molecular mechanisms of the effect of luminal calcium (Ca) on the facultative water absorption in the collecting duct have been recently understood. Luminal Ca through its CaSR receptor hinders the ADH-dependent translocation of aquaporins to the luminal tubular membrane thus impairing water reabsorption. While this mechanism seems to be relevant in severe pathological conditions, whether it may be disclosed also in "paraphysiological" conditions such as idiopathic hypercalciuria is not known. We have investigated this issue in stone patients with idiopathic hypercalciuria.

Materials and Methods: From our database of 852 renal stone patients, we selected those with hypercalciuria at their first calcium stone episode who hadn't had any treatment or "stone clinic" suggestion before laboratory evaluation. All had to be idiopathic for both hypercalciuria and stone disease. Forty-nine (23 women) patients were found. They were analyzed according to UCa: group females1 and males1, respectively, with UCa 5.6-6.7 mg/kg/day; females2 and males2 with UCa 4.8-6.4 mg/Kg/day.

Results:

	$Females_1$	$Females_2$	$Males_1$	$Males_2$
N° of patients	12	11	13	12
Age, years	35.4 ± 6.1	33.6 ± 4.9	34.2 ± 4.3	32.3 ± 5.6
Ca Intake, mg/day	980 ± 328	1279 ± 451		
S_K, mEq/l	3.94 ± 0.06	3.69 ± 0.07*	4.35 ± 0.04	4.16 ± 0.05
U_{Ca}, mg/kg/day	4.8 ± 1.6	6.4 ± 1.5**	5.6 ± 1.7	6.7 ± 1.4**
V, ml/min	1.17 ± 0.05	2.05 ± 0.08**	1.22 ± 0.05	2.24 ± 0.07**
CCr, mL/min/1.73 m^2	123 ± 29	132 ± 15	128 ± 23	131 ± 18
UCI, index	105 ± 18	156 ± 24**	133 ± 23	153 ± 18**
U_{Osm}, mOsm/kg H_2O	586 ± 89	403 ± 53**	643 ± 98	458 ± 120**
COsm, ml/min	0.84 ± 0.01	1.62 ± 0.03*	0.92 ± 0.01	1.59 ± 0.03**
E-C_{H20}	-1.37 ± 0.05	-1.02 ± 0.06*	-1.59 ± 0.08	-1.44 ± 0.07*
WB-EFWC, l/day	0.115 ± 0.06	0.626 ± 0.05**	0.158 ± 0.04	0.539 ± 0.08**
NEAP, mM/day	38 ± 9	37 ± 10	44 ± 13	43 ± 12
$U_{Na}V$, mM/day	156 ± 44	218 ± 34*	187 ± 42	233 ± 56*
U_KV, mM/day	45 ± 12	55 ± 11	58 ± 13	65 ± 9
$U_{citrate}$, mg/day	488 ± 97	354 ± 68**	564 ± 187	390 ± 101**
U_P, mg/day	676 ± 137	856 ± 199*	1129 ± 329	1325 ± 289*
UCa vs WB-EFWC	r = 0.046, ns	0.361**, p < .001	r = 0.049, ns	r = 0.418, p < .001

Values are means ± SD. *P < .005; **P < .001. Correlation coefficients (r) **P < .001 or ns.

Conclusions: Our study shows that diuresis, is increased in subjects with very high levels of UCa. The increased urinary volume induces a significant decrease in E-CH20 and WB-EFWC thus indirectly supporting a teleological protective effect against the risk of intratubular calcium salt precipitation.

70 – EFFECTS OF BODY COMPOSITION ON BONE DENSITY IN HEALTHY WOMEN AND IN WOMEN WITH IDIOPATHIC CALCIUM NEPHROLITHIASIS

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Objectives: To analyze body composition (lean mass, fat mass and mineral mass) in women with idiopathic calcium nephrolithiasis (ICN) and controls and to evaluate the associations between anthropometric parameters (weight and height), body composition (lean mass and fat mass) and bone density.

Materials and Methods: 37 women with ICN (group A) and 96 controls (group B) were assessed according to menopausal status: group A1 pre-menopausal stone formers (n. 21), group A2 post-menopausal stone formers (n. 16), group B1 pre-menopausal healthy women (n. 70), group B2 post-menopausal healthy women (n. 26). No women had osteoporosis in her history or therapies interfering calcium, phosphate or bone metabolism. All women were subjected to an assessment of body composition by Dual Energy X-Ray Absorbtiometry (DEXA) and collection of clinical history targeted to detect minimal trauma fractures and physical activity.

Results: Lean mass and total fat mass, trunk fat and lean, legs fat and lean, their relationship and the percentage of fat mass on total mass were not different in controls and stone formers women, both in pre- and post-menopausal status. Only the trunk lean/legs lean ratio was significantly higher in post-menopausal stone formers compared to controls (group A2 1.68 ± 0.17 vs group B2 1.55 ± 0.20, p = 0.031). The bone mineral density (BMD) was significantly worse in stone formers both as absolute values and as T-and Z-score, particularly in the femur area (p < 0.05); however, the percentage of women with previous minimal trauma fractures was not statistically different in 4 groups.

In the group B1 (pre-menopausal controls) the lean mass was positively associated with almost all bone parameters and fat mass; after correction for body weight, it was negatively associated with total body and limbs BMD. In the group A1 (pre-menopausal stone formers), the lean mass was positively associated only with femoral bone density and, after correction for body weight, leg fat mass was negatively associated with total body (T e Z score).

In the group B2 (post-menopausal controls) the entire body mass was positively associated with all measured bone parameters, except total body and arm BMD. In post-menopausal stone formers only femur bone density was positively associated with body mass (total, lean and fat). The percentage of women performing physical activity was significantly higher in controls compared to women with ICN (35% vs 16%; p = 0,003).

Conclusions: Body composition of women with ICN differs from controls only for bone density, which is lower in stone formers. The effects of body composition on BMD are more evident in the controls. Further studies should confirm these data with particular regard to the role of physical activity.

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71 – POLYMORPHISMS OF THE CALCIUM-SENSING RECEPTOR GENE AND STONES IN PRIMARY HYPERPARATHYROIDISM.

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Objectives: Calcium-sensing receptor (CaSR) regulates water and calcium excretion in kidney tubule. In patients with primary hyperparathyroidism (PHPT), calcium stones were associated with the activating R990G polymorphism (SNP) located on the CaSR gene exon 7. In a recent study, idiopathic calcium stones were associated with the haplotype characterized by three SNPs (rs7652589, rs4678013 and rs1501899) located in the CaSR gene first block including the gene promoters. Thus, we tested the association of these four SNPs with stones in PHPT patients.
Materials and Methods: 296 PHPT patients and 453 healthy controls were genotyped for R990G, rs7652589, rs4678013 and rs1501899 SNPs. Allele frequency was associated with kidney stones.
Results: Allele frequency was not significantly different in PHPT patients and controls. Stone forming PHPT patients (SF) were 155; non-stone forming PHPT (NSF) were 141. 990G variant allele was more frequent in SF than NSF (7.4% vs 1.8%, RR = 4.4, p = 0.001). The most common haplotype at the promoter region (GGG, including the more common alleles at the three SNPs) was less frequent in SF than NSF (37.4% vs 50.3%, RR 1.7, p = 0.0015). Considering together R990G and the haplotype of promoter region, the risk of stones was 1.66 in homozygous patients for 990R allele carrying a diplotype different from GGG/GGG (p = 0.041, homozygotes for both GGG and 990R as reference group). It was 3.6 in patients carrying GGG/GGG diplotype and one or two copies of the 990G variant allele (p = 0.06). In patients carrying one or two copies of the 990G allele and a diplotype different from GGG/GGG, the stone risk was 9.5 (p = 0.004). PHPT patients carrying one or two copies of 990G variant allele had higher calcium excretion than homozygotes for 990R allele (p = 0.035). Patients carrying GGG/GGG had higher serum ionized calcium than patients with any other haplotypes (1.50 ± 0.178 vs 1.46 ± 0.122 mmol/l, p = 0.04) similar to inactivating mutation effect.
Conclusions: Our findings suggest that SNPs/haplotype modifying CaSR gene promoter activity favor stone formation in PHPT patients and reduce CaSR expression in parathyroid and kidney tubular cells. Their pro-stones effect may be multiplicative with that of R990G SNP.

72 – PERSISTENCE OF HYPERCALCIURIA AFTER SUCCESSFUL SURGICAL TREATMENT OF PRIMARY HYPERPARATHYROIDISM

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Persistent hypercalciuria despite normalization of serum calcium and PHT have been described after parathyroid surgery. Its frequency and causes have not been well studied. We selected 111 patients with primary HPT who underwent PTx and were re-evaluated during followup (24 ± 19 months). Prior to surgery 38.7% had normocalciuria and 61.3% had hypercalciuria (HC). Of the 68 hypercalciuric patients 56 were included in this study: 46 women (52.9 ± 9 years) and 10 men (53.8 ± 19 years), ratio W/M: 4.6: 1. Kidney stones were present in 50% of women and 90 % of men. Before de surgery the glomerular filtration (GFR) was 87.4 ± 32 ml/min for women and 91.3 ± 22 ml/min for men. PTH and serum calcium normalized in all of the HC patients after surgery. Despite this 30% of the women and 50% of the men do not corrected their calciuria after surgery. In patients with persistent hypercalciuria no changes were seen after PTX in GFR and the sodium urinary excretion. Filtered load of calcium was the same as in those patients that corrected hypercalciuria,while fractional excretion of calcium and urinary calcium/100 ml FG remained higher both in men and women in which hypercalciuria persisted. We conclude that persistent hypercalciuria is a frequent finding after successful parathyroid surgery. An impaired in renal tubular calcium reabsorption may be the main factor determining hypercalciuria produced by prolonged hypercalcemia prior to surgery which produces alterations in kidney and tubular function.

73 – NEPHROLITHIASIS IN MEDULLARY SPONGE KIDNEY

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Introduction: Medullary Sponge Kidney (MSK) is a congenital abnormality of the renal medulla characterized by the precalyceal collecting tubules ectasia. The frequence of MSK in patients with nephrolithiasis is controversial. Furthemore a variety of metabolic anomalies causing stone formation have been reported. This study was carried out to report our experience .
Materials and Methods: Between January 1984 to December 2008 among 974 patients with recurrent calcium stones 71(7.3%) had the characteristic features of MSK on intravenous pyelograms, i.e radial distribution of calcification around enlarged papillae, flattened calyces and dilated collecting tubules with or without cystic deformities. In 68 patiens the defect was bilateral and in all cases tubular ectasia involved three or more papillae. For this study all radiographs were reviewed by one of us and at least one radiologist unaware of the previous diagnosis and diagnostic conclusion was confirmed in 100% of the cases. All patients underwent complete metabolic protocol. Three 24 h urine samples were analyzed for levels of oxalate, uric acid, citrate, creatinine, sodium and potassium. A fasting venous blood was drawn for calcium, phosphate, uric acid, creatinine; morning spot urine was also collected for urine analysis and culture. Passed or removed stone were analyzed whenever possible.
Results: Hypercalciuria (defined as 24 h urine calcium excretion greater than 300 mg) was present in 31(44%) patients, hypocitraturia (as less than 350 mg) in 33(46%), hyperuricosuria (as above 800 mg) in 20 (28%) and hyperoxaluria (as more 40 mg) in 16(22%). In 3 patients distal renal tubular acidosis (RTA) was present. Ten patients were hypercalciuric and hypocitraturic, 4 hyperuricosuric and hypercalciuric and 5 hyperuricosuric, hypercalciuric and hypocitraturic. In 13 (18%) no metabolic anomaly was found. No patient was hypercalcemic and none had hyperparathyroidism. The

chemical analysis of stones was calcium-oxalate and /or calcium phosphate in all patients but 5 who had mixed (calcium oxalate-uric acid).
Conclusions: Patients with MSK usually come to the attention of physicians because of kidney stones. The frequency of radiographic features of MSK may vary from to 2.3 to 21% of patients with calcium stones. Differences in radiological criteria may account for the various prevalences reported according to the number of papillae involved (all, half or at least three in one or both kidneys). The incidence of MSK in our patients with recurrent calcium nephrolithasis was 7.3%. Furthemore, in our case population, metabolic anomalies were observed in 82% of patients. Although anatomical abnormalities, which determine stasis of urine and infection, may cause stone formation, a careful metabolic evalution and appropriate therapy may prevent nephrolithiasis in MSK patients.

74 – EFFECT OF SEX HORMONES ON CALCIUM OXALATE FORMATION IN RAT UROLITHIASIS MODEL

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Objectives: The incidence of urolithiasis in men has been reported to be 2.4 times greater than that in women in Japan. Although its pathogenesis is multifactorial and intricate, the difference in incidence between sexes is thought to be caused by sex hormones. In the present study, we investigated the effects of experimentally induced changes in levels of sex hormones on endogenous oxalate synthesis and oxidative stress in regard to calcium oxalate stone formation caused by ethylene glycol (EG) treatment in male and female rats.
Materials and Methods: Sprague Dawley rats aged 10 weeks at the time of stone induction were used for the study. They were divided into 7 groups (4 male groups and 3 female groups) with 6 rats in each group, as follows. The M-1 group was composed of intact male rats used as male controls. M-2 was castrated male rats. M-3 was intact male rats subcutaneously implanted with a 60day sustained release dose of testosterone (25 mg). M-4 was intact male rats subcutaneously implanted with a 60day sustained release dose of estradiol (2.5 mg). F-1 was intact female rats used as female controls. F-2 was castrated female rats, and F-3 was intact female rats implanted in the same manner as M-3. At 10 weeks of age, all rats were fed 0.5% EG in drinking water and forced-fed with 0.5µg of 1,25-dihydroxy vitaminD3 every other day for 1 week. Following that treatment, all were euthanized, and their kidneys and livers were immediately harvested. Crystal depositions in each group were visually examined under a polarizing microscope. Important enzymes in oxalate synthesis are alanine:glyoxylate aminotransferase (AGT) and glycolate oxidase (GO), and are found in liver peroxisomes. The levels of AGT and GO activities in each group were measured using real time RT-PCR. To evaluate oxidative stress, immunofluorescence was performed to determine the amount of 8-OHdG in paraffin embedded kidney sections from each group. Further, level of super oxide dismutase (SOD) and catalase (CAT) activities in the kidney were also measured using real-time RT-PCR. NADPH activity in the kidney was measured using a lucinigen-enhanced chemiluminescence method.
Results: Kidney tissue microscopy showed extensive crystal depositions in the male, whereas there were very few crystals in the females. Testosterone administration enhanced the crystal depositions, while estradiol inhibited them.
Furthermore, testosterone also enhanced GO activity, which increased urinary oxalate excretion. As for oxidative stress, castration and testosterone administration in the females inhibited antioxidant enzyme activity and enhanced NADPH oxidase, castration and estradiol enhanced antioxidant enzyme activity and inhibited NADPH oxidase in the males.
Conclusions: Testosterone promotes urolithiasis and estradiol inhibits calcium oxalate stone formation, because of their effects on oxalate synthesis and oxidative stress.

75 – THE RELATIONSHIP BETWEEN METABOLISM OF THE GLYOXYLATE AND THE SPECIES

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Objectives: Urinary oxalate is one of the major risk factors in urinarystone formation. The precursor of oxalate is glyoxylate and serine:pryvate/alanine:glyoxylate aminotransferase (SPT/AGT) is essential liver enzyme for its metabolism. The defect or deficiency of SPT/AGT leads to primary hyperoxaluria type 1 (PH1). The subcellular distribution of SPT/AGT is the species-specific and food habit-dependent. In carnivores like the dog, SPT/AGT is localized in mitochondria. In the human and herbivores like the rabbit, on the other hand, SPT/AGT is localized in peroxisomes. This study was loaded L-hydroxyproline (Hyp) and glycolate, each precursor of glyoxylate, to dogs and rabbits and urinary excretion of metabolites was measured.
Materials and Methods: Dogs (n = 6) were sequentially loaded every 4 days normal foods (Normal), 71 mol/day (Low) and 152 mol/day (High) of Hyp or glycolate mixed with foods, respectively. Rabbits (n = 5) were sequentially loaded every day none (Normal), 20 mol/day (Low) and 40 mol/day (High) of Hyp or glycolate mixed with water under anesthesia, respectively. Statistical analysis was used two-way ANOVA and Bonnferoni's multiple comparison. Results are presented as the mean ± SEM and statistical significance was set at $P < 0.05$ for all comparisons.
Results: In dogs; urinary excretion of creatinine (Ìmol/day) loaded glycolate 1.17 ± 0.2 (Normal), 1.81 ± 0.19(Low) and 1.77 ± 0.27 (High), respectively, and that of loaded Hyp were 2.02 ± 0.24 (Normal), 1.99 ± 0.27 (Low) and 2.30 ± 0.49 (High), respectively. Oxalate/creatinine ratios (mol/mol) loaded glycolate were 56.4 ± 4.7 (Normal), 228.6 ± 19.9 (Low) and 549.3 ± 49.8 (High), respectively, and that of loaded Hyp were 48.2 ± 3.9 (Normal), 114.8 ± 15.2 (Low) ($p < 0.05$), 144.5 ± 34.8 (High) ($P < 0.001$). In rabbits; urinary excretion of creatinine (µmol/day) loaded glycolate 0.632 ± 0.046 (Normal), 0.670 ± 0.106 (Low) and 0.562 ± 0.076 (High), respectively, and that of loaded Hyp were 0.832 ± 0.052 (Normal), 0.434 ± 0.136 (Low) and 0.622 ± 0.106 (High), respectively. Oxalate/creatinine ratios (mol/mol) loaded glycolate were 85.22 ± 10.44 (Normal), 106.94 ± 21.89 (Low) and 183.36 ± 21.12 mol/mol (High), respectively, and that of loaded Hyp were 114.8 ± 16.06 (Normal), 75.89 ± 23.01 (Low) and 96.70 ± 34.49 (High) ($P < 0.05$), respectively.
Conclusions: These results suggest that an important role of mitochondrial SPT/AGT in carnivores and peroxisomal SPT/AGT in herbivores is to convert Hyp- or glycolate-derived glyoxylate into glycine in situ, preventing undesirable overflow into the production of oxalate. In the human as well as herbivores, SPT/AGT was localized in peroxisomes,

urinary excretion of oxalate may be increased when Hyp is loaded, resulting in a part of causes of urinary stone.

76 – ETHYLENE GLYCOL-INDUCED HYPEROXALURIA INCREASES PLASMA AND RENAL TISSUE ASYMMETRICAL DIMETHYLARGININE LEVELS IN RAT: A NEW PATHOGENETIC LINK IN HYPEROXALURIA INDUCED DISORDERS

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Objectives: Pathogenesis of kidney stones is still elusive. There are some evidence that hyperoxaluria may affect vascular endothelium and many studies link renal stones to atherosclerosis. Besides renal vascular endothelial cells have been shown to regulate proximal tubule epithelial cell function. The aim of this study was to determine the effect of hyperoxaluria on plasma and tissue levels of assymmetrical dimethyl arginine (ADMA) levels. Secondary aim was to determine the effect of verapamil on ADMA levels.
Materials and Methods: A total of 64 Sprague Dowley rats have been included into study. Group IA and B: Hyperoxaluria induced group for 7-day or 28-day period were given a hyperoxaluria inducing diet for 2-week period. Group IIA and B: Hyperoxaluria + verapamil group; for 7-day or 28-day period. Group III: Control group; No specific medication but distilled water. Blood samples were obtained at 24 hour and at the end of study and kidney samples obtained at 1 or 4 weeks for histopathologic evaluation.
Results: Plasma ADMA levels increased early in hyperoxaluric group ($p = 0.0002$). The effect retained at the end of the study period ($p = 0.01$). There was no increase in ADMA levels in verapamil group either in short or long term. Hyperoxaluria induced significantly dense statining pattern in renal tissue ADMA ($p = 0.01$). Administration of verapamil did not create significant tissue ADMA staining compared to controls.
Conclusions: Increase in both systemic and local tissue ADMA may help to explain the pathogenetic mechanisms of hyperoxaluria induced disorders such as nehprolithiasis and atherosclerosis.

77 – EFFECT OF THE INGESTION OF TAURINE ON THE EXCRETION OF URINARY GLYCOLATE

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Taurine is an amino acid which has been shown in previous animal model studies to have beneficial effect as an antioxidant. In the present study it was administered as a component (1000 mg) of a commercially available energy drink (250 ml) to 20 healthy male subjects who ingested one dose while on a standardized diet. No changes in urinary glycolate and oxalate were observed.

78 – EFFECT OF A DIETARY OXALATE CHALLENGE ON RENAL INJURY AND OXIDATIVE STRESS IN TWO DIFFERENT ETHNIC GROUPS

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Previous studies have suggested an association between calcium oxalate stone disease, renal tubular damage and oxidative stress. In the present study, three different dietary oxalate challenges were administered for periods between 1-3 days, to black (n = 10) and white (n = 10) subjects while on controlled diets. Counterintuitively, urinary oxalate increased in black subjects but not in whites. Urinary N-acetyl-B-glucosaminidase (NAG) and 8-hydroxydeoxyguanosine (8-OHdG) did not change in either group.

79 – ROLE OF OXALOBACTER FORMIGENES IN OXALATE METABOLISM OF CALCIUM OXALATE STONE PATIENTS

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Objectives: Oxalobacter formigenes is a Gram-negative anaerobe, which degrades dietary oxalate in the intestine, thus limiting its absorption. The primary goal of this study was to assess the role of O. formigenes in the metabolism of oxalate, i.e. intestinal absorption, plasma oxalate concentration and urinary oxalate excretion in calcium oxalate stone patients.
Materials and Methods: Thirty-seven calcium oxalate stone formers participated in this study. Twenty-six patients who tested negative for O. formigenes were compared with 11 patients that tested positive for O. formigenes. Analysis of blood samples, two 24 hour urines and $[^{13}C_2]$oxalate absorption test were performed on standardized conditions.
Results: Intestinal oxalate absorption did not differ with the presence or absence of O. formigenes colonization. However, plasma oxalate concentrations were significantly higher in patients without O. formigenes (5.79 µmol/l) than in colonized stone formers (1.70 µmol/l) ($p = 0.003$). Urinary oxalate excretion was significantly lower in O. formi¬genes-positive patients (0.318 and 0.367 mmol/24h) than in those who were O. formigenes-negative (0.454 and 0.474 mmol/24h, respectively) ($p = 0.003$ and $p = 0.043$, respectively). The relative supersaturation with respect to calcium oxalate was significantly higher in patients without O. formigenes colonization.
Conclusions: Colonization with O. formigenes could be associated with a reduced risk of calcium oxalate stone formation resulting from a decreased excretion of urinary oxalate. It is suggested that higher intestinal concentration of oxalate is available for absorption at a constant intestinal absorption rate.

80 – UNDUE ACIDITY – A PATHOGENETIC FACTOR ONLY IN URIC ACID UROLITHIASIS?

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Objectives: The main risk factor for uric acid stone formation is a disturbed acidification of the urine with permanently low pH-levels. The pathogenesis is unclear. Nutritional factors and a genetically determined abnormality in the glutamine metabolism resulting in reduced ammonia excretion are discussed. Clinical observations show that permanently low urine pH is also found in calcium oxalate stone formers

(CaOx). We therefore systematically studied this phenomenon in Ca and examined whether there it is prognostic factor.
Materials and Methods: n = 150 patients with CaOx stones were investigated. Stone analysis was performed by x-ray diffraction. In all patients the following parameters were determined: age, sex, BMI, stone frequency, diabetes mellitus; blood: creatinine, uric acid, calcium; urine: pH-profiles, volume, calcium, uric acid, citrate, ammonia and urea. According to urine pH levels, two groups were divided: 1. patients with undue acidity (pH permanently ≤ 5.9); 2. patients with normal pH levels.
Results: Undue acidity was observed in 21% of our patients, 79 % showed normal urine pH levels. The stone frequency was similar (1.4 ± 0.5 vs. 1.4 ± 0.9 episodes). Patients with undue acidity had a significantly higher BMI (30.3 ± 5.9 vs. 27.3 ± 3.0), a significantly higher serum uric acid (6.3 ± 1.7 vs. 4.6 ± 1.1 mg/dl) and by definition a significantly lower urine pH. All the other parameters showed no significant differences.
Conclusions: Our results demonstrate that undue acidity is present in more than 20% of CaOx stone formers. Therefore, it is not an exclusive finding in the pathogenesis of uric acid lithiasis. Metabolic evaluation showed that undue acidity is related to parameters of the metabolic syndrome. Concerning recurrence rate, however, it is not a prognostic factor.

81 – NEED FOR REPEATED URINE ANALYSIS IN THE STONE CLINIC

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Objectives: In most urinary stone clinics, urinary deposits are not routinely analyzed before the treatment modalities and dosages are decided. Treatment is usually based on the presence of stone in the ultrasound/x-ray. Antibiotics are given routinely for most patients. This produces and unhealthy trend in the management of stone patients. Patients are given unnecessary antibiotics and unscientific chemotherapeutic/chemoprophylactic regimes. The objective of this study was to identify the relevance of repeated urine examination in stone patients to help modify treatment schedules.
Materials and Methods: 250 stone patients attending the stone clinic for the first time during 2007-008 were investigated for the stone problem by collecting four urinary samples for routine urine studies and the routine metabolic work up of the patients. Early morning urine and random samples were collected on the first day and the reporting day and analysed thus making four samples from each patient (total 1000 samples-study group). The variation and pattern of urinary finding and crystals and other urinary deposits was done in the different samples. All patients had at least one urinary deposit result performed before the first attendance at the clinic (250 samples-control group). These results were compared with those of the study group.
Results: In the study group, all patients showed variations in the urinary findings in the four samples. There was variation between the findings of the first day and the last day. RBCs, pus cells and crystals were more in the early morning urine. Deposits were significantly more in the samples of first day compared to the last day. This could be explained by the fact that many patients attended the clinic first at the time of symptoms. The findings of the study group compared with the control group of urine deposit reports showed that samples without any significant findings were 16% and 47% respectively. Deposits were present in 84% vs 32%; pus cells 23%, 21%; RBCs 17%, 15%; Calcium Oxalate Monohydrate 33%, nil; Calcium oxalate dihydrate 32%, 8%; uric acid 18%, 3%; ammonium urate 3%, 0.5%, phosphates 25% 12%; Crystal aggregation 8%, nil; and crystal clumping 3%, nil. Calcium oxalate monohydrate crystals, crystal aggregation and crystal clumping were not recorded in any of the control group.
Conclusions: It is concluded that study of urinary deposits should be repeated as many times as possible in order to identify the real nature of urinary pathology indicating stone disease. Early morning urine sample is more likely to positive finding than the random sample. COD crystals seen more in the random samples as it is likely that activity of the patient will permit the movement down of the spiculated COD crystals and thus produced increased % of COD crystals in random sample.

82 – METABOLIC EVALUATION AND RISK OF RELAPSE IN A LARGE COHORT OF PATIENTS WITH KIDNEY STONES

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Objectives: The aim of the study was to perform the metabolic evaluation in a large cohort of patients with kidney stones recruited in 2 different Italian centres, in North (Centre A – Turin) and South (Centre B – Bari) of Italy, to estimate the lithogenic risk and the possible factors responsible for the risk of relapse of nephrolithiasis.
Materials and Methods: In this cross-sectional study we evaluated the metabolic profile of 1624 patients who suffered from kidney stones [922 from Centre A (431 M, 491 F; mean age 49.7 ± 16.7 years) and 702 patients from Centre B (302 M, 400 F; mean age 46.5 ± 22.8 years)]. In 1153 patients we evaluated the urine state of supersaturation (β) with calcium oxalate (βCaOx), calcium phosphate (βbsh) and uric acid (βAU) using a validated software (LITHORISK). In 299 patients followed for at least 2 years the risk of relapse and the possible covariates were analyzed by Kaplan-Meier method and multivariate Cox proportional hazard method.
Results: There were no significant differences between the Centre A and Centre B, except for diuresis (22.8 ± 8.5 dL/24h vs 17.4 ± 6.7 dL/24h; $p < 0.001$), oxaluria (30.1 ± 12.9 mmol/24h vs 26.3 ± 10.5 mmol/24h; $p < 0.001$) and uricuria (479.9 ± 177.6 mg/24h vs 540.4 ± 202.2 mg/24h; $p = 0.002$). Hypercalciuria occurred in 30% of the patients, hyperoxaluria in 11%, hypocitraturia in 17%, hyperuricuria in 9%, other abnormalities in 15%. No change was seen in 18%. The analysis of stones in 1010 patients showed as the main component calcium oxalate (69.2%), calcium phosphate (11.8%), uric acid (14.4%), other types (4.6%). In 647 patients with calcium stones disease, 26.2% had hypercalciuria, 12.3% hyperoxaluria, 35.6% hypocitraturia and 14.5% hyperuricuria. In the long term follow-up (mean follow-up 105 ± 93 months) 76/299 (25.4%) patients had a relapse. The probability of relapse in these patients was 14%, 28%, 36%, 46% at 5, 10, 15, 20 years respectively. At the multivariate analysis only baseline BMI (HR 1.10; CI 95% 1.03-1.19) and modification at two years of diuresis (HR 0.93; CI 95% 0.88-0.97) and urinary specific gravity (HR 1.50; CI 95% 1.10-2.10) were indipendent predictors of the risk of relapse.
Conclusions: Small differences were observed in biochemical

and urinary parameters in 2 italian centres, probably due to dietary habits and enviromental factors. In the long term follow-up, modification of diuresis and urine specific gravity reduced the risk of relapse. Moreover Body Mass Index may be a novel predictor of relapsing kidney stones.

83 – DIAGNOSTIC VALUE OF PHYSICAL AND BIOCHEMICAL PARAMETERS OF URINE IN METAPHYLAXIS OF UROLITHIASIS

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Objectives: Definition of the diagnostic value of physical and biochemical parametres of urine in metaphylaxis of urolithiasis.
Materials and Methods: Object of the research were 60 subjects with age ranging from 19 to 67 years. The first group comprising 40 patients with diagnosis of urolithiasis and the second group comprising 20 healthy voluntary people were investigated about their physical and biochemical urine characteristics.
Results: The results in the first group were: kinematic viscosity -1,28 ± 0,07, superficial free energy -70,11 ± 0,34, electroconductivity -0,020 ± 0,005, osmolarity -862,4 ± 48,5, crystal-inhibiting activity -1,22 ± 0,03, ionization of calcium -31,9 ± 3,8, ionization of magnesium -22,2 ± 1,1, diuresis -0,98 ± 0,07. The results in the second group of healthy people: kinematic viscosity -1,07 + 0,02, superficial free energy -65,3 ± 0,32, electroconductivity -0,027 ± 0,005, osmolarity -650,4 + 46,1, crystal-inhibiting activity -1,45 ± 0,03, ionization of calcium -25,5 ± 2,2, ionization of magnesium -25,6 ± 1,5, diuresis -1,53 ± 0.08. The results significantly ($p < 0,05$) differ from each other. They show that early characteristics of urolithiasis are: decrease of total crystal forming abilities of urine, reduction of its superficial free energy by a background hyperosmia, hypodipsia, increase of ionization of calcium and decrease in ionization of magnesium of urine. The changes of degree of ionization of calcium and magnesium have important prognostic value. The level of ionization of calcium of urine reflects a saturation of active ions of calcium in unit of the investigated environment, and the level of ionization of magnesium reflects a degree of saturation of urine active inhibiting crystallization.
Previous research allowed to establish an essential decrease of electroconductivity in the urine of patients of the first group. Part of the ions of urine is in the free dissociated condition, and the others take part in the formation of a double electric layer on a surface micelle. Reduction of crystal activity depends on the number of the free ions, capable to enter electrochemical interaction under influence of ionic and covalent communications. With reduction of number of free ions decreases electroconductivity urine and the risk of crystallization raises.
Conclusions: The use of the above-stated physical and biochemical parameters of urine as diagnostic methods, allows to find out urolithiasis on early phases of development and also to carry out pathogenetic metaphylaxis.

84 – DIAGNOSTIC DIFFICULTIES WITH ESTIMATION OF THE CAUSE OF NEPHROLITHIASIS-CASE PRESENTATION

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Objectives: Between patients with recurrent urolithiasis there are some in which we cannot estimate the cause of stones forming. We present one such case picturing our failure of making correct diagnosis despite of very broad spectrum of laboratory investigations.
Case report: 18 years old girl with recurrent urolithiasis was admitted to Department of Nephrology, Renal Transplantation and Hypertension of Children's Memorial Health Institute in November 1999 at the age of 9years. There was nephrolithiasis in her father's family. In our patient the disease was diagnosed while looking for the cause of recurrent urinary tract infections. There were many stones in both renal pelvises. Bilateral pyelolithotomy, then ESWL had been performed in local hospital. The stone had been composed of calcium oxalate and in 10% of cystine. During ten years observation in Children's Memorial Health Institute we found in repeated examinations: good renal function, hypomagnesemia without hypomagnesuria, hypercitraturia, normal levels of calcium and phosphorus, PTH 53,6-72,3 pg/mL, 25OHD3 3,6-23,8 ng/mL, normal excretion of Ca, P, Mg and uric acid in 24h urine collection. Metabolic diseases leading to stone forming were excluded. There were normal excretion of free aminoacids in urine. She had correct total BMD and L2-L4 BMD. In renal scintigraphy we found bilateral renal scars. Many times she excreted concrements consisted of: in 10.1999- calcium oxalate and in 10% cystine; in 11.2000- calcium phosphate and traces of Mg and Cl; in 01.2001- calcium phosphate and traces of K; in 02.2009- calcium oxalate and ammonium- magnesium phosphate. The patient has been on low NaCl, oxalate and purine diet and large amount of low- mineral water. She has been treated with captopril and potassium citrate until cystinuria was excluded. Many times ESWL was performed.
Conclusions: In this patient with recurrent urolithiasis the reason of concrements forming was not found. It is possible that constant presence of stones made diagnosis more difficult. In such cases decision as to the treatment method one can make only analyzing consistency of excreted concrement.
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85 – PARAMETERS OF METABOLIC SYNDROME IN URIC ACID AND CALCIUM OXALATE STONE FORMERS

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Objectives: Previous investigations showed that the metabolic syndrome (MS) as an expression of insulin resistance plays a major role in the pathogenesis of uric acid stones. This is in correspondence to the characteristics found in uric acid stone formers (UASF). Obesity, for example, is seen, however, also in many calcium oxalate stone formers (CaOxSF) and has been described as a risk factor. Therefore we compared parameters of MS and metabolic risk factors in

UASF and CaOxSF to see whether MS influences the risk for stone formation in a special way.
Materials and Methods: We studied n = 100 consecutive CaOxSF and n = 50 UASF treated in our hospital. The following parameters were examined: Age, sex, stone frequency, stone analysis, arterial blood pressure, diabetes mellitus, serum levels of creatinine, calcium and uric acid and 24 h-urine parameters (volume, pH, calcium, uric acid, citrate, urea, and ammonia). For statistical analysis Gaussian distribution and equal variance were checked. Significance was analyzed by Student's t-test or Mann-Whitney-test respectively.
Results: BMI (27.7 vs. 25.3) and urinary calcium (7.3 vs. 4.2 mmol/d) were significantly higher in CaOxSF, systolic blood pressure (161 vs. 148 mmHg) and serum uric acid (6.3 vs. 5.3 mg/dl) in UASF. All the other parameters examined were not significantly different.
Conclusions: We could demonstrate that parameters of MS are equally prevalent in CaOxSF and UASF. MS is not a characteristic finding only in UASF. There was no clear relation of these parameters to the special pathogenesis of uric acid lithiasis. Especially urinary pH was not significantly different between CaOxSF and UASF. MS seems to be a general finding in stone patients and cannot be related to a special stone composition.

86 – URIC ACID METABOLISM IMBALANCE AT METABOLIC SYNDROME

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Objectives: The aim of our research is to find answer on two questions: can we speak about additional pathogenetic mechanism of stone formation from uric acid with men who have late onset hypogonadism and is it possible to normalize level of uric acid by means of lowered testosterone level correction.
Materials and Methods: Criteria of including into the task group were the following: hyperuricemy and/or hyperuricosuria, reduction of testosterone level and also symptoms of metabolic syndrome such as abdominal visceral obesity, glucose tolerance imbalance, dyslipidaemia and arterial hypertension. Nine men have been included into the examination by today. Four of the patients included had X-ray negative stones, not more than 1 cm in size.
All the patients receive androgen substitutive therapy with gel form of testosterone "Androgel" 50 ml once a day. Urine acidity is corrected with citrate mixture till pH 6,0-6,5 level at individual adjustment of dosage. Diuresis is increase by means of taking Canephron N 50 drops 3 times a day and by means of changing of water consumption till urine density not more than 1,015 g/l. Length of taking Androgel and citrate mixtures till control study have been determined as 3 months. Intake dosage of Canephron N is 10 days every month. By today control study has been made with 4 patients.
Results: Before treatment patients got following parameters: level of urine acid — 490,0 ± 130,0 micromole/l, urine acid in the urine — 6,98 ± 2,03 millimole/l, cholesterol — 8,3 ± 2,4 millimole/l, testosterone — 8,6 ± 4,2 nmol/l, pH urine — 5,2. After the treatment: level of urine acid — 230,0 ± 21,0 micromole/l, urine acid in the urine — 3,21 ± 1,08 millimole/l, cholesterol — 5,2 ± 0,8 millimole/l, testosterone — 14,3 ± 6,3 nmol/l, pH urine — 6,3.
Conclusions: Purine metabolism imbalance together with classical components of metabolic syndrome (arterial hypertension, pancreatic diabetes, cholesterol metabolism imbalance, abdominal visceral obesity) results in increase of uric acid level. Because of disorder of secretion ammonium kidney acid forming function changes lead to high risk of stone formation from uric acid. In our opinion, treatment response in that case is determined by prescription of testosterone in the form of gel "Androgel", which is applied on skin every day. Reduction of uric acid and pH urine level happen in that case due to normalization of purine metabolism in the result of reduction of symptoms which form metabolic syndrome.

87 – EFFECT OF HIGH DIETARY SALT INTAKE ON URINARY RISK FACTORS FOR URIC ACID STONE FORMATION

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Objectives: A high dietary salt (sodium chloride) intake has been reported to increase urinary calcium excretion, which may enhance the risk of forming calcium-containing urinary stones. Aim of the present study was to examine the physiologic effects of an increased salt intake on urinary risk factors for uric acid stone formation.
Materials and Methods: Ten healthy men, with a mean age of 27 years, received a standard diet for 5 days with a daily constant intake of 9 g sodium chloride (153 mmol/d sodium), 215 mg purines and a constant fluid intake. During the test phase the subjects were maintained on the same standard diet for 5 days. In addition, they took 13 g sodium chloride (221 mmol/d sodium) per day with the meals for a total sodium chloride intake of 22 g/d (374 mmol/d sodium). Urine was collected for 24 hours on each day.
Results: During the test phase, urinary sodium and chloride excretion were significantly greater than during the control phase. The high salt intake resulted in a significant decrease in urinary uric acid excretion during the last 3 days of the test phase (2.99 mmol/24h on day 5 of the test day versus 3.58 mmol/24h on day 5 of the control phase). There were no significant differences in 24h urine volume, pH, potassium, magnesium, ammonium, sulfate and citrate excretion between the last three days of each phase. The relative supersaturation with respect to uric acid did not change significantly.
Conclusions: The reduction in urinary uric acid excretion could be explained by the retention of uric acid. It is suggested that the mechanism responsible for the decrease in uric acid excretion is comparable to that attributed to saluretics. Further studies are necessary to clarify, whether a high dietary salt intake may increase plasma uric acid concentration as a result of decreased uric acid excretion.

88 – DIFFERENCES IN 24-HOUR URINE COMPOSITION BETWEEN DIABETIC AND NON-DIABETIC STONE-FORMERS

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Objectives: To examine the differences in 24-hour urine composition among stone-formers with and without diabetes mellitus.

Materials and Methods: A retrospective review of a database of 24-hour urinalyses from a metabolic stone clinic was performed. Patients who presented for their initial metabolic stone workup and who were ≥ 18 years of age were eligible for the study. Electronic medical records were reviewed for past medical history and medications.
Multivariate linear regression adjusted for possible confounders including age, gender, race, BMI, hypertension, thiazide use, potassium citrate use, and 24-hour urine chemistries (volume, pH, calcium, citrate, creatinine, oxalate, magnesium, phosphate, potassium, sodium, sulfate, and uric acid).
Results: Four hundred sixteen (416) patients without diabetes mellitus and 46 patients with diabetes mellitus were included in the study. On multivariate analysis, compared with non-diabetic stone-formers, those with diabetes mellitus excreted significantly greater amounts of oxalate (6.4 mg/day, 95% CI 1.26 to 11.6) and volume (0.38 L/day, 95% CI 0.13 to 0.64). Diabetic stone formers also excreted less phosphate (-0.11 g/day, 05% CI-0.48 to -0.21) and had significantly lower urine pH (-0.34, 95% CI -0.48 to -0.21).
Conclusions: Significant differences exist in 24-hour urine chemistries between diabetic and non-diabetic stone-formers. Diabetic stone-formers had significantly lower urine pH (a risk factor for uric acid nephrolithiasis) as well as significantly higher daily oxalate excretion (a risk factor for calcium oxalate nephrolithiasis). Knowledge of these differences will be useful in the evaluation and treatment of these patients and prevention of stone recurrence.

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89 – NEPHROLITHIASIS AND THE RISK OF HEART DISEASE IN OLDER WOMEN

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Objectives: The etiology of nephrolithiasis is incompletely understood. Nephrolithiasis has been linked to several systemic diseases (hypertension, diabetes mellitus, obesity, metabolic syndrome) and there is a small amount of evidence suggesting that nephrolithiasis and vascular disease may share a common mechanism. We undertook this study to examine the relationship between prevalent nephrolithiasis and prevalent cardiovascular disease in older women.
Materials and Methods: A total of 9704 white women were recruited in 1986-1988 from 4 clinical centers to participate a longitudinal cohort study, the Study of Osteoporotic Fractures. Of these, 9054 attended a second clinic visit (1988-1990) at which time basic medical, dietary, and lifestyle history was obtained.
Prevalent heart disease (myocardial infarction (MI), angina, congestive heart failure (CHF) was examined in patients with and without a history of nephrolithiasis. In addition, atherosclerotic mortality (confirmed by death certificates) was ascertained during a median of 13.7 years of follow-up. Multivariable logistic regression and proportional hazards models were adjusted for age, diabetes mellitus, hypertension, waist circumference, body mass index, smoking, aspirin use, and calcium and vitamin D intake.
Results: The 426 (4.7%) women with a history of nephrolithiasis at baseline had significantly greater prevalence of MI (13% versus 6.9%, p < 0.001), angina (18.3% versus 12.2%, p < 0.001), and CHF (5.8% versus 2.9%, P < 0.001) than women without a history of urinary stone disease. There was no significant difference in cardiovascular mortality between the two groups (14.7% versus 12.2%, p = 0.14). In adjusted analyses, the odds ratios for the association with nephrolithiasis were 1.8 for MI (95% CI: 1.2-2.6), 1.6 for angina (95% CI:1.2-2.2), and 2.2 for CHF (95% CI: 1.3-3.8). There was a no increase in cardiovascular mortality associated with nephrolithiasis (hazard ratio, 1.2, 95% CI: 0.8-1.8).
Conclusions: Cardiovascular disease was significantly more prevalent in older women with a history of nephrolithiasis than those without a history of urinary stones, but a history nephrolithiasis did not appear to increase subsequent cardiovascular mortality. This evidence suggests that there is a common physiologic mechanism linking urinary stone disease and cardiovascular disease, independent of diabetes, hypertension, and metabolic syndrome. Further investigation is necessary to understand the mechanisms underlying these associations.

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90 – METABOLIC STRESS RESPONSE PATTERNS IN URINARY COMPOSITIONS OF IDIOPATHIC CALCIUM OXALATE STONE FORMERS, STONE FORMERS WITH CHONIC BOWEL DISEASES AND CONTROLS

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Objectives: Stress is a multi-stage disease which is, inter alia, associated with increased hormon release, increased blood-sugar level, heart rate and blood pressure, and weakening of the immune system. Emotional stress burden clearly affects metabolism. Whether chronic stress exposure leads to altered urinary compositions with increased risk of CaOx stone formation was examined by investigating the relation between stress burden and urinary composition.
Materials and Methods: The study included 29 controls (CG), 28 idiopathic CaOx stone patients (SF), and 28 CaOx stone formers suffering from chronic inflammatory bowel diseases (CIBD) who were all kept to a controlled diet for 5 days.
The stone patients were advised to pause any stone metaphylaxis related medications. At day 5, a 24h-urine was collected. Urinary volume, pH and the renal excretions of, inter alia, Ca, oxalic acid (OA), citric acid (CA), and Mg were analyzed. AP risk index for CaOx formation was calculated. Subjective stress levels experienced by the study participants during the past 3 months were assessed with the Trier Inventory for the Assessment of Chronic Stress, a standardized 57-item self-report scale for the differentiated assessment of the different specifications of chronic stress, e.g. job overload, pressure to succeed, lack of social recognition and social isolation.
Results: Mean AP at CG, SF and CIBD amount to 0.8 (± 0.3), 1.2 (± 0.7) and 1.9 (± 1.2), respectively. Increased AP at SF is

mainly attributed to an increased excretion of promotors (Ca, OA), whereas at CIBD this is caused by both increased promotoric urine compositions and lowered excretions of inhibitoric risk factors (CA, Mg, V).
None of the stress scales is linearly correlated to any urinary parameter or AP with r> 0.572. However, some of these correlations are statistically significant ($p < 0.05$ and $p < 0.01$). Whereas at SF only one combination, "lack of social recognition" vs. Ca, shows statistical significance, at CIBD a multitude of combinations are significantly related. In particular, urinaryNa concentration affected by increasing stress. At CG, increasing stress levels are directly related to CA, i.e. in case of increasing stress burden, protection against urinary stone formation tends to increase.
Conclusions: Even statistically significant on a considerably high level, it must be noted that the obtained linear correlations are small. It remains difficult to decide, whether stone formation at CIBD is the result of bowel disease prior to stress burden or persistent stress elicited in fact bowel disease leading to pathologically altered urine compositions. However, it is remarkable that stress perception is most associated with altered urinary compositions at this patient group.

91 – NEPHROLITHIASIS RISK IN PATIENT WITH RENAL TRANSPLANTATION

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Objectives: The aim of this study was to estimate the lithogenic risk in renal transplant recipients, focusing on the pathogenetic role of the immunosuppressive therapy.
Materials and Methods: We performed a case-control study, comparing 100 transplant patients with the same number of healthy subjects. In both groups we analysed the promoting factors (phosphaturia, calciuria, uricuria and oxaluria) and the inhibitors (magnesuria and citraturia) of crystallization for the main types of kidney stones. We evaluated the state of relative urine supersaturation with calcium oxalate, calcium phosphate and uric acid using a validated software (LITHORISK).
Results: Calciuria, phosphaturia and oxaluria were within the normal range in our study population. However, the mean calciuria was significantly higher in transplant recipients than in normal subjects ($p = 0.0271$); oxaluria was lower and phosphaturia was slightly higher in the group of transplant recipients than in the control group. The uricuria values were comparable in the two groups. Rapamycin-treated patients presented calciuria ($p < 0.01$) and phosphaturia ($p < 0.01$) levels significantly higher than the patients on calcineurin inhibitors therapy.
Interestingly transplant recipients showed a remarkable reduction of citrate urinary levels ($p = 0.0001$) and an increase, altough not significant of magnesium ($p = 0.06$), compared to control group. Moreover, urinary pH of our transplant patients was significantly lower ($p = 0.0001$) compared to the control group. Transplant recipients showed a significantly lower risk to form calcium phosphate stones ($p < 0.001$) and calcium oxalate stones ($p < 0.0001$) compared to the control group. For the uric acid the risk was the same in the 2 groups. In addition we studied the role of familiarity and we observed that transplant patients with a positive family history for kidney stones had a greater risk to form calcium oxalate stones ($p < 0.05$). Finally, rapamycin-treated patients resulted with a higher risk to form calcium oxalate and calcium phosphate stones compared to patients on calcineurin inhibitors-based therapy.
Conclusions: The lithogenic risk in patients with renal transplantation is low, but the therapy with rapamycin may influence the urinary excretion of calcium and phosphate which, in association with the low level of citrate, might result in a significant of such a risk.

92 – THE SURVEILLANCE OF PATIENTS WITH LOWER CALYCEAL STONE AND METABOLIC RISK FACTOR

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Purpose: The intervention time of asymptomatic small sized lower calyceal stones remains controversial. In this prospective study we evaluated the natural history and progression rate of asymptomatic small sized (< 4 mm) lower calyceal stone patients with metabolic high risk factors.
Materials and Methods: we followed patients every 6 months. The patients were examined 3-D computerized tomography or intravenous pyelography. We examined every 1 year if the patients were no stone size change without symptom development. The patients were found a chance checkup medically. All of them were metabolic checkup including imaging study. Disease progression was defined as pain experienced during followup, stone growth or need for intervention.
Results: A total 43 patients, 22 male and 21 female, were followed for a mean of 58.3 months(range 24 to 78). All of them had small sized lower calyceal stone, of the 43 patients 9 had bilateral lower calyceal stone. Measured stone size was mean 4.5mm under the 3-D CT or IVP. The patients were followed every 6 months, and then 1 year followed if no size variation. Metabolic study of urinary stone check up the hypercalciuria, hyperuricosuria, hyperoxaluria and hypocitriuria. Body mass index(BMI) was a mean 105.8 kg/m^2, the patients expressed slightly obesed state. The 34 patients were hypercalciuria(mean 283.2 mg/day), 28 patients were hyperoxaliuria(mean 52.5 mg/day), 12 patients were hypocitriuria(mean 336.5 mg/day). During the mean followup, 28 patients (65.1%) were disease progression and 15 patients (34.9%) were need intervention.
Conclusions: Our study showed that asymptomatic, small sized lower calyceal stone can be followed safety but the patients with metabolic abnormalities, obesity need early intervention or closed surveillance.

93 – THE EFFECT OF FOLIUM PYRROSIAE (SHI WEI) ON CALCIUM OXALATE KIDNEY STONE RISK FACTORS: AN IN VIVO STUDY ON SOUTH AFRICAN MALES

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Folium Pyrrosiae has been suggested as being a potential inhibitor of kidney stone disease because of its effect on cal-

cium oxalate (CaOx) crystal nucleation. In the present study, this herb was administered to healthy black (n = 9) and white (n = 9) males for 7 days in a double-blind, placebo-controlled study. Urinary CaOx crystallization kinetics and biochemical risk factors for CaOx stone formation were measured. However no statistically significant effects were observed. These results do not support the findings of previous studies.

94 – THE EFFECTS OF VITAMIN E (DL-α-TOCOPHERYL ACETATE) AND OMEGA-3 FISH OIL (SALMON OIL) ON RISK FACTORS FOR CALCIUM OXALATE UROLITHIASIS IN BLACK AND WHITE SOUTH AFRICAN SUBJECTS

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The effects of fish oil (1000 mg) ingestion alone (protocol 1) and in tandem with vitamin E (400 IU) (protocol 2) on urinary calcium and oxalate excretion, as well as on plasma uric acid, α-tocopherd and free malondialdehyde (MDA) were investigated. Results showed that protocol 1 had no significant effect on any of the urinary or plasma kidney stone risk factors in the two race groups while protocol 2 favourably and significantly raised plasma α-tocopherol in both groups but did not have any effect on the other parameters.

95 – THE THERAPEUTIC USE OF POTASSIUM CITRATE IN UROLITHIASIS AND PREUROLITHIASIS IN CHILDREN

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Objectives: The process of stone formation is initiated by imbalance between promotors and inhibitors of crystallization. Citrates are effective inhibitors in case of oxalate and calcium- phosphate urolithiasis. The aim of the study was estimation of usefulness of potassium citrate in urolithiasis and preurolithiasis state in children.
Materials and Methods: 36 children (23 girls, 13 boys) aged 2-18 years with urolithiasis or preurolithiasis state qualified to citrate potassium treatment. All were previously diagnosed as to the kind of formed stones, had ultrasonography and urine pH profile. The indication for treatment were hyperoxaluria, hypercalciuria and hyperuricosuria (single or mixed pathology). We performed 24 hours urine collection with enzymatic estimation of citrate excretion. We recognized hypocitraturia for citrate urine level beneath 1,5 mmol/l. There were 3 courses of treatment- 3 months each. After every course we checked citrate excretion, urine pH profile and ultrasound examination.
Results: in 34 children we obtained intended urine pH profile. Mean urinary citrate excretion had been: 0,604 mmol/l at the beginning of the study, 0,956; 1,309 and 1,555 mmol/l after each course of treatment. In 25 children there were no stones after 3 courses of treatment, in 5 children we observed increasing of stone dimension and in 6- the same picture as before treatment. Intended urine pH level were obtained in all, exept two, children; increased excretion of citrate was observed in all.
Conclusions: There is advantageous influence of potassium citrate in the majority of examined children.

96 – DISSOLUTION OF RADIOLUCENT RENAL STONES BY ORAL ALKALINIZATION WITH POTASSIUM CITRATE/POTASSIUM BICARBONATE

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Aim: Uric acid stone disease is dependent on three pathogenetic factors: acid urine pH, low urine volume, and hyperuricosuria. However, the most important factor for uric acid stone formation is persistently acidic urine that represents a prerequisite for uric acid stone formation and growth. Urinary alkalization with alkali administration has been advocated for dissolution of stones on the basis of estabilished clinical experience. The aim of this study was to evaluate the clinical efficacy of therapy with potassium citrate/potassium bicarbonate for dissolution of radiolucent stones. **Patients and Methods:** A total of 8 patients with radiolucent stones (< or = 15 mm) in functioning kidneys were enrolled (4 M, 4 F; mean age 66+/-2 years) Ultrasonography (or computed tomography scan) was done to confirm stone presence and burden and plain X-ray to exclude calcified stones. At basal a blood sample was drawn for glucose, creatinine and uric acid measurement and a 24 hour urine sample was collected for evaluation of daily uric acid excretion. Urine coltures were also performed in order rule out urinary tract infection. All patients at presentation and weekly during the study period filled out urinary pH and volume diaries. Each study day three samples of urine were collected for pH and volume measurement (morning from 8 AM to 2 PM; afternoon from 2 PM to 8 PM, and night from 8 PM to 8 AM). Two study periods were considered: during the first 6 week period a daily water intake of 1500 ml was prescribed whereas in the following 6 week period the same water intake plus potassium citrate 40 mEq and potassium bicarbonate 20 mEq (divided in two doses). Potassium alkali were chosen in order to reduce the risk of calcium precipitation because of their calcium-lowering effect. The effects of treatment on stone dissolution was evaluated by ultrasonography after each study period (6 weeks and 12 weeks).
Results: During the first period of treatment stone burden remained unchanged in all patients. On the contrary after 6 weeks of potassium citrate/bicarbonate treatment, complete stone dissolution was found in three of the patients. In the other five cases a partial dissolution was observed and in two of them complete dissolution of the stone was achieved after prolongation of the treatment for 4 and 6 month respectively. Mean urinary volumes were unchanged during all the two study periods. Mean urinary pH was significantly higher during the potassium citrate/bicarbonate treatment period in comparison to the first study period (morning 6.60+/1.06 vs 5.53+/-0.51, p = 0.030; afternoon 6.53+/-0.70 vs 5.63+/- 0.41, p = 0.007; night 6.57+/-0.51 vs 5.98+/-0.80, p = 0.092). Tolerance of the drug was good, and no serious effects were observed sufficient to interrupt treatment. None of the patients required subsequent interventions for stone treatment.
Conclusions: Urinaryalkalization with potassium citrate/bicarbonate is a well tolerated and highly effective treatment, resulting in dissolution of nonobstructing uric acid stones .

97 – METABOLIC EFFECTS OF ANTIANDROGENIC TREATMENT

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Introduction: Androgen deprivation therapy has a variety of

metabolic effects including obesity, insulin resistance, lipid alterations and osteoporosis that can influence the lithogenic urinary potential.
Materials and Methods: We reviewed the medical literature using the PubMed search terms prostate cancer, androgen deprivation therapy, calcium, oxalate, osteoporosis, obesity, insulin resistance, and lipids.
Results: Osteoporosis is a complication that may be associated with long-term androgen deprivation therapy in men. Testosterone may be an important factor in bone formation, although the role of androgens on bone metabolism appears to be mediated indirectly through their conversion to estrogens. As a consequence androgen deprivation increases bone resorption and has been associated with an increased risk of skeletal fracture. Furthermore androgen deprivation therapy decreases insulin sensitivity and increases low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglycerides.It also decreases lean mass and increases fat mass and risk of obesity. Some of these effects overlap with features of metabolic syndrome, although in contrast to the metabolic syndrome, androgen deprivation therapy increases subcutaneous fat and high density lipoprotein cholesterol. Finally experimental studies in the rat indicate that androgens increase and estrogens decrease urinary oxalate excretion, plasma oxalate concentration, and kidney calcium oxalate crystal deposition. Conversely subcutaneous implantation of exogenous testosterone restored calcium oxalate stone formation in castrated ethylen glicole (EG) treated male rats and enhanced urolithiasis in castrated female rats receiving EG.
Conclusions: Physicians need to be aware of the potential for metabolic effects of androgen deprivation therapy for prostate cancer in order to recognize and properly address them. The cumulative effect on the lithogenic risk has to be evaluated (increased calcium excretion, decreased oxalate excretion, metabolic syndrome-like effect).

98 – PROPHYLACTIC DRUG DOSE ADJUSTMENT BASED ON SYMPTOMS

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Objectives: Patients with urinary stone are administered various prophylactic regimes like potassium citrate either alone or in combination with magnesium or pyridoxine, sodium bicarbonate and other drugs with out assessing their biochemistry properly. This usually ends in non compliance due to gastric upsets and other side effects. This paper intends to project the importance of scientific decision making in the urinary stone prophylaxis, based on dose adjustment of drugs depending on symptoms and extent of urinary deposits.
Materials and Methods: 500 randomly selected stone patients from the urinary stone clinic who were administered allopurinol and pyridoxine were followed up for minimum of two years for metabolic correction, urinary deposits, stone passage and clearance of symptoms and urinary deposits. At the first visit, they were radiographed, sonologically assessed, metabolically investigated and urinary deposits studied. Patients needing stone retrieval were excluded from the study. Based on results, the patients were administered the drugs in appropriate doses. When they returned for review after two moths, the severity of the symptoms and extent of urinary deposits were noted. Based on observed findings, the dose was adjusted. The extent of symptomatic relief and clearance of urinary deposits were recorded. Presence of passable stones, excruciating pain and presence of frank haematuria invited high dose therapy in 87 with allopurinol 300 mgs. and pyridoxine 120 mgs (HDC). Patients with varying grades of crystalluria and moderate symptoms without definite stones or back pressure were started with low dose treatment in 413 with allopurinol 100 mgs and pyridoxine 40 mgs (LDP). The dose was adjusted during each review.
Results: Of the 500 patients selected, 122 had stones retrieved with no residual radiological stone, 249 were colic patients (138 had USS identified stones < 5 mm, 37 with back pressure in USS without evident stone and 74 with associated crystalluria) and 129 were crystallurics with low back ache. The most common metabolic abnormalities identified were hyperoxaluria (63%), hyperuricosuria (47%) and hyperuricaemia (12%) in that order. At two months, among the patients with HDC, three had to increase the dose, two for persistent symptoms and one for persistent significant crystalluria. 22 patients had to continue on HDC (12 for symptoms 5 for crystalluria and 5 for combination) 62 had reduction in dose. Among patients on LDP, 94 needed increase in dose (45 for symptoms and 49 for increased or persistent urine deposits), 52 had to continue the same dose and 267 could reduce the dose. At follow up at 2 years, 345 had interrupted treatment at various periods of time, 67 of whom returned with symptoms, 87 restarted drugs by themselves at recurrence of symptoms, and the rest 191 had taken the drugs with interruption. At the end of two years 3 patients developed recurrent stones. All the three had defaulted prophylaxis in between.
Conclusions: It is concluded that the dose adjustments in prophylaxis should be based not just on the symptoms of the patients, but also on presence of urinary deposits.

99 – NON COMPLIANCE AND RECURRENCE OF URINARY STONE

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Objectives: Patients with urinary stone disease are administered various chemotherapeutic/chemoprophylactic regimes. Many of these patients stop coming to the clinic for a long time. Many return with significant symptoms. This paper is based on the experiences of the authors in the management of stone clinic for 10 years during the period 1999 to 2009. 500 patients who attended the urinary stone clinic after stopping of prescribed chemotherapy/ chemoprophylaxis were studied. The objective of the paper was to identify the reasons for non compliance and find the pattern of recurrence.
Materials and Methods: 500 urinary stone patients who came to the urinary stone clinic for follow up after discontinuation of the original advice were assessed. The duration of the stone disease, period of compliance, duration of non compliance, and indication for return were noted. The patients were asked for the reasons for non compliance.
Results: Of the 500 patients, who returned for review after non compliance of chemo prophylaxis/chemotherapy, 39% of patients came back with severe symptoms, 28% returned with moderate symptoms, 20% returned with mild symptoms and 13% had no symptoms. 8% had radiological stones without any symptoms. The period of non compliance ranged from two months to 8 years (2 to 6 months - 65%, 6 months to 1 year - 18%, 1-2 years - 7%, 2-5 years 7% and

over 5 years - 3%). The reasons for non compliance were lack of information regarding need for long term drug prophylaxis (23%), absence of symptoms (53%), cost factor (8%), non availability of the prescribed drugs (7%), shifting to other systems of medicine (7%) and fear of side effects (2%). Among the patients with recurrence, 67% had symptoms of pain, 13% had dysuria, 5% had haematuria and 3% had lithuria. The group of patients had significant urinary deposits, namely rbc - 27%, pus cells - 23%, COM - 17%, COD - 16%, Phosphates - 5% and uric acid - 7%. 23% of the patients had radiological stones and 33% had Ultrasonic evidence of stone without radiological confirmation. It was noted that the patients who were given clear instruction in the printed format tended to return for review in spite of not have any recurrent symptoms. The finding of 65% of the patients returning with recurrence within a period of 6 moths indicates that in case of recurrence, majority will develop within a period of six months.
Conclusions: Proper patient education is the most important advice to be given to the patients at the time of discharging from the stone clinic. That is concluded that patient education is as important as administering chemoprophylaxis and dietetic prophylaxis in stone patients.

100 – ECONOMICS OF MEDICAL TREATMENT

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Objectives: Urinary stone patients are administered blind chemophrophylaxis and chemotherapy without performing appropriate metabolic assessment by allopathic, ayurvedic, homeopathic and naturopathic physicians. The extent of recurrence in these patients is very high. Several patients are administered citrates, sodium bicarbonate, thiazides and a host of unscientific preparations and plant extracts. This study was conducted to find out the cost effectiveness of the various modalities of treatment in a long term basis.
Materials and Methods: The cost of different drugs available in the market was calculated on a per year basis for a moderate dose. The extent of compliance to treatment was noted among the patients. The utility of the drugs with regard to symptomatic relief and clearance of crystalluria were recorded. The patients were followed up for a minimum period of 2 years to assess the extent of stone recurrence.
Results: The total annual cost of the drugs and their efficacy are detailed in the table.

Drug	Annual Cost in US$	No. of patients	Stone episode %*
Allopurinol	20	250	-82
Pyridoxine	5	250	-82
Hydrochlorothiazide	48	34	-28
Sod. Bicarbonate	10	16	-45
Sodium citrate	620	27	-32
Sodium Pot. citrate	1500	56	-68
Potassium citrate	720	67	-35
Calcury	20	16	+ 2
Cystone	20	45	+ 9

* Reduction in stone activity indicated by – and progress in stone activity marked by +.
The total expenditure of administering allopurinol and pyridoxine combination was acceptable for most patients and the combination did not present any adverse reaction in the dose administered. The effectiveness of the treatment had to be assessed by the presence of tolerability problems, side effects and the usefulness in terms of clearness of urinary deposits like RBC's Puscells and Crystalls.
Conclusions: It is concluded that the most cost effective treatment would be administration of appropriate biochemical agents. For idiopathic Calcium Oxalate stone disease important metabolic abnormalities are hyperuricosuria, hypoxaluria and hyperuricaemia in that order. Even in the presence of other metabolic abnormalities, it would be advisable to correct the uric acid and oxalate metabolism by administering allopuinol and pyridoxine.

101 – SIDE EFFECTS OF DURG THERAPY IN UROLITHIASIS

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Objectives: Various drugs are administered by various physicians for stone patients with different types of urinary stones disease. In this paper and attempt was made to assess the side effects of the patients consuming different types of chemotherapeutic regimes.
Materials and Methods: 480 patients consuming different chemotherapeutic regimes namely Allopurniol + pyridoxine, Hydrochlorothiazide, Rowatinex, Sod. Bicarbonate, sodium citrate, sodium Pot. Citrate, potassium citrate, Calcury, Cystone and Distone were studied. The number of days the patients could tolerate before stopping was noted. The clinical effects on symptoms and urinary deposit findings were recorded.
Results: The details of the drugs consumed and the side effects are given below.

Drug	No	Months	GIT %	Skin rashes %	Nervous %	Others %
Allopurinol + B6	220	24	1	1	Nil	Nil
Hydrochlorothiazide	23	4	8	Nil	8	Nil
Rowatinex	18	5	10	Nil	15	Nil
Sod. Bicarbonate	12	6	50	Nil	Nil	Nil
Sodium citrate	62	2	32	Nil	Nil	Nil
Sodium Pot. citrate	78	15	Nil	Nil	Nil	Nil
Potassium citrate	45	7	34	Nil	Nil	Nil
Calcury	9	6	Nil	Nil	Nil	Nil
Cystone	18	13	Nil	Nil	Nil	Nil
Distone	13	10	Nil	Nil	Nil	Nil

The most common adverse reaction of the drugs was gastro intestinal upset. This was primarily identified in all forms of citrates except hexa sodium hexapotassiumm hydrogen citrate.
The combination of allopurinol 100 mgs. and pyridoxine 40 mgs. was identified to be best suited for the stone patients.
Conclusions: It is seen the patients consuming different types of citrate could not tolerate the drug because of gastrointestinal upsets.
Other drugs were mostly unscientifically given are hence not recommended.
It is concluded that appropriate chemotherapy/chemoprophylaxis should be instituted based on the metabolic status and type of stone formed.

Poster D

PCNL & OTHER

102 – ASSESSMENT OF DEMOGRAPHICS, OPERATIVE DETAILS AND RESULTS IN 500 CONSECUTIVE CASES OF PERCUTANEOUS NEPHROLITHOTOMY IN A MAJOR UK TERTIARY REFERRAL CENTRE

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Objectives: To assess the patient mix, methods of operating and results for PCNL in a major London teaching hospital serving as a tertiary referral centre for the South East of England

Materials and Methods: 500 consecutive patients operated on at UCLH, over a period of two and a half years, analysing operation record, notes and electronic patient records where necessary.

Results: two thirds of our patients were male, with a mean age of 51.2 years. 20% of our cases were Staghorns. Mean stone size of non Staghorns was 1.7cm per stone, with the largest mean (2.4cm) within the renal pelvis. There were mean 2.5 stones per case. All punctures were performed by a radiologist who stayed in theatre and assisted with each case. 25% of stones were treated with a direct puncture onto the stone. The rest with an indirect puncture that was via the upper pole in 54% of cases. 83% involved 1 puncture. In those with 2 or more punctures, all included an upper pole puncture. We had a 74% stone free rate for all-comers, included complex Staghorns on 1 sitting, and 93% if full stags were excluded. 22% were performed fully tubeless. There was a mean blood loss of 1.1 g/dl. A transient creatinine rise occurred in 1.5% of patients. Failed access rate was 1.7%, Transfusion rate 0.7% and sepsis 3%. Despite the fact that upper pole punctures were use in over 50% of cases, our pneumothorax rate was 3%. Embolisation rate was 0.2%, bowel injury 0.3%. 46% of our stones were calcium oxalate, 27% Magnesium Ammonium Phosphate and 15% Cysteine.

Conclusions: We report the results of a major UK centre for PCNL. Almost 200 cases are performed a year. We can treat complex stones with minimal complications and would recommend that complex cases are sent to tertiary referral centres where outcome can be world class. We would recommend tandem work with radiologists as part of a multidisciplinary approach, and suggest the upper pole access results in excellent clearance of the upper and lower poles, good access to the renal pelvis & ureter (only 5% needed a primary stent) and should be recommended.

103 – TUBELESS MINI-PNL VS. CONVENTIONAL PNL FOR SOLITARY KIDNEY STONES

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Introduction: Percutaneous nephrolithotomy (PNL) remains the standard therapy for larger renal calculi. The introduction of smaller nephroscopes (so-called "Mini-PNL") and abandonment of nephrostomies after uncomplicated procedures may reduce morbidity.

Aim of this study was to compare a consecutive series of PNL and Mini-PNL (tMP) procedures, focusing on peri- and postoperative morbidity.

Materials and Methods: 2x25 pat. were treated either by PNL (26 F. working sheath, ultrasound lithotripsy, 22 F. nephrostomy) or Mini-PNL (18 F. working sheath, holmium laser lithotripsy, antegrade DJ-placement and tract closure with thrombin matrix; all instruments Karl Storz Endoscopes, Germany) for solitary renal calculi < 25 mm. Recorded peri- and postoperative parameters included complications, visual-analogue pain scale, use of analgetics and length of hospital stay.

Results: Patients characteristics were comparable (age, gender, BMI) except of stone size being slightly lower in the tMP group (tMP 18 vs. PNL 18 mm; p = 0.042). OR time was longer in the tMP group (57 vs. 48 min., n.s.). Significant complications did not occur (PNL: 1 pelvic perforation, 2 venous bleeding, tMP: 1 venous bleeding, n.s.). Transfusions were not necessary in both groups. Immediate stone free rate was comparable (tMP 24/25 vs. PNL 23/25). Postoperative pain (VAS/analgetics) was little lower in the tMP group (p = 0.048). Fever > 38.5°C occurred in 5/25 (PNL) vs. 3/25 (tMP) pat. Length of stay favored tMP (3.8 vs. 6.9 days). Significant complications did not occur in both groups.

Conclusions: Both, conventional and Mini-PNL are safe procedures with comparable low complication rates. However, less postoperative pain and shorter hospital stay may support tubeless tMP in patients with limited stone mass.

104 – IS THERE A "RATIONALE" EXPLAINING THE LOWER RISK OF COLONIC INJURIES DURING SEMI-SUPINE VERSUS PRONE PERCUTANEOUS NEPHROLITHOTOMY?

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Objectives: Iatrogenic lesion of colon represents a rare major complication of percutaneous nephrolithotomy (PNL). Several studies have underlined that colonic injuries rate is lower during semi-supine than during prone PNL, as resulting by the medical records on adverse events. Aim of this prospective study was to analyze the displacements of the ascending/descending colon and the omolateral kidney in semi-supine and prone position, by means of preoperative abdominal computed tomography (CT) in both positions.

Materials and Methods: Seventeen stone patients candidate to PNL preoperatively underwent computed tomography (CT) scan of the abdomen, with and without contrast, in prone and semi-supine position. Exclusion criteria were: congenital anatomical anomalies of the kidney or of the upper urinary tract; skeletal or abdominal abnormalities; previous upper urinary tract surgical treatments or infections and previous abdominal surgery. Semi-supine position was obtained placing a roll, 10 cm in diameter, under the abdominal flank omolateral to renal stone, obtaining an oblique inclination of the surgical side of about 30°. To analyse the abdominal topography in prone and semi-supine positions, we identified two anatomical parameters, the colon-axial angle and the reno-colic angle, directly measured using the CT images.

Results: The semi-supine position was characterized by a

median oblique inclination of 30° (R.I. 25°-35°). CT scan in semi-supine position evidenced a more medial displacement of colon respect the same in prone position, withdrawing that from the puncture area. Statistical analyses of the considered angles evidenced a significant difference between their values in prone e semi-supine position, confirming a medial colon displacement in semi-supine position. Stratifying our patient group for gender, as far as for body mass index (≤ 25 and > 25) and umbilical waist circumference (≤ 100 cm e > 100 cm), it has been confirmed the presence of a similar statistically significant difference between prone and semi-supine position.

Conclusions: Our study supports the clinical observations that percutaneous approach to the lower renal pole in semi-supine position is characterized by a lower risk of colonic injury than in the prone. The rationale is that, rolling from prone to semi-supine position, there is a medial displacement of the colon far from the site of ideal percutaneous puncture of the kidney. This reduction of iatrogenic colonic injuries is independent of gender, build and central body fat release.

105 – THE BART'S MODIFIED VALDIVIA POSITION: OUR EXPERIENCE WITH SIMULTANEOUS ANTEROGRADE AND RETROGRADE URINARY TRACT ACCESS FOR COMPLEX ENDOUROLOGICAL PROCEDURES

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Objectives: Complex endourological entities such as renal and upper ureteric stones, co-existing UPJ or ureteric strictures and migrated or encrusted stents often necessitate both retrograde and anterograde access. The lack of a one-step combined retrograde and anterograde procedure may increase operating time and morbidity, especially in high-risk patients in the prone position. We present our experience and success with the use of our positioning technique for achieving simultaneous anterograde and retrograde access in such complicated cases.

Methods: 22 patients (14 males, 8 females) with a mean age of 55 years had simultaneous anterograde and retrograde upper urinary tract procedures carried out in the Bart's modified Valdivia position. We place our patients in the lithotomy position with the pelvis tilted at 45º supported by a foam wedge, while the torso is twisted to the contra-lateral side with the shoulders perpendicular to the operating table. The leg of the operated side is flexed and relatively adducted following the lateral rotation of the trunk, while the contra-lateral leg remains fully abducted. Twelve patients (including one with a horseshoe kidney) had pelviureteric junction (PUJ) obstruction with concurrent impacted PUJ stones, 3 patients had dense upper ureteric strictures from retroperitoneal fibrosis, 3 patients had impacted upper ureteric stones as a result of a stricture distal to the stone, 1 patient had an upper ureteric stone with no stricture, 2 patients had heavily encrusted JJ stents and one patient with a solitary kidney had hydronephrosis due to a distal ureteric stone in a ureter which had been reimplanted into a neobladder following nephro-ureterectomy and cysto-prostatectomy.

Results: All twelve patients undergoing endopyelotomy (8 anterograde and 4 retrograde) and stone extraction had a successful initial procedure with stone clearance from the PUJ. Two patients needed adjuvant ESWL to clear small calyceal stones inaccessible during surgery. Radionucleotide scanning at mean follow-up of 22 months confirms relief of obstruction in 10 out of the 12 cases (83%). In the other 2 cases there is borderline obstruction but the patients are asymptomatic. We achieved successful recanalisation of all ureteric strictures using this position and placed ureteric Memokath stents across the narrow segments. The ureteric stone clearance rate has been 100% so far using the anterograde and retrograde approach simultaneously. One of two patients with heavily encrusted JJ stents was rendered stone free while the other required ESWL for small residual kidney stones to be rendered stone free. The patient with a solitary kidney and ureteric implantation into a neobladder was rendered stone-free. No perioperative or postoperative complications such as bleeding or splanchnic injury were experienced.

Discussion: Our modification to the Valdivia position is safe and effective during complex endourological procedures and importantly allows two surgeons to work simultaneously. High risk patients take advantage of reduced operating time and better cardiovascular and respiratory function that is enabled by the more lateral position we use compared to the Valdivia technique. This position offers more flexibility in terms of access points as the loin is more exposed and we can achieve a steeper access if necessary. Percutaneous access is achieved by combined ultrasonographic and fluoroscopic guidance as conventional landmarks do not apply.

106 – PERCUTANEOUS ENDOUROLOGICAL PROCEDURES IN HIGH RISK PATIENTS IN THE LATERAL DECUBITUS POSITION

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Background and Purpose: Percutaneous endourological procedures are most commonly performed with the patient in the prone position under a general anaesthesic. In high risk patients, this approach can lead to circulatory and respiratory compromises. Operating on such patients in a full lateral position will minimize the haemodynamic and respiratory risks and – if combined with spinal anaesthesia – will allow for increased patient comfort (despite the regional anaesthesia) and safety.

Patients and Methods: After rigorous pre-operative assessment, a total of 27 medically high risk patients (12 males, 15 females) with a mean age of 62 years and an ASA score of > 3 were included in this study. The majority (78%) had regional (spinal/epidural) anaesthesia and were fully awake and alert during the operation. In the majority of these cases we perfomed an initial retrograde renal study/ filling with contrast medium in lithotomy position to aid the kidney puncture. The percutaneous procedure was then performed with the patient in the lateral decubitus position and access was performed under fluoroscopic guidance. In the remaining patients where there was no first stage, the puncture was performed under ultrasound guidance. Twenty-two percutaneous nephrolithotomies (PCNL), 3 anterograde endopyelotomies (AEP), 1 percutaneous resection of renal pelvic transitional cell carcinoma, and 1 percutaneous renal cyst sclerotisation were performed.

Results: 11 patients were stone free after PCNL and a further 8 after adjuvant SWL for small residual fragments. One renal

access failed. Two procedures were aborted because of haemorrhage after tract dilatation. Nuclear medical renal scanning after 3 months showed relief of obstruction in all three AEP patients. Ultrasound confirmed complete resolution of the sclerotized renal cyst. None of our patients with regional anaesthesia required conversion to general anaesthesia. In two patients experiencing mild to moderate discomfort a top-up with local anaesthesia solved the problem.
Conclusions: The full lateral position – which whilst requiring expertise and experience to gain proficiency in performing good renal access – is safe and effective in medically high risk patients. Complex percutaneous renal procedure can be safely and effectively performed under regional (spinal/epidural) anaesthesia avoiding the risks of general anaesthesia and allowing for patient – anaesthetist communication throughout the procedure. Cardiac and respiratory parameters are improved, stable and easily controlled. In morbidly obese patients the lateral position under spinal anaesthetic not only reduces circulatory and respiratory complication but allows for easier access to the kidney when compared to the prone position.

107 – THE EFFICACY OF LEVOBUPIVACAINE INFILTRATION TO NEPHROSTOMY TRACT IN COMBINATION WITH INTRAVENOUS PARACETAMOL ON POSTOPERATIVE ANALGESIA IN PERCUTANEOUS NEPHROLITHOTOMY PATIENTS

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Objectives: Our aim was to evaluate the efficacy of intraoperative local anesthetic infiltration in combination with intravenous paracetamol infusion on postoperative pain management in patients who underwent percutaneus stone surgery.
Design and methods: Sixty patients who were older than 18 years were included into the study. Percutaneus nephrolithotomy (PNL) has been performed via single subcostal access in all patients. Patients were randomized into three groups including 20 cases in each. In the first group (Group SP), 20 ml saline was infiltrated through the whole (cutaneous, subcutaneous and muscle layers) nephrostomy tract intraoperatively and this was followed by intravenous paracetamol (4x1 gr) infusion postoperatively. In the second group (Group LP), 20 ml of 0, 25% Levobupivacaine infiltration to the nephrostomy tract in a similar manner followed by IV paracetamol infusion. The third group (Group LS) 20 ml of 0,25% Levobupivacaine infiltration to the nephrostomy tract in a similar manner followed by IV saline infusion. In the postoperative period, pain status of patients were evaluated in the recoveryunit (hour 0) and in the ward at postoperative 2, 4, 6, 8, 12 and 24'Th hours by using the visual analogue scale (VAS). In patients who did not completely respond medication (VAS ≥ 3), meperidine 1 mg/kg intramuscular was given as on additional "rescue"analgesic. The patient satisfaction from the postoperative analgesia management was assessed by 5 points scale.
Results: Three groups were compared regarding the demographic features, parameters on pain control, the adverse effects due to agents used in analgesia, surgical complications and postoperative hospital stay. The factors those have impact on these parameters have been analyzed. There was no statistically significant difference between 3 groups regarding the demographic characteristics. Our findings revealed that in group LP, the amount and frequency of opioid used was lesser, VAS score was lower, time period until full mobilization was shorter and patient satisfaction score was higher when compared to the other 2 groups.
Conclusions: According to the results our studies, Levobupivacaine infiltration through the nephrostomy tract in combination with intravenous paracetamol infusion was shown to be safe and efficious as an analgesia method following PNL. However, to have more reliable results, this study should be conducted in larger group of patients.

108 – MINIMAL INVASIVE PCNL IN OLDER PATIENTS – ANALYSIS OF OUTCOME AND MORBIDITY IN 57 CONSECUTIVE PATIENTS AGED 70 AND ABOVE

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Objectives: Minimal invasive PCNL (MPCNL) is used in the treatment of nephrolithiasis as an alternativ treatment to shock wave lithotrypsy or conventional PCNL in suitable cases. Previously published data demonstrated a high efficiency and low morbidity of the method.
This study analyses the data of 57 consecutive patients aged 70 years (y) or above compared with 278 younger patients to evaluate the applicability of the method in aged patients.
Materials and Methods: 57 patients (range 70 to 92 y, mean age 75.0 ± 4.2 y) were treated by a miniaturized PCNL (MPCNL) equipment, including a 12 F nephroscope and an 15 F Amplatz sheath. Data on the stone size and location, stone-free rate, blood transfusions, operating time and complications were recorded prospectively. Results were compared with the data of 278 consecutive younger patients. Student´s t-test or Chi-square test were used for statistical testing.
Results: Average stone size was 4.7 cm^2 on the plain x-ray film and did not differ from controls (4.2cm^2). Furthermore no statistically significant differences could be detected for mean operating time (62 ± 28 min. vs. 68 ± 30 min.), stone-free rate (90% vs. 89 %), and transfusion rate (1.8% vs. 1.8%). The necessity for retreatment to achieve endoscopically and radiographically assured absence of residual fragments tended to be lower (21% vs. 32%) but did not reach statistical significance. A significant difference ($p < 0.05$) however was revealed for postoperative febrile episodes. There was no relevant fever episode in older patients (0%) whereas fever was observed in 7.9% of controls.
Discussion: MPCNL demonstrated to be well applicable in older patients. Results are independent of age in terms of stone-free rates and treatable stone burden. There was no higher morbidity in aged persons compared with younger individuals. Therefore, in aged patients MPCNL can be regarded a safe and reliable alternative treatment modality to SWL and PCNL in suitable cases, as well.

109 – MINIMAL INVASIVE PCNL IN THE TREATMENT OF NEPHROLITHIASIS – ANALYSIS OF EFFICIENCY AND MORBIDITY AFTER 443 CONSECUTIVE PATIENTS.

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Objectives: Extracorporal shock wave lithotripsy (SWL) or percutaneous nephrolithotomy (PCNL) are the treatment

modalities of choice in nephrolithiasis. SWL however is associated with a relatively high probability of residual fragments, whereas PCNL demonstrates better results, but is more prone to complications. To reduce the invasiveness and consequentially the complication rate a miniaturized 18F instrument for PCNL (MPCNL) has been developed. 443 consecutive patients were prospectively evaluated to determine the status of the method.

Materials and Methods: 443 patients (mean age 53.8 ± 12.9) were treated. Data on the stone size and location, stone-free rate, blood transfusions, operating time and complications were recorded. A subgroup with a stone mass larger than 5cm^2 on the plain x-ray film (n = 139) was analyzed separately to determine the applicability to larger stone loads.

Results: In 440 patients access was possible. On average retreatment rate was 0.29 (subgroup: 0.37). The mean stone size was 4.4 cm^2 (subgroup: 9.4 cm^2) The average operating time was 66 ± 47 min. (subgroup: 75 ± 25 min). Overall stonefree rate was 92.7% (subgroup: 92.1%). Blood transfusion were needed in seven cases (1.7%, subgroup: 1.4%). Febrile pyelonephritis was observed in 29 patients (6.5%, subgroup: 7.9%). Except one arterio-venous fistula, which had to be treated by interventional radiology, no major complications were observed.

Discussion: MPCNL was a reliable alternative to SWL for renal calculi with a size from 1 to 3 cm located in the renal pelvis and calices, especially the lower calix. Advantages are short treatment time and the high stone-free rate. Complication rate is similiar to that of SWL and significantly lower when compared to conventional PCNL. Despite the reduced diameter of the instruments treatment of larger stone burden is possible with just slightly increased operating time. As high stone-free rate and low level of complications are maintained, MPCNL is worth to be considered alternatively to conventional PCNL in suitable cases.

110 – A TEN YEAR SINGLE CENTER EXPERIENCE OF LARGE PROXIMAL URETERAL STONE TREATMENT: COMPARISON OF EFFICACY BETWEEN RETROPERITONEOSCOPIC URETEROLITHOTOMY AND PERCUTANEOUS NEPHROLITHOTOMY

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Objectives: The surgical treatment for ureteral stones has changed dramatically since the development of extracorporeal shock wave lithotripsy (ESWL) and endourologic procedures. To date, most patients with upper urinary stones have been treated with ESWL. However, some patients with large proximal ureteral stones still have had to undergo open ureterolithotomy or endourologic procedures such as percutaneous nephrolithotomy (PNL) and retroperitoneoscopic ureterolithotomy (RPU). In view of these findings, we performed RPU or PNL for the patients with large proximal ureteral stone (> 1 cm) and analyzed the efficacy of two surgical treatments.

Materials and Methods: We reviewed retrospectively 72 cases of surgical treatments for large proximal ureteral stones (> 1 cm) between 1998 and 2008. 18 patients underwent PNL while 54 patients underwent RPU. PNL was performed after large proximal ureteral stones were lifted up into the renal pelvis with open end catheter or retrograde ureterorenoscopy. RPU was performed by retroperitoneal approach.

Results: There was no significant differences between PNL group and RPU group in patient age (52.2 years: 46.1 years), stone size (1.54 cm: 1.5 cm), operation time (194 minutes: 190 minutes), transfusion rate (11%: 6%), hospitalization day (6.61 days: 6.74 days), hemoglobin decrement (1.2 g/dl: 1.3 g/dl), complication rate (11%: 15%) and stone free rate (94.4%: 96.3%). But, compared with RPU group, PNL group had lower double-J catheter insertion rate (56%: 94%, p = 0.044) and shorter double-J catheter indwelling duration (14 days: 36 days, p = 0.002).

Conclusions: Our results suggest RPU is as effective as PNL for large proximal ureteral stones except for double-J catheter indwelling.

111 – PERCUTANEOUS NEPHROLITHOTRIPSY IN THERAPY FOR NEPHROLITHIASIS

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Objectives: The retrospective analysis and estimation of efficiency of percutaneous nephrolithotripsy in the therapy of nephrolithiasis.

Materials and Methods: We considered data of 127 patients (age range from 23 to 75 years) with various clinical forms of nephrolithiasis who underwent percutaneous nephrolithotripsy in the period 2005-8. All patients presented with stones of 1,8 cm or above. Unilateral stones were observed in 74 (58,3%), bilateral stones in 36 (28,3%), coralliform stones in 17 (13,4%) (10 bilateral and 7 unilateral). In 115 (90,6%) patients there was leukocyturia, microhematuria and bacteriuria. In case of bacteriuria antibacterial therapy was started 7 days prior to operative intervention (cephalosporin 3-4 generation or quinolones). Patients with sterile urine received antibiotics (cephalosporin) directly ahead of operation

Results: In 119 (93,7%) patients stones were successfully removed, but in 5 patients the procedure has to be stopped because of a significant bleeding who requested an hemostatic drainage. In 2 obese patients pecutaneous tract was lost during the procedure and it was not possible to remove the stones. In all 7 patients stones have been removed with a repeated attempt after 1-2 months. Duration of operation ranged from 40 to 120 minutes (on the average 70 minutes). Average blood loss was 100-150 ml.

The postoperative period in all patients proceeded without complications. A nephrostomy drainage in all patients was left for 4-7 days. Patients were discharged from the hospital 6-8 days after the operative intervention in satisfactory condition.

Conclusions: Percutaneous nephrolithotripsy is an effective method of therapy for nephrolithiasis, reducing postoperative complications and hospital stay.

112 – PERCUTANEOUS NEPHROSTOMY FOR OBSTRUCTING NEPHROLITHIASIS

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Objectives: The retrospective analysis and estimation of efficiency of percutaneous nephrostomy (PN) for urolithiasis.

Materials and Methods: We considered data of 52 patients who underwent PN for urinary upper tract obstruction during last years. (24 men (46,2%) and 28 women (53,8%)). In 5 case (9,6 %) stones were located in the pelviureteric junction, in 4 (7,7%)in the pelvis, in 16 (30,8%) in the lower third of the ureter, in 10 (19,2%) in the upper third, and in 5 (9,6 %) patients in the mid ureter. Staghorn calculi were present in 7 (13,5%). The sizes of the stones ranged from 0,8 up to 4,0 cm. In 5 (9,6%) patients radiolucent stones were diagnosed. PN was performed by means of the ultrasonic scanner "Bruel and Kjear" with the probe 3,5-5 MHz.
Results: Procedure was urgent in 38 (73,1%) patients, due to infrarenal obstruction and associated obstructive pyelonephritis Restoration of urine outflow in association with adequate antibacterial therapy achieved complete and fast cure of all 52 patients. In 12 (23,1%) the nephrostomy tract was used for carrying out percutaneous nephrolithotripsy. Contact ureterolithotripsy was performed in 14 (26,9%) patients. The presence of a nephrostomy considerably reduced the risk of postoperative complications. 26 (50%) patients, including 4 with staghorn calculus, underwent extracorporeal lithotripsy without risk of obstruction after fragmentation of the stone.
Conclusions: PN under the control of ultrasound is the most effective method of treatment of obstructing stones, reducing the rate of postoperative complications and time of hospital stay.

113 – ENDOUROLOGICAL TREATMENT OF CALYCEAL DIVERTICULUM STONES – INDICATIONS AND RESULTS

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Due to the anatomical conditions of calyceal diverticulum stones results of extraxcorporal shockwave lithotripsy (SWL) are very poor. Even after successful desintegration, the stonefree rate is only about 50% because of diverticulum neck obstruction. Since introduction of new miniaturized endourological instruments the technical feasibility of these procedures has been significantly improved. The main advantage is to combine treatment of the morphological obstruction and the removement of the stone.
37 patients were treated in total. 8 patients underwent ureterorenoscopy (URS) (A). 20 patients underwent minimal invasive percutaneous nephrolithotomie (MPCNL) (B) and 9 received a combination of both procedures (C).
The overall stonefree-rate was 81,8%. In the patients who underwent URS a stone-free rate of 75% was achieved. The stone-free rate with URS for the upper calyceal group was 84%, for the middle calyceal group 100% and for the lower calyceal group 50%. In group B, overall stone-free rate was 96%, 100% in the upper calyceal group, 100% in the middle calyceal group and 91% in the lower calyceal group. For group C, a stone-free rate of 78% was achieved. 50% in the upper calyceal group, 100% for the middle and the lower calyceal group. It was possible to treat the calyceal diverticulum neck every time.
In comparison with SWL a high stone-free rate can be achieved with new minimal-invasive endourological instruments. The advantage of this method is the additional treatment of the obstruction due to the calyceal diverticulum neck, which is neccessarry to prevent stone-recurrence. The complication-rate of endourological treatment was very low. In conclusion the endourological approach to calyceal diverticulum stones is superior to SWL. The decision whether to use MPCNL or URS should depend on the stone localization.

114 – SIMULTANEOUS ABLATION OF RENAL CYST AND LITHOTRIPSY OF RENAL STONE WITH LAPAROSCOPIC APPROACH: FIRST CASE REPORT

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Objectives: Laparoscopic pyelolithotomy is an effective and feasible procedure. However, it can be tricky in case of staghorn stones, especially if located inside a calyx. We describe a combined procedure in a symptomatic patient affected by renal cyst and pielic stone. After cyst removal and pielotomy, a rigid nephroscope allowed a ballistic lithotripsy (Swiss LithoClast®) of the stone, with subsequent removal of the fragments.
Materials and Methods: A 55 years-old man complaining of relapsing renal colic and haematuria, was diagnosed by contrast CT a renal cyst (12 cm) and 5 pielic and middle caliceal stones. A laparoscopic approach was preferred compared to a percutaneous one because of the uncertain features of the cyst (enhancement patterns in the peripheral wall), in order to obtain an adequate histological specimen. With the patient positioned on the flank (45°), 4 transperitoneal trocar (10-12 mm for 2 and 5 mm for 2 trocars) were inserted and renal cyst removal was easily performed. After the pyelotomy, a flexible nephroscope was introduced inside a 10-12 mm trocar, to obtain visualization of the excretory ways. The use of laparoscopic forceps allowed the retrieval of pielic stones, but the extraction of the caliceal one required the use of a rigid instrument with ballistic lithotripsy. After fragments removal, a double J ureteral stent was inserted by an anterograde route and renal pelvis has been sutured. Follow up was performed with ultrasound 1,2 and 6 months after surgery.
Results: Operative time was 175 minutes, and both the procedure and the following course were ordinary, without significant bleeding. Patient was discharged 4 days after laparoscopy, and pathological exam showed a simple renal cyst. Stent removal was carried out 20 days later, and the subsequent follow up was uneventful (without hydronephrosis or residual stones).
Conclusions: Laparoscopic approach allows the simultaneous treatment of different diseases as described in the present case. The introduction of a nephroscope inside a pyelotomy represents a safe procedure, that offers the advantages of an ample visualization of the excretory ways, an adequate irrigation, and application of energies to perform lithotripsy. The ballistic device was particularly effective in stone fragmentation, and laparoscopic approach avoids parenchymal and uretelial potential damage.

115 – ENDOUROLOGIC TREATMENT OPTIONS IN COMPLICATED NEPHROLITHIASIS

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Objectives: In recent years new treatment options emerged in the treatment of nephro- and ureterolithiasis. Flexible

ureterorenoscopes, semirigid ureteroscopes and a minaturised PCNL equipment (MiniPCNL) have been developed and prepared the ground for a more active endoscopic management of urolithiasis. Modern guidelines take these techniques into consideration and define their role in the treatment of standard situations. Beyond that they are able to contribute in the care of nephrolithiasis in the setting of more complicated circumstances.
Materials and Methods: During January 2005 and March 2009 more than 1.000 active endoscopic treatments of nephrolithiasis have been performed. Six recurrent situations with increased level of difficulty could be identified. These include nephrolithiasis in patients with ileum neobladder, double kidney with ureter fissus or duplex, horseshoe kidneys, with single kidney, transplant kidney or with diverticulum stones. The treatment modalities used were reviewed and typical cases selected for presentation.
Results: Retrograde and antegrade flexible ureterorenoscopy and the percutanous approach by MiniPCNL offered treatment options for all of the before mentioned situations. The endoscopic techniques provided a high efficiency while treatment morbidity is moderate.
Discussion: Difficult nephrolithiasis situations arise from anatomical variations and/or individually increased risk factors for treatment. Modern endourological techniques offer new treatment options. Thus typical improvements of these methods like short treatment time, reduced complications and low morbidity can be offered to these patients as well.

116 – TRAINING OF UPPER URINARY TRACT ENDOSCOPY – EXPERIENCE WITH A NEW MODEL USING PORCINE URINARY TRACT

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Introduction: Endourological procedures are of high significance in diagnosis and treatment of upper urinary tract diseases. In order to improve surgical skills it is advisable for the urological surgeon to perform in vitro exercises. So far just two-dimensional training models were available. A new three-dimensional training model using a porcine urinary tract allows to learn and practice endourological techniques close to reality.
Materials and Methods: The transportable training model consists of a stainless steel torso covered with a neoprene cover. The relief of the retroperitoneum is imitated by a wire grating. The porcine urinary tracts are fixed by use of special granulate material. The urethra is fixed by suturing into a flexible silicone funnel to allow easy access to the urinary tract. All components are easy to clean and provide good hygienic conditions.
Results: The elastic fixation of the urinary tract allows the use of semirigid and flexible ureterorenoscopes in conditions close to reality. It is possible to prepare the urinary tract with artificial stones to practice the use of holmium laser-lithotrypsy. The training model was used successfully in many endourological workshops. So far more than 150 urologists have been trained successfully.
Conclusions: The newly developed training model allows to learn and practice endourological techniques close to reality because of its special three-dimensional configuration and the use of porcine urinary tract. It was successfully used in education of urologists.

117 – IMPROVED TRAINING MODEL FOR PERCUTANEOUS NEPHROLITHOTOMY

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Objectives: Percutaneous nephrolithotomy (PCNL) and similar endourological procedures require an advanced level of skills. To facilitate the training of the proper technique, simulators are helpful. Non-biological models, useful to learn the basic steps, do not represent the clinical situation in an ideal way. Several years ago, we developed a porcine urinary tract model for PCNL using silicone and gelatine respectively. When dilating the percutaneous tract silicone and gelatine quite frequently were damaged thus inhibiting proper working with the endoscopes. Therefore we improved our training model and made it closer to the clinical situation in humans.
Materials and Methods: The kidney with the ureter is dissected off the retroperitoneal organ package of freshly slaughtered pigs. The kidneys were put into bags cut into parts of the thoracic/abdominal wall of these pigs. The renal pelvis can be filled with saline to simulate hydronephrosis; stones can be implanted for PCNL.
Results: Our new model allows for even better training of all percutaneous endourological procedures (e.g. percutaneous nephrostomy, PCNL, endopyelotomy). Especially puncturing is extremely close to the situation in humans as the porcine thoracic/abdominal wall in principal has the same anatomy as the human one.
Conclusions: Our new training model has already been used with great success in hands-on courses. Concerning "tissue feeling", the anatomic relations and the great variety of procedures that can be trained, it is superior to non-biological models. Nevertheless, it is easily available and inexpensive.

118 – FEASIBILITY OF MINIATURIZED ENDOUROLOGICAL TREATMENT IN CHILDREN WITH DIFFICULT STONE SITUATIONS

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Objectives: The difficulty of stone treatment in children if shockwave lithotripsy (SWL) has failed is the particular anatomy, the small diameter of the ureter and the necessity of miniaturized instruments. In the oncoming abstract we present our results in 11 children treated with minimal invasive percutaneous nephrolithotomy (MPCNL) as well as our experience with stones in a Mainz-Pouch of a 4 year old boy and a difficult ureteral stone in a two year old boy. The challenge in the treatment of kidney stones in children is the difficulty of the access. Especially if the ureteral access is not possible a percutaneous access is necessary. With the conventional percutaneous nephrolithotomy the damage caused to the infantile kidney is significant so that this method is not practicable. With the development of the MPCNL which requires less widening, the path for the percutaneous treatment of kidney stones in children was opened.
Results: In 11 treated children, an overall stone-free rate of 100% was achieved. In 50% of the children a second look was needed. No major complications were observed.
A special challenge was given in a 4 year old boy with a Mainz-Pouch after a cystoprostatovesiculektomy due to a

myosarcoma. Due to non-absorbable sutures, apatit stones had developed in his pouch. A complete removal of all stone material was achieved by means of MPCNL through the pouch-nipple. There was no alteration of the pouch detected. The continence of the child was not affected. In addition to the complete stone-removal in the pouch, an upper calyceal stone was removed from the kidney by MPCNL.
In a two year old boy with a big impacted ureteral stone, first an ureterorenoscopy was tried which remained unsuccessful because of the tight anatomical conditions of the infantile ureter. Over a percutaneous access, antegrade flexible ureterorenoscopy was done for stone-removal.
Conclusions: Endourological approach to stone disease in small children is feasible. Due to miniaturized instruments almost all regions of the calyceal system and ureter of children can be reached today. In summary minimal-invasive percutaneous approach, antegrade flexible ureteroroscopy and retrograde endourological treatment can be recommended even in small children.

119 – PERCUTANEOUS NEPHROLITHOTOMY IN PEDIATRIC PATIENTS: DICLE UNIVERSITY EXPERIENCE

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Objectives: We retrospectively evaluated the percutananeous nephrolithotomy (PCNL) results done in our pediatric patients.
Materials and Methods: We planned PCNL to totally 48 pediatric patients between September 2004- April 2009. Urine cultures were done before surgery in all patients. 26F Storz or 24F Olympus nephroscopes were used during procedure. Pneumatic lithotriptor (Swiss Lithoclast®) preferred for lithotripsy. Either re-entry catheter or Pesser catheter was replaced as nephrostomy following lithotripsy. Fluoroscopic screening and PCNL time and stone burden were recorded.
Results: We performed PCNL to totally 47 children including 27 boys and 20 girls aged between 4-16 (med. 11.5 ± 5.8). The stone location in renal pelvis only, in renal pelvis and lower calyx, in lower calyx only, in middle calyx only,and in upper calyx only were respectively as 23,13,6,2,1. Two patients had staghorn calculi. During PCNL only two patients switched to open surgery, one was because of renal pelvis perforation during the procedure, the other was because of transcolonic access. In one patient we did open surgery primarily as we detected retrorenal colon in computerised tomography.In the rest PCNL performed 45 patients, the mean stone burden was 445 ± 225 (110-800) mm^2,mean operating time was 51 ± 23 (25-80) minutes and mean fluoroscopic screening time was 6,1 ± 2.7 (3-10) minutes. Even though PCNL was performed only, in patients with sterile urine culture, the fever of two patients was over 38 C0. Intraoperative blood transfusion was necessary only in one patient and 10ml/kg blood transfused.
Nephrostomy catheters were removed medially 2, 4 (1-4) days. In two patients the double J stent insertion was necessary for prolonged urine drainage from the nephrostomy tract. In post-operative control x-rays 34 of 45 patients (76%) were stone free, in five patients (11%) there was clinically unimported residual stones and in six patients (13%) there was residual stones. All residual fragments were treated by ESWL.
Conclusions: PCNL is a safe and an efficient treatment of kidney stones in paediatric patients. Stone free rates are directly related to clinical experience.

120 – MANAGEMENT OF SYMPTOMATIC URETERAL CALCULI COMPLICATING PREGNANCY

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Objectives: To review our experiences with management of symptomatic ureteral calculi complicating pregnancy.
Materials and Methods: Between January 2001 and December 2007, 48 pregnant women were treated for symptomatic ureteral stone. The medical records of these patients were retrospectively reviewed.
Results: The mean patient age was 23 (range 17-37) years and gestational age at presentation was 21 weeks (12-38). Most ureterolithiasis cases during pregnancy (60%) occurred in the third trimester. Flank pain was the common presenting symptom (90%), 10 percent had associated fever and 20 percent had irritative voiding symptoms. Ultrasonography was the initial test confirming the diagnosis. By conservative management with analgesics and hydration, spontaneous passing of stones was noted in 13 cases (27%). In ten patients (20.8%) symptomatic relief occurred without spontaneous passing of stones until the end of pregnancy with no complication. Definitive treatment performed after birth in these cases. Invasive management required during pregnancy in 25 patients (52%) due to persistent pain and/or ureteral obstruction. Of these, in twenty patients; ureteral calculi were treated successfully by ureteroscopy. Stones were extracted by pneumatic lithotripsy and/or basket catheter or forceps. In five patients; only double-J stent was inserted during ureteroscopy due to unreached or migrated stone. Majority of the patients (62%) had lower ureteric calculi. The mean size of the stones retrieved was 7 mm (4-13mm). No obstetric or urologic complications were noted.
Conclusions: When conservative treatment fails, ureteroscopy is an effective and safe therapeutic option in symptomatic ureteral calculi complicating pregnancy.

REVIEW

The origin of nephrocalcinosis, Randall's plaque and renal stones: A cell biology viewpoint.

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Summary

Medullary nephrocalcinosis is a rare condition typically observed in metabolic conditions prone to renal calcium stones. Randall's plaques are very frequently observed in the common idiopathic calcium-oxalate nephrolithiasis. These plaques are apatite mineral structures, and we propose they also are an example of nephrocalcinosis. While these calcium deposits are generally considered to be the consequence of purely physico-chemical phenomena, we advance the hypothesis that they form because of a true ectopic biomineralization in the renal tissue. Henle's loop epithelial cells, or pericyte-like interstitial cells, or papillary stem-cells differentiating along a bone lineage could be involved.

KEY WORDS: *Apatite; Pericytes; Stem cells.*

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INTRODUCTION

Medullary nephrocalcinosis is a rare condition typically observed in metabolic conditions prone to renal calcium stones, such as the primary hyperoxalurias, distal tubular acidosis, primary hyperparathyroidism, medullary sponge kidney (MSK), and the very rare X-linked recessive nephrolithiasis (Dent's disease).

There is no clear definition of nephrocalcinosis other than a non-specific, generalized increase in the calcium content of the kidneys (1). It is not clear whether the definition implies an involvement of the tubular lumen and/or epithelium and/or tubular-interstitial space, alone or in different combinations, because little information is available on the microscopic appearance of kidneys affected by the various diseases causing nephrocalcinosis. These conditions are diagnosed on clinical and biochemical grounds, not on renal histopathology. Unfortunately, renal histopathological findings in patients with end-stage renal disease (ESRD) due to the above nephropathies are uninformative because the picture is severely distorted by fibrosis, atrophy and inflammation. Only occasional biopsies have been performed in the early stages of renal conditions associated with nephrocalcinosis, i.e. in Dent's disease, in which cases the calcium deposition occurred not in the nephronic lumen (with the sporadic observation of few calcified casts) or tubular epithelium, but in the renal interstitium (2, 3).

We suggest that calcium deposition in the interstitium should be the histopathological definition of nephrocalcinosis. Of course, intratubular cell crystallization, with or without intra-epithelial involvement, may occur in some conditions, but those depositions seem to belong to a different situation with a different pathogenesis, as discussed below (a true physicochemical and toxic phenomenon?).

Variable degrees of chronic interstitial nephritis with cellular infiltration, tubular atrophy, foci of calcification around and within epithelial cells, and glomerular sclerosis have been described in these renal disorders (4), but only Dent's disease and the primary hyperoxalurias are very frequently associated with ESRD. This suggests that nephrocalcinosis is not per se a condition leading to ESRD. In Dent's disease, in fact, there may be even severe medullary nephrocalcinosis, but progression to ESRD is unrelated to its severity and, in a few patients, ESRD develops even in its absence (2, 5).

While the clinical, biochemical and genetic aspects of the diseases causing nephrocalcinosis are fairly well established, little is known about the pathogenesis of nephrocalcinosis in itself. The issue has been investigated mainly in models of hyperoxaluria, but this is a very specific condition: it is a calcium-oxalate (CaOx), not an apatite nephrocalcinosis, in which both cortical and medullary

nephrocalcinosis occurs, and the toxic effect of high oxalate concentrations on the tubular epithelial cells is prominent (6-8).
Based on our proposed definition of nephrocalcinosis, we believe that Randall's plaque is a further example of nephrocalcinosis, given the recent findings in CaOx stone formers reported by the Indianapolis group (9), which confirm and expand on Randall's original observations (10) and the report from *Stoller et al.* (11) on the interstitial origin, composition and location in the papilla of the sites of apatite deposition.

Pathogenesis of nephrocalcinosis: a neglected issue

Interstitial CaOx deposition will not be discussed here for the reason mentioned above; the focus here is on apatite deposition. The principal hypothesis for explaining this deposition is purely physicochemical, i.e. spontaneous calcium phosphate crystallization in the interstitium due to its oversaturation with calcium phosphate salts. The purported triggering mechanisms behind calcium phosphate crystallization in the renal substance include an alkaline interstitial environment associated with a higher calcium concentration in renal tubular acidosis (though whether this is true nephrocalcinosis has recently been challenged by *Evan et al*. (12), since they found no interstitial concretions in the papilla, but only intratubular apatite crystal deposits in the collecting and Bellini ducts - deposits that they judged to be surgically removable stones), or a higher calcium concentration alone in primary hyperparathyroidism and other hypercalcemic-hypercalciuric conditions. As for the pathogenesis of Randall's plaque, *Bushinsky* (13) has again advanced a physicochemical hypothesis, albeit in great detail, which associates the particular situation created by the countercurrent mechanisms in the papillary environment (leading to oversaturation with calcium phosphate salts) with the effect of an extracellular matrix protein (that provides the site for these salts' heterogeneous crystallization).
A study on intraoperative biopsies of the renal papilla taken from 15 CaOx stone formers has described the histopathology of Randall's plaque in detail (8). Microscopic observation disclosed hydroxyapatite deposits located in the interstitial space and following bundles of thin loops of Henle and vasa recta up to the inner medulla. These calcifications ranged from single spheres as small as 50 nm to large clusters entirely surrounding loops of Henle or, more rarely, collecting ducts. Such presumably initial deposits seem to occur in or near the basement membrane of the limb of the loop of Henle and of the vasa recta, subsequently spreading from there through the interstitium to underneath the papillary urothelium. Very similar findings were described in 1982 by *Gusek et al*. (14) and interpreted in much the same way as in *Evan et al.* (8).
In our opinion, such a putative sequence of events involving the vasa recta basement membrane too as the initial site of apatite deposition rules out another hypothesis on the pathogenesis of nephrocalcinosis recently detailed by *Kumar et al*. (15), who suggested that crystals attach to the epithelium (in the case of Randall's plaque this has to occur at the tip of the long loop of Henle), from where they migrate to the interstitium in the papilla to the renal pelvis, eventually becoming incorporated in the plaque).
As concerns the papilla, however, there is no evidence to support such a hypothesis in the detailed histopathological analysis performed in Indianapolis (8). As a matter of fact, no crystals were found in the lumen of the loops of Henle (the only site where calcium salts, and calcium phosphate in particular, can crystallize spontaneously) (16), nor in the corresponding epithelium or papillary interstitial cells, and no plaque was seen in the papillae where crystals aggregates adhering to the epithelium in the collecting ducts (in patients with intestinal hyperoxaluria or renal tubular acidosis). The proposed hypothesis is most likely only applicable to very severe conditions of hyperoxaluria and phosphaturia (17), when spontaneous calcium crystallization departs from the proximal segment of the nephron, where a number of investigators (18-20) have shown in vitro that oxalate and crystals give rise to inflammatory, oxidative, chemotactic, and fibrogenic loops.
In the same, previously-mentioned paper, *Kumar et al*. (14) suggested that nanobacteria (also known as nanoparticles, since there is still no compelling evidence to show that they are true bacteria) may have a role in the pathogenesis of nephrocalcinosis because they look very like the tiny, 50 nm spheres observed near the basement membrane of the thin loop of Henle and the vasa recta in the papilla of stone formers (8). The existence of these elusive life forms (in stones, renal tissues and urine, at least) still awaits confirmation, however, since the structures observed and described as nanoparticles might in fact be a form of biomineralization initiated by non-living macromolecules, possibly similar to matrix vesicles (21, 22).
A third hypothesis advanced few years ago by our group (23) was that resident renal cells might be induced to trans-differentiate along an osteogenic lineage under the influence of the paraphysiological urinary and/or interstitial conditions observed in CaOx idiopathic stone formers (in the case of Randall's plaque) or in other renal disorders associated with nephrocalcinosis.

Nephrocalcinosis as a biomineralization phenomenon

Myazawa et al. (24, and personal communication) have presented data demonstrating that CaOx crystals upregulate vimentin gene transcription in normal rat kidney proximal cells. Vimentin is an embryonic marker of multipotent kidney mesenchyme and is not expressed by normal epithelial cells. It is hardly surprising, however, that tubular epithelial cells should express vimentin because they derive from the renal mesenchymal blasteme. The phenomenon of tubular epithelial cell differentiation into cells with the mesenchymal phenotype is also well known in chronic kidney disorders. A number of observations have shown that renal interstitial myofibroblasts derive from renal tubular cells which have undergone epithelial-mesenchymal transformation

(25). But greater interest, in relation to our hypothesis, lies in the recent findings by *Kumar et al.* (15), showing that inner medullary collecting duct cells grown in a calcifying media tend to form calcific nodules that are positive for typical bone proteins, osteopontin and bone sialoprotein. These observations support the notion that renal cells can acquire an osteoblast-like phenotype. According to the hypothesis generated by the Indianapolis group's observations (8), however, the inner medullary collecting duct epithelium should not be involved in the pathogenesis of Randall's plaque; it would be much more relevant if the same were to occur in epithelial cells of the thin loop of Henle (but unfortunately there is no cell culture available for them). It also remains to be seen whether certain "*stone risk*"-related conditions or "*extreme*" physiological conditions that might occur in the papilla or the loop of Henle can trigger such a trans-differentiation along the osteoblastic lineage.

The phenomenon of trans-differentiation is not limited to the kidney or to the epithelial cell, since there are numerous well-known examples of trans-differentiation in other cells and tissues too. For instance, it may occur in a special kind of pericyte, the liver Ito cell (26), and in a subpopulation of smooth muscle cells in the intima of arteries, which may coincide with pericytes. Smooth muscle cells have the ability to undergo osteoblastic trans-differentiation and mineralization (27), and this seems to be responsible for vascular ectopic calcifications. Vascular calcification was long thought to result from passive degeneration, but in fact involves a complex, strictly regulated process of biomineralization resembling osteogenesis (28). There is evidence to indicate that proteins controlling bone mineralization are also involved in regulating vascular calcification. Cultured artery smooth muscle cells are also induced to become osteogenic by inflammatory stimuli, reactive oxygen species and hypoxia (29).

A similar phenomenon may occur in the renal papilla. CaOx crystals and/or oxalate at paraphysiologically high concentrations or, more likely, a high pre-urine CaOx supersaturation in conjunction with an unfavorably low oxygen tension may trigger inflammation in the long loop of Henle cells on a level with the bend. This would then induce the trans-differentiation of these cells towards the osteogenic lineage, determining the synthesis of typical bone osteoid proteins (osteopontin, osteocalcin, BMP-2, etc.) and a true biological hydroxyapatite mineralization of the Henle's loop basement membrane (beneath the differentiating cells). While both hydroxyapatite and brushite have been recognized in stones, depending on the clinical phenotype (30), the existence of brushite in calcified tissue has been ruled out (31). Hence, the reports from *Evan et al.* (8) and *Khan et al.* (32) that Randall's plaque and the preceding crystalline structures in the basement membrane and papillary interstitium are composed of bone-like hydroxyapatite crystals support the hypothesis that they are the consequence of an active process of biomineralization, and therefore that the Henle's cells may be capable of differentiation.

Concerning the active process of biomineralization, it is worth noting that osteopontin has been found localized in the Golgi apparatus of descending thin loop of Henle cells in the normal rat kidney (33). Osteopontin was detected in the lamellae and striations of the organic matrix in human calcium oxalate monohydrate stones (34); this observation and in vitro findings have prompted the suggestion that it is a powerful inhibitor of CaOx crystallization (35), which may well be the case. We speculate, however, that it might also reflect the biomineralization process occurring at Henle's tip/papillary level: this hypothesis is supported by the colocalization of osteopontin with the apatite concretions observed by the Indianapolis group (36).

An alternative possibility is that the interstitial medullary pericytes, rather than the Henle loop cells, differentiate along the bone lineage when exposed to "stone risk-related or "*extreme*" physiological conditions in the papilla or the Henle's loop tubular lumen. Pericytes are perivascular cells closely associated with precapillary arteries, capillaries and postcapillary venules; they have many features in common with myofibroblasts and it is not always possible to distinguish between these cells. Very like the smooth muscle cells in larger vessels, pericytes play a part in regulating blood flow in the microcirculation and this has been considered their prevalent role in the kidney (37). Cross-talk between the Henle loop epithelium and the pericytes enables vasa recta resistance and medullary circulation to be adapted to the metabolic needs of the nephron. In a recent study on a model, NO generation by Henle's loop cells should be capable of modulating pericyte activity (38). Pericytes also regulate vessel permeability and provide mechanical support and stability for the vessel wall through their interaction with endothelial cells and the synthesis of basement membrane proteins (39).

Pericytes have also been shown, however, to have the potential for differentiation into many different cell types, including osteoblasts, chondrocytes, adipocytes, smooth muscle cells and fibroblasts, suggesting that they serve as a source of adult progenitor cells in situations of repair, inflammation and disease (38). That pericytes have the potential to calcify was demonstrated in cultures of retinal capillary pericytes, where they form three-dimensional nodule-like structures that become mineralized (40). These mineralized nodules produced by pericytes in culture are considered to be the in vitro equivalent of the process of bone formation (41). They contain type I collagen, osteopontin, matrix Gla protein and osteocalcin, strongly resembling the matrix found in bone, and the mineralized component is apatite, as in bone (38). These findings thus suggest that pericytes may have a role in mediating ectopic calcification.

As for the calcifying vascular cell of the arterial wall (42), and for mesenchymal precursor cells in a site of osteoinduction (43), a putative subsequent step of these cells condensing – a stage preceding biomineralization, which is always associated with an epithelium and epithelial basement membrane *in vivo* – may explain why hydroxyapatite mineralization occurs in the Henle loop basement membrane.

Finally, a third cell type might hypothetically form Randall's plaque. Due to its particular conditions of low oxygen tension, the papilla is a niche for stem cells (44), which have

been shown to differentiate into myofibroblasts and cells expressing neuronal markers, and to spontaneously form cellular spheres. These renal stem cells are able to migrate to other parts of the kidney, and to the medullary tubular epithelia in particular (43, 45). Since stem cells recovered from other tissues are capable of differentiating along the bone lineage, a third potentially mineralizing cell population in the kidney is that of the papillary stem cells.

Why is nephrocalcinosis so frequent at papillary level?

A very low oxygen tension exists at papillary level, so the papilla is particularly susceptible to ischemia and ischemic lesions of the papilla in diabetic and analgesic-related nephropathies are well known. A 47% incidence of nephrocalcinosis has been recorded in the latter disease (46) and the calcified papillae have even been known to become ossified in this condition (47).
Thus, in the subischemic microenvironment of the medulla/papilla, where there may be a high concentration of reactive oxygen species, the Henle's loop cells, or the pericytes, or the stem cells might be very sensitive even to mild toxic insult, or to high calcium, oxalate or phosphate concentrations. Cell differentiation could occur as a consequence, leading to nephrocalcinosis or Randall's plaque formation.

Conclusions

We have presented data supporting the theory that nephrocalcinosis is not a passive biomineralization phenomenon, but an active, biological one, though to prove this theory it is necessary to verify whether osteogenic cells really exist in the papillary biopsies containing Randall's plaque, and whether the machinery for bone matrix synthesis is operating. We need to investigate whether tubular epithelial cells and papillary cells (Henle's loop cells, pericytes or stem cells) can indeed differentiate in vitro into an osteogenic lineage, especially at very low oxygen tensions, under paraphysiological oxalate, calcium and phosphate concentrations. Attempts to culture renal papillary specimens might also prove extremely interesting for investigating the phenomenon in detail. Finally, we need to investigate these same issues in other forms of medullary nephrocalcinosis, e.g. in Dent's disease, to develop a general theory of nephrocalcinosis. Confirmation of our hypothesis might possibly point to new therapeutic approaches for this neglected renal disorder.

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ORIGINAL PAPER

Risk factors for renal calcium stone formation in South African and European young adults.

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Summary

Objectives: The different susceptibility to renal stone disease of white and black people has been previously explained in terms of intrinsic (genetics) and extrinsic (diet, lifestyle) factors. However, in South Africa, the absence of stone disease in the black population has not yet been fully explained by either of these. The aim of the present study was to identify potential differences between black and white subjects in South Africa and white subjects in Europe with respect to their relative dietary and urinary risk factors for renal stone formation.

Materials and Methods: A total of 72 healthy subjects (45 males and 27 females, age range 21-30 years) with no previous history of renal stone disease or specific diseases predisposing to renal stone formation were recruited in South Africa (SA) and in Italy (IT). They were divided in three groups: South African blacks (SA-B), South African whites (SA-W) and Italian whites (IT-W). Each participant provided a 24-hour dietary record and 24-hour urine sample taken over the same period. Nutrients and calories were calculated by means of food composition tables using a computerised procedure. Urinary concentrations of potassium, sodium, calcium, phosphate, oxalate, urate, citrate, magnesium, and creatinine, together with the pH and urinary volumes, were measured.

Results: The mean carbohydrate intake was significantly higher in SA-B (293+90 g/day) than in both SA-W (194+74, p = 0.002) and IT-W (212+/-81; p = 0.000). Daily magnesium intake was higher in SA-B (290+124 mg/day) than in IT-W (176+73 mg/day, p = 0.002).

The mean daily urinary excretion of calcium was significantly (p = 0.029) lower in SA-B (3.07+/-1.68 mmol/day) with respect to SA-W (4.65+/-2.44 mmol/day) and IT-W (4.51+/-1.89 mmol/day) whereas mean daily urinary excretion of citrate was significantly (P = 0.012) higher in SA-B (3.36+/-1.4 mmol/day) than in SA-W (3.09+/-1.45 mmol/day) and IT-W (2.36+/-0.98 mmol/day).

Conclusion: Although the carbohydrate intake and the percent of energy from carbohydrate of black subjects in this study were higher with respect to white controls, we were not able to show any other relevant difference of the known dietary stone risk patterns between black and white subjects.

On the other hand the urinary patterns of black controls seem to be more favourable in term of risk for stone formation than those of white controls showing a lower calcium excretion and a higher citrate excretion in the urine. Our result of higher carbohydrate intake in black subjects is counter-intuitive as it suggests a higher risk of stone formation in this group. This puzzling result may have arisen because our subjects were recruited from the urban population rather than from rural areas, suggesting that western diets and lifestyles may ultimately change the stone incidence profile in the black population.

KEY WORDS: *Urinary calculi; Epidemiology; Diet; Race.*

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Introduction

In South Africa, urinary stone disease in the black population has been described as a rare event with an hospitalisation annual rate of 0.03% or lower (1, 2).

A probable explanation was identified in the type of diet, which could involve a low excretion of phosphates and calcium. More particularly, it has been observed that the diet in the black population has a high phytic-acid content (unleavened bread, coarse cereals, maize, sorghum, beans, pumpkin) and a low protein content (little meat) (3, 4).

In the sub-Saharan Africa, vesical lithiasis in infancy is less common than in Asia, in spite of widespread poverty, probably because it is common practice to prolong breast-feeding.

Since the beginning of the 20th century in Europe and North America, as affluence has spread to all social classes, calcium renal stone disease has progressively increased involving high prevalence rates (5-15%) in all the countries of these geographical areas (5).

On the other hand renal stones have also been reported as a common finding in the South African white population who seem to be stone-prone with prevalence rates comparable to those observed in Westerncountries.

The different susceptibility to renal stone disease has been explained in terms of intrinsic factors (genetic background), but also in terms of extrinsic factors. Although South African blacks and whites share some of the potential extrinsic factors (eg climate), diet and genetic factors could differ between the groups.

The aim of this study was to identify any differences between black and white subjects in South Africa and Europe in the dietary and urinary risk factors for renal stone formation which might provide insights into explaining the rarity of stones in black South Africans.

Materials and methods

A total of 72 healthy subjects (45 male and 27 female, age range 21-30 years) with no previous history of renal stone disease or specific diseases predisposing to renal stone formation were recruited in South Africa (SA) and in Italy (IT).

They were divided in three groups: South African blacks (SA-B) (10 males and 7 females), South African whites (SA-W) (16 males and 2 females) and Italian whites (IT-W) (19 males and 18 females).

The subjects were investigated while they followed their normal activities and ate their usual diet.

Each participant was investigated with respect to a 24-hour dietary record and 24-hour urine sample taken over the same period.

Nutrients and calories were calculated by means of food composition tables using a computerised procedure (Terapia Alimentare Windows Release 5.00.00 - Dietosystem).

Daily potential renal acid load (PRAL) was calculated according to *Remer* and *Manz* (6) by considering the mineral and protein composition of foods, the mean intestinal absorption rate for each nutrient and the metabolism of sulfur-containing amino acids.

Urinary concentrations of potassium, sodium, calcium, phosphate, oxalate, urate, citrate, magnesium, and creatinine, together with the pH and urinary volumes, were measured.

Sodium and potassium concentrations were measured by atomic absorption (SA) or flame photometry (IT), calcium by atomic absorption (SA) or a Corning 940 calcimeter (IT), magnesium by atomic absorption (SA-IT), urinary pH by pHmeter. Phosphate, urate and creatinine were measured by conventional colorimetric methods.

Table 1.

Daily intake of nutrients and potential renal acid load (PRAL) in different groups of healthy controls.

	SA Whites	SA Blacks	European	Sig	Post hoc Bonferroni
PRAL	3.56+/-29.6	17.4+/-16.9	16.43+/-19.11	0.090	
Energy (Kcal)	1540+/-467	1928+/-527	1562+/-546	0.049	
Protein (g)	78+/-33	87+/-23	78+/-24	0.489	
Vegetable protein (g)	22+/-6	29+/-11	21+/-9	0.017	2 *vs* 3 P = 0.019
Animal protein (g)	53+/-33	55+/-18	52+19	0.911	
Carbohydrate (g)	194+/-74	293+/-90	212+/-81	0.001	1 *vs* 2 P = 0.002 2 *vs* 3 P = 0.005
Fat (g)	54+/-23	53+/-17	49+/-26	0.767	
Calcium (mg)	685+/-253	619+/-330	570+/-357	0.476	
Sodium (mg)	895+/-539	1126+/-740	2171+/-3013	0.093	
Potassium (mg)	3049+/-1374	2827+/-841	2369+/-1003	0.077	
Magnesium (mg)	203+/-76	290+/-124	176+/-73	0.003	2 *vs* 3 P = 0.002

Table 2.

Daily excretion of urinary risk factors in different groups of healthy controls.

	SA Whites	SA Blacks	European	Sig	Post hoc Bonferroni
PH	6.09+/-0.30	6.20+/-0.37	6.01+/-0.37	0.17	
Potassium (mmol)	55+/-38	50+/-28	51+/-18	0.86	
Sodium (mmol)	216+/-189	237+/-130	181+/-69	0.27	
Calcium (mmol)	4.65+/-2.44	3.07+/-1.68	4.51+/-1.89	0.029	2 *vs* 3 P = 0.045
Magnesium (mmol)	3.41+/-1.29	3.47+/-1.52	3.44+/-2.16	0.99	
Urate (mmol)	3.72+/-1.12	3.35+/-1.04	3.30+/-1.35	0.49	
Oxalate (mmol)	0.29+/-0.05	0.28+/-0.06	0.28+/-0.07	0.90	
Citrate (mmol)	3.09+/-1.45	3.36+/-1.40	2.36+/-0.98	0.012	2 *vs* 3 P = 0.018

Oxalate (oxalate oxidase) and citrate (citrate lyase) were measured enzimatically.
Mean values were calculated and compared by one-way ANOVA with the Statistical Package for the Social Sciences (SPSS).
Difference between groups were evaluated by post-hoc Bonferroni analysis.

Results

The mean (+ SD) daily intakes of nutrients and the mean values of urinary risk factors for stone formation in the three groups are shown in Tables 1 and 2 respectively.
The mean carbohydrate intake was significantly higher in SA-B (293+90 g/day) than in both SA-W (194+74, p = 0.002) and IT-W (212+/-81; p = 0.000). Daily magnesium intake was higher in SA-B (290+124 mg/day) than in IT-W (176+73 mg/day, p = 0.002).
No significant difference in the mean PRAL value and in mean intakes of energy, protein, fat, calcium, sodium and potassium was observed in the three groups.
No significant difference in the mean daily urinary excretion of sodium, potassium, magnesium, urate and oxalate in the three groups.
The mean daily urinary excretion of calcium was significantly (p = 0.029) lower in SA-B (3.07+/-1.68 mmol/day) with respect to SA-W (4.65+/-2.44 mmol/day) and IT-W (4.51+/-1.89 mmol/day) whereas mean daily urinary excretion of citrate was significantly (p = 0.012) higher in SA-B (3.36+/-1.4 mmol/day) than in SA-W (3.09+/-1.45 mmol/day) and IT-W (2.36+/-0.98 mmol/day).

Discussion

Although the carbohydrate intake and the percent of energy from carbohydrate of black subjects in this study were higher with respect to white controls, we were not able to show any other relevant difference of the known dietary stone risk patterns between black and white subjects.
On the other hand the urinary patterns of black controls seem to be more favourable in term of risk for stone formation than those of white controls showing a lower calcium excretion and a higher citrate excretion.
It should be pointed out that we studied a group of urbanised students who are not representative of subjects from rural or peri-urban settlements constituting the majority of the black population in South Africa.
In fact, it has been shown that black subjects from informal and formal peri-urban settlements show energy intakes below the recommended dietary allowance (RDA) for both men and women with inadequate micronutrient and dietary fiber intake (7, 8).
However more recent data (9) have shown that shifts in dietary intake towards the Western diet are occurring among urban blacks, but that these shifts are less apparent among rural African dwellers.
Urban subjects consumed less maize porridge but more fruits, vegetables, animal-derived foods and fats and oils than rural subjects. As a consequence % energy from fats and protein increased among urban blacks while % energy from carbohydrate decreased. A recent population-based survey confirmed that the urbanisation of blacks influences the nutrition and health transition in South Africa culminating in a subsequent emergence of risk factors for diseases previously uncommon among blacks such as coronary heart disease (CHD), hypertension and diabetes. Indeed, in the predominantly black community of Soweto, 78% of subjects were found to have at least one major risk factor for heart disease, with the most prevalent (55%) risk factor in women being obesity associated with physical inactivity (11, 12).
In our opinion the shift in the dietary pattern of the black population towards the Western diet could also involve a concomitant increase in the risk of renal stone formation. In fact in the United States where nephrolithiasis disproportionately affects the white and black populations, an increase in the incidence of stone disease in the black populations has been recently observed (13) in conjunction with an increase in the energy intake and the amount of food consumed in all race and gender groups (14). The risk of stone formation is aggravated by lower intakes of vegetables, potassium, and calcium.
On the other hand in renal stone patients, all racial groups have demonstrated a similarity in the incidence of underlying metabolic abnormalities suggesting that dietary and environmental factors may be as important as ethnicity in

the etiology of stone disease (15). In particular hypocitraturia, hyperuricosuria, hyperoxaluria, gouty diathesis and high sulphate levels were equally represented among all ethnic groups. Also, in the KwaZulu Natal province of South Africa, only a few variations in the metabolic risk factors between Indians and Whites renal stone formers were observed (16).

In conclusion, our results suggest that if dietary profiles of recently urbanised blacks are not improved with respect to reducing stone formation risk factors a "*stone wave*" similar to that experienced by western countries in the 20th century could be experienced by the black population (17).

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ORIGINAL PAPER

Management of urolithiasis in renal transplantation.

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Summary

Objective: To report our experience with extracorporeal shock wave treatment for upper urinary tract stones in transplanted kidneys.
Patients and Methods: A total of eight patients underwent extracorporeal shock wave lithotripsy (SWL) in prone position under analgosedation with the Dornier MPL 9000 lithotripter or the Storz Modulith SLX lithotripter employing ultrasound targeting. The stones had overall diameter ranging 7-12 mm and were located in the renal calices in 5 cases and in the ureter in 3 cases. Five stones were radiopaque and 3 radiolucent.
Results: Stone fragmentation was obtained in 87% of the patients and 75% became stone free within 90 days. Serum creatinine values and creatinine clearances remained stable within 30 days post-operatively in all the treated patients.
Conclusions: SWL in transplanted kidney is feasible and simple to perform when the patient is treated in prone position with ultrasound targeting and without any complication or deterioration of renal function. Results similar to those achievable in native kidneys can be obtained also in graft kidneys with limited endourological antero-retrograde ancillary manouvres.

KEY WORDS: Urinary calculi; Renal transplantation; Extracorporeal shock wave lithotripsy; Treatment.

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INTRODUCTION

The formation of urinary tract stones following renal transplantation is a rare complication, but it could be associated to a high morbidity.
The prompt diagnosis and removal of stones can prevent adverse effects on renal graft outcome although the treatment of these patients could be complicated by immunosuppressive therapy and border-line renal function.
Advancements in endourology and interventional radiology influenced the management of renal transplant complications that can be actually treated efficiently and effectively with these minimally invasive modalities minimizing the potential risk to the recipient and for the renal allograft.
The aim of this study was to determine the feasibility, safety and efficacy of SWL for stones in renal allograft and to review etiologic, diagnostic, and management aspects of stone disease in renal transplant recipients and donors.

PATIENTS AND METHODS

In a 5-year period we observed 12 patients with renal or ureteral graft stone referred from the Kidney Transplant Unit of the IRCCS Ospedale Maggiore of Milan.
Out of them eight patients underwent extracorporeal shock wave lithotripsy (SWL) in prone position under analgosedation with the Dornier MPL 9000 lithotripter or the Storz Modulith SLX lithotripter employing ultrasound targeting (Table 1-2).
The stones had overall diameter ranging 7-12 mm and were located in the renal calices in 5 cases and in the ureter in 3 cases. Five stones were radiopaque and 3 radiolucent.
Ureteral stones were treated with in situ ESWL but patient n. 7 who underwent echoguided nephrostomy with ante-ro-retrograde ureteral catheterization and stone push-up before SWL treatment. Antibiotic prophylaxis was administered to all patients. Patients were followed up with renal ultrasound on the first day after treatment and thereafter at 1 month, 3 month and 12 month visit.
Renal function was monitored with serum creatinine and creatinine clearance serial evaluation.

RESULTS

Stone fragmentation was obtained in all the patients but patient n. 8 who underwent surgical ureterolithotomy and re-do ureterocystoneostomy.

Table 1.
Characteristic of transplanted patients with stone treated by extracorporeal shock wave lithotripsy.

Pt n.	Sex	Age to stone presentation after Tx (years)	Time	Clinics	UTI alterations	Matabolic abornomalities	Anatomic
1	F	65	15	Pain fever	No	No	No
2	F	32	8	Pain fever hematuria	Yes	Hypercalcemia	No
3	M	42	5	Pain	No	HPT – hypercalcemia	No
4	F	22	14	Pain	No	Hyperuricemia	No
5	F	66	3 (renal ultrasound)	Hydronephrosis	No	No	No
6	F	22	7	Renal ultrasound	No	Hyperuricemia	No
7	F	49	9	Pain fever anuria	Yes	No	No
8	F	51	3	Renal ultrasound	No	No	Yes

Table 2.
Characteristic of stones and modalities of shock wave treatment.

Pt n.	Stone location	Stone size (mm)	Shock Wave n.	Kv	Treatment n.	Lithotripter
1	Lower calix	8	2600	19	2	*Dornier MPL 9000*
2	Upper/middle c.	12	3100	16	3	*Dornier MPL 9000*
3	Upper calix	11	1500	17	1	*Dornier MPL 9000*
4	Upper calix	10	1560	16	2	*Dornier MPL 9000*
5	UPJ	12	800	15	1	*Dornier MPL 9000*
6	Lower calix	7	1100	16	1	*Dornier MPL 9000*
7	Pyelic (push up)	10	5000	15	3	*Storz Modulith SLX*
8	Distal ureter	7	2500	17	1	*Storz Modulith SLX*

Table 3.
Serum creatinine values and creatinine clearances before and after shock wave treatment.

Pt n.	Serum creatinine range (mg/dl)			Creatinine clearance range (ml/min)		
	Pre-operative	Post-operative 30 days	Post-operative 360 days	Pre-operative	Post-operative 30 days	Post-operative 360 days
1	1.2-1.7	1.6-1.8	1.5-1.6	53-38	38-35	42-38
2	1.3-1.7	1.5-1.7	1.5-2.0	39-30	34-30	33-24
3	1.6-1.8	1.7	1.7-1.9	53-48	50	50-44
4	1.8-3.0	3.2-3.3	3.2-6.7	25-15	14-13	14-6
5	0.9-1.3	-	0.9	50-35	-	50
6	1.9-2.4	2.0-2.5	2.3-2.5	43-34	40-32	36-33
7	1.9-2.3	1.5-2.2	1.3-1.6	38-31	46-31	52-43
8	1.3-1.4	1.4-1.5	1.0-1.1	60-55	55-52	70-56

Creatinine Clearance calculation according to Cockcroft = (140-age) x weight (Kg)/ Serum creatinine (mg/dl) x 72
In females the calculated value is 15% lower

All the patients became stone free within 90 days but patient n. 2 who died 16 months after the stone treatment because of respiratory distress.
Serum creatinine values and creatinine clearances remained stable within 30 days post-operatively in all the treated patients. At 12 month follow up patient n. 4 who presented preoperatively with chronic rejection developed a progressive renal failure requiring haemodyalisis and a

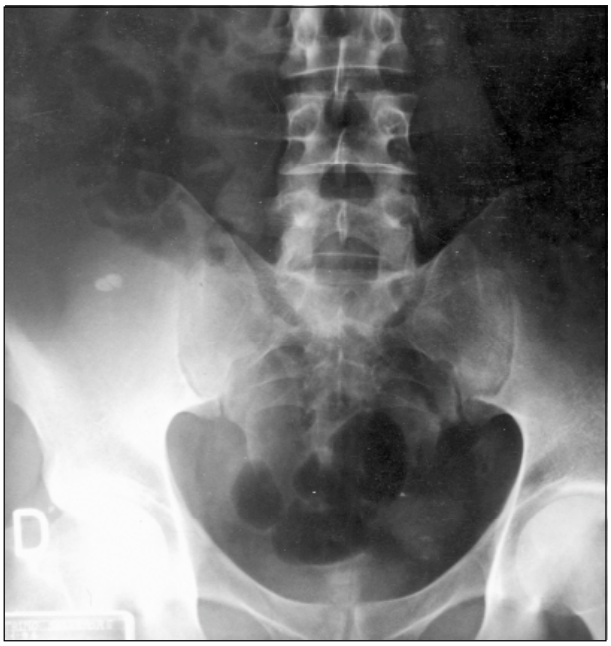

Figure 1.

Patient n. 3: pre-operative plain Rx.

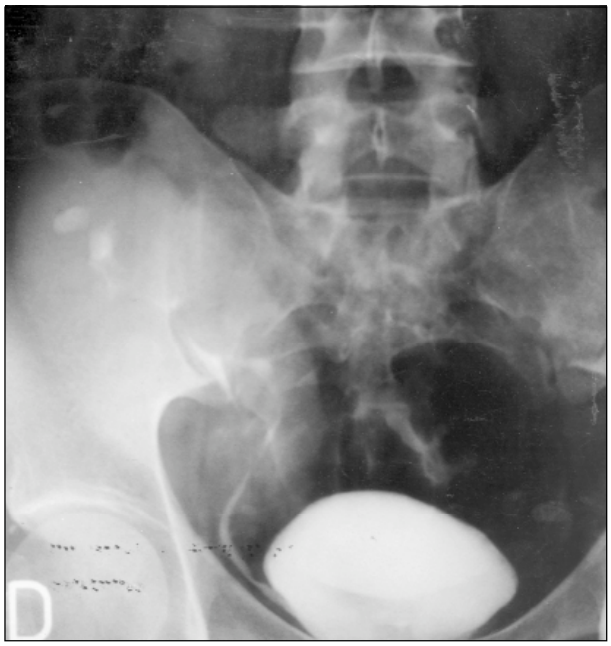

Figure 2.

Patient n. 3: pre-operative intavenous pyelography (IVP).

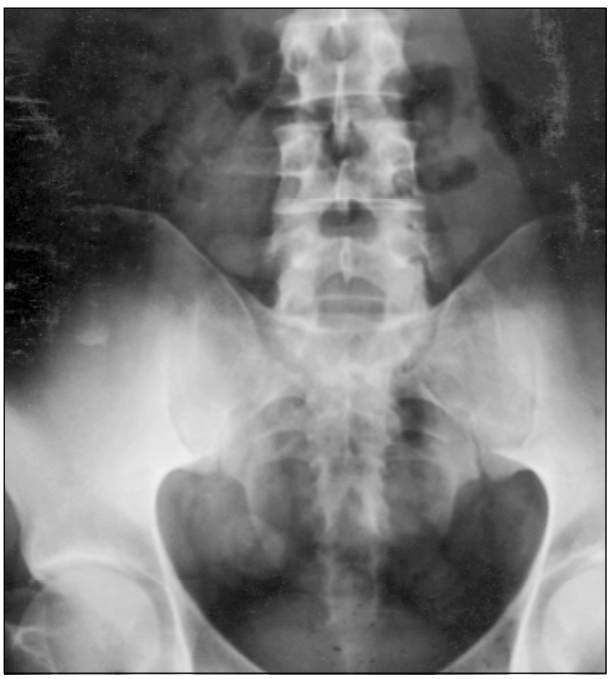

Figure 3.

Patient n. 3: post-operative plain Rx demonstrating complete stone fragmentation.

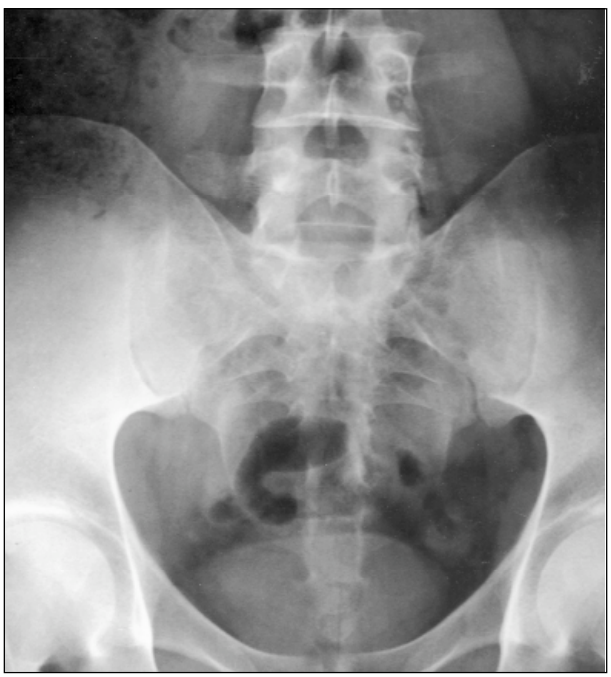

Figure 4.

Patient n. 3: post-operative plain Rx demonstrating stone-free status.

successive new kidney transplantation. In the remaining seven patients no significant variation of serum creatinine values and creatinine clearances was observed.

Discussion

Prevalence and incidence

Urinarystone formation following kidney transplantation is reported as a rare complication with a prevalence ranging from 0.8 to 1.8% (1-7).

In 1997 the annual United States incidence rate of hospitalisation for urinary stones in renal transplant recipients has been computed as 0.104% (*National Hospital Discharge Survey*) (8).

In pediatric patients urolithiasis seem to be more frequent with about 2.7-5% of pediatric transplants developing stones (9, 10).

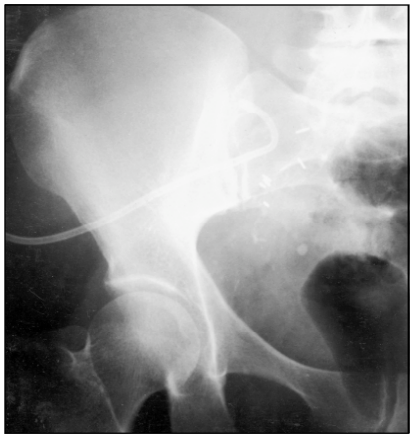

Figure 5.

Patient n. 7: pre-operative plain Rx with nephrostomy.

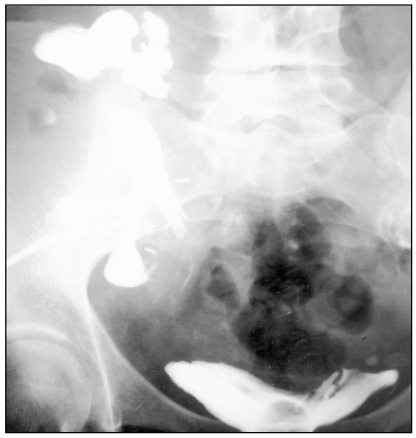

Figure 6.

Patient n. 7: pre-operative trans-nephrostomic pyelography.

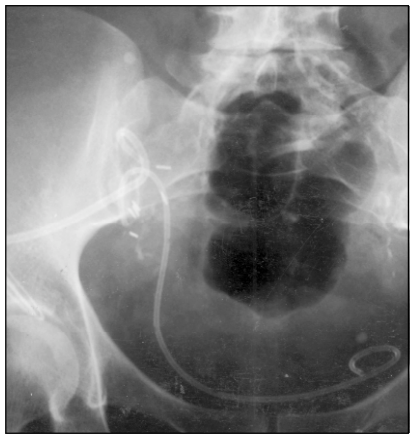

Figure 7.

Patient n. 7: pre-operative plain Rx after push-up and double J ureteral stenting.

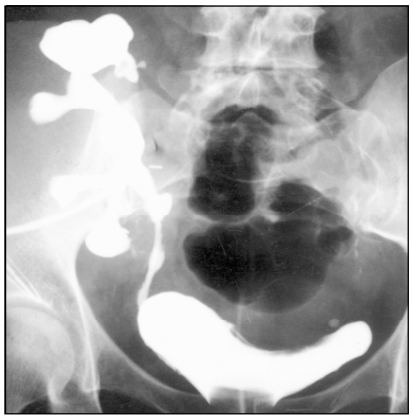

Figure 8.

Patient n. 7: pre-operative trans-nephrostomic pyelography after push-up.

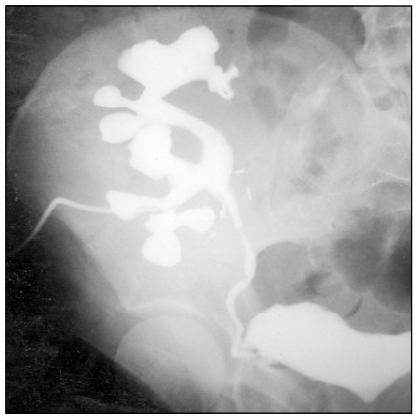

Figure 9.

Patient n. 7: post-operative trans-nephrostomic pyelography.

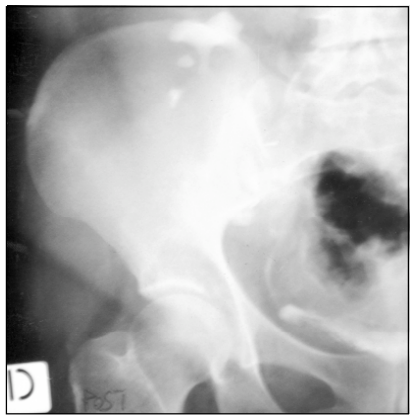

Figure 10.

Patient n. 7: 3-month post-operative IVP.

Diagnosis

The clinical features of stones after transplantation differ from those observed in non-transplant patients.

Renal colic or pain is usually absent and rarely resembles acute rejection. Presenting features of urinary calculi are urinary tract infection (UTI), gross or microscopic haematuria, dysuria without infection. Stones can remain silent in about 20% of cases (10). Anuria can be the only clinical sign at presentation (11).

To detect stones and determine their location and size, ultrasonography appears to be the most useful diagnostic tool that should be used routinely for early detection of problems in the post transplantation period.

Stone composition

The composition of stones after renal transplantation is similar to those of patients with native kidneys.

Calcium oxalate (mono- and di-hydrate) and calcium pho-sphate were found in the majority of stones (3), but infected stones consisting of struvite or mixed form of struvite and calcium phosphate are also relatively common (2, 10).

Etiology

Urinary calculi observed after renal transplantation can be due to de novo stone formation after transplantation or be transferred in the donor graft.

De novo stone formation is related to several causes such us: metabolic factors, drugs, urinary infection or stasis, foreign bodies (retention of suture material, incrusted double J stent).

Metabolic causes

Metabolic alterations have been described in 60-75% of cases (3, 4).

Tertiary hyperparathyroidism, hypercalciuria and hypocitraturia are the most common risk factors, but often there are multiple factors which predispose to stone formation (2, 10).

Calcineurin inhibitor treatment after kidney transplantation in children can lead to significant hypocitraturia, especially in patients receiving the highest dose of medication whereas hyperoxaluria can be primarily the result of a removal of significant body oxalate stores, deposited during dialysis (12).

Table 4.
Serum creatinine values and creatinine clearances before and after shock wave treatment.

Author	Institution	Renal transplants (n.)	Stones (n.)	
Prevalence in adult age				
Montanari et al. 1996 (1)	IRCCS Ospedale Maggiore, Milano	1200	12 (1%)	
*Kim et a*l. 2001 (1980-1997) (2)	Rogosin Institute/ The Weill-Cornell Medical Center, New York, USA	849 functioning renal grafts for 3 or more months	15 (1.8%)	M > F (2:1) 3rd-4th decade 8 from living donors 7 from cadaveric donors. 3-109 months after transplantation (mean 17.8 months). 5 recurrent. bladder = 11, kidney = 3, multiple = 1. Size 3.4-40 mm (mean 12 mm).
To rrecilla Ortiz C et al. 2001 (1980-2000) (3)	Servicio de Urologia, Ciudad Sanitaria y Universitaria de Bellvitge, Hospitalet de Llobregat, Barcelona, Spain	1198	22 (1.8%)	Kidney graft = 15, ureter = 3, bladder = 4 7 from cadaveric donors.
Challacombe et al. 2005 (1977-2003) (4)	Department of Urology, Guy's and St Thomas' Hospitals, London, UK.	2085	21 (1.01%)	17 adults, 4 children.
Klingler 2002 (5)	Department of Urology, University of Vienna, Vienna, Austria.			28 months (range 13 to 48).
Millain Rodriguez et al. 2003 (6)	Servicio de Urologia Fundacion Puigvert, Cartagena, Barcelona, Spain	850	15 (1.76%)	
Streeter 2002 (7)	Department of Urology and Oxford Transplant Centre, Churchill Hospital, Oxford, UK	1535	13 (0.8%)	Ureter = 9, Bladder = 3.
Annual hospitalisation rate				
Abbott et al. 2003 1997 (8)	United States Renal Data System		0.104% per year	F > M (2.84:1) kidney > ureter
Prevalence in pediatric age				
Nuininga et al. 2001 (1977-1999) (9)	Department of Urology, University Medical Center St Radboud, Nijmegen The Netherlands	146 (183 renal allografts)	5 (2.7%)	
Khositseth et al. 2004 (1983-2003) (10)	Department of Pediatrics, University of Minnesota Medical School, Minneapolis, Minnesota, USA.	399	20 (5%)	Time to stone presentation was 19 ± 22 months post-KTx

Stones transferred in the donor graft

Stones are frequently transplanted with allografts; *Klinger et al.* reported that about 50% of stones observed in allograft kidneys were actually transplanted (5).

Possible pre-existent lithiasis in a donor kidney should not be overlooked; therefore, preoperative imaging of the donor or intraoperative screening by ultrasonography are mandatory.

In the living related donors stones can be initially treated by ESWL. On the other hand detection of renal calculi in cadaveric renal donors is not a reason to refuse the graft for further transplantation.

In 75% of cases stones detected before transplantation can be successfully removed by an endoscopic procedure (5). Pyelotomy at the back table during the transplantation could be an alternative option (14). On the contrary

observation is the best treatment for caliceal stones smaller than 5 mm (3).

Treatment

Management of allograft stones is mainly based on anecdotal experience, rather than on the analysis of larger series. Possible treatment options are extracorporeal shock wave lithotripsy (SWL), flexible ureteroscopy and in situ lithotripsy, percutaneous nephrolithotomy (PCNL), open pyelolithotomy and open cystolitholapaxy. SWL is the treatment of choice for caliceal stones sized 5 to 15 mm whereas for stones greater than 15 mm or for ureteral stones, antegrade endoscopic procedures seem to be more favorable (5). Small stones (4 mm or less) may be closely followed up, because they can pass spontaneously.

Spontaneous passage

Spontaneous passage was descibed in 15-30% (2, 5).

SWL

SWL is the recommended treatment for medium-sized calculi in transplant kidneys.

In large series about 30-70% of patients were treated by extracorporeal lithotripsy with a reported success rate ranging 87-100% and no complications (3-5). Successful result of SWL were not related to size and location of the stone, but success rate was higher in solitary stones with respect to multiple stones (6). The best result was found for solitary stones located at the ureteral anastomosis. Multiple sessions are often required in order to obtain a stone-free condition. Double J stent insertion before ESWL might be needed in stones larger than 10 mm or to relieve obstruction. Largest stones more often require the placement of a nephrostomy tube (6) and a transient nephrostomy was needed in about 40% of the patients treated with ESWL (5).

PCNL

In the Abbott series (8) percutaneous procedures were more common than ureteroscopy or extracorporeal shock wave lithotripsy whereas according to *Klinger et al.* about 20% of stone in renal allograft could be removed percutaneously with complete clearance and without renal impairment (5).

Successful percutaneous nephrolithotomy (PCNL) for staghorn stones and percutaneous anterograde treatment of ureteral obstructive stones in renal allografts were also reported (15, 16).

Finally percutaneous nephrolithotomy remains the "gold standard" procedure even in cases of external urinary diversion. A percutaneous nephrolithotomy was reported for surgical treatment of a coralliform lithiasis that occurred in a renal allograft in association with a Bricker ureterointestinal anastomosis for urinary diversion (17).

m-PCNL

Recently the results of minimally percutaneus nephrolithotomy (mPCNL) in patients with upper urinary tract stones in transplanted kidneys have been reported (18). A 16 F peel-away sheath and a 8.5/11.5 F nephroscope or a 8/9.8 F ureteroscope were used for the procedure with a mean operative time less of an hour and a mean haemoglobin decrease less than 1 g/dL. All patients were rendered stone-free after a single procedure, with no complications during or after surgery and stable renal allograft function in all patients and no recurrence of stone at a mean follow-up of 23 months. It has been concluded that mPCNL is safe and effective for managing calculi in transplanted kidneys, and it can be the initial therapy for most cases of upper urinary tract stones in transplanted kidneys, except for simple and small stones in the middle or lower calyx.

URS

Ureteroscopy has been demonstrated as a safe and effective method for the management of ureteral stones after renal transplantation (19).

After failure of extracorporeal shock-wave lithotripsy ureteroscopies were performed with a 67% success rate using a semi-rigid 9.8 F ureteroscope after insertion of a guide-wire into the allograft ureteral orifice.

Recurrence

After stone removal stones recurred in 0-20% of the transplant patients (3, 5).

No changes in graft function at diagnosis and after removal of stones were observed in the majority of cases.

Conclusions

The incidence of urolithiasis in renal transplant patients is low. There is a high incidence of metabolic causes and therefore renal transplant patients with urolithiasis should undergo comprehensive metabolic screening.

Management of these patients requires a multidisciplinary approach by renal physicians, transplant surgeons and urologists (20, 21).

In our experience SWL in transplanted kidney is feasible and simple to perform when the patient is treated in prone position with ultrasound targeting and without any complication or deterioration of renal function. Results similar to those achievable in native kidneys can be obtained also in graft kidneys with limited endourological antero-retrograde ancillary manouvres.

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ORIGINAL PAPER

Urinary citrate and renal stone disease: The preventive role of alkali citrate treatment.

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Summary

Hypocitraturia or low urinary citrate excretion is a common feature in patients with nephrolithiasis, particularly in those with calcium stone disease. Citrate is a weak acid that is synthesized inside Krebs' cycle. It can also enter the body through dietary intake. Differences in intestinal handling, serum concentration as well as filtered load of citrate were not found between kidney stone formers and normal subjects. On the contrary, several metabolic abnormalities, such as metabolic acidosis, hypokalemia and starving, seem to influence the renal handling of citrate by inducing a decrease in the urinary citrate excretion. Hypocitraturia is defined as urinary citrate excretion lower than 320 mg/day. Literature data show a large prevalence of hypocitraturia in patients with nephrolithiasis, ranging from 8% up to 68.3%. The protective role of citrate is linked to several mechanisms; in fact citrate reduces urinary supersaturation of calcium salts by forming soluble complexes with calcium ions and by inhibiting crystal growth and aggregation. Furthermore, citrate increases the activity of some macromolecules in the urine (eg. Tamm-Horsfall protein) that inhibit calcium oxalate aggregation. Citrate seems able to reduce the expression of urinary osteopontin. A role of citrate in pathogenesis of metabolic bone diseases has been recently suggested and citrate measurement in urine has been proposed as a predictor of both bone mass loss and fracture risk. Idiopathic calcium stone disease, with or without hypocitraturia, can be treated with alkaline citrate, as well as other forms of nephrolithiasis and different pathological conditions. The therapy with potassium citrate, or magnesium potassium citrate, is commonly prescribed in clinical practice in order to increase urinary citrate and to reduce stone formation rates. Our data as well as those of the literature confirm that alkali citrate induces both an increase of protective urinay analytes (eg. citrate, potassium and pH) and a decrease of calcium oxalate supersaturation. Moreover, alkali treatment reduces the rate of stone recurrence and increases the clearance rates and dissolution of stone fragments. Last but not the least, an increasing number of papers pointed out the protective role of alkali citrate in preserving bone mass in stone formers as well as in healthy subjects with bone loss.
Nevertheless, the evaluation of urinary citrate in patients with kidney stones and the treatment of these patients with alkali salts namely with potassium citrate are still scarce.

KEY WORDS: *Citrate; Stone disease; Alkali therapy.*

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The critical role of citrate in the pathogenesis of kidney stone disease is well known and the efficacy of treatment with alkali salts, in patients with nephrolithiasis, has been demonstrated by several authors (1). Nevertheless, the evaluation of urinary citrate excretion in stone formers is still scarce and the treatment of these patients with alkali salts, namely with potassium citrate, is far from routine use. More recently citrate has been involved in the pathogenesis and treatment of metabolic bone diseases and citrate measurement in urine has been proposed as a predictor of both bone mass loss and fracture risk (1, 2). Alkali salts can prevent bone loss by means of several mechanisms (3-5): they seem to have a direct action on osteoclastic bone resorption (5) and, indirectly, when given as potassium citrate, they are able to reduce urinary calcium excretion, thus preventing bone resorption (3, 6, 7). Finally, some studies suggested that alkali may also stimulate bone formation (3, 8). Citrate is a weak acid that is synthesized inside Krebs' cycle. It can also enter the body through dietary intake. About 4 grams of citrate are daily introduced with the diet and they undergo a rapid and almost complete intestinal absorption. The small intestine presents a citrate

transporter similar to the sodium dependent dicarboxilate carrier observed in the proximal renal tubule. After an oral intake of alkaline salts, citrate is absorbed and metabolized thus producing an alkaline load that, ultimately, increases urinary citrate excretion (1). On the contrary both a decreased dietary intake or intestinal absorption may induce a hypocitraturic condition (9). Plasma citrate is filtered at glomerular level and then reabsorbed in the proximal tubule mainly in the convoluted and straight segments. Citrate is reabsorbed in the apical membrane of the proximal tubule by a Na+/citrate2- cotransporter, which was cloned and named Na+/dicarboxylate co-transporter (NaDC- 1) (10, 11). NaDC-1 is a major determinant of urinary citrate excretion; human NaDC-1 gene (hNaDC-1) contains 12 exons consisting of 1953 base pairs in its cDNA and encodes 593 amino acids. *Okamoto et al*. (12) evaluated in 105 recurrent calcium stone formers (RSF) and in 107 age-matched healthy controls, the 1550V polymorphism. In both groups, subjects with a BB genotype (homozygous for the digested BcL-I allele) showed a significantly lower urinary citrate excretion than subjects with a bb genotype (homozygous for the undigested allele). Although subjects with the BB genotype were observed more frequently in the RSF group than in healthy controls, the genotype distributions of these two groups were not significantly different in this study. The results of these authors suggest that the B allele of 1550V polymorphism of hNaDC-1 may be associated with a reduction in urinary citrate excretion and that it contributes to hypocitraturia in RSF. Hypocitraturia is one of the principal factors promoting stone formation in idiopathic stone disease, with a prevalence of hypocitraturia ranging from 8% up to 68.3% (1). Hypocitraturia is frequently found in patients with idiopathic calcium stone disease and several cut-offs have been suggested to define it: these different values may help to explain the wide range of hypocitraturia prevalence observed in the literature (Table 1). Furthermore, the prevalence of hypocitraturia may be modified when this parameter is considered alone or together with other metabolic alterations (13). Also the gender and food intake may influence the prevalence of hypocitraturia. In fact, hypocitraturia appears to be greater in stone former males than in females and a relevant difference in daily citrate excretion will occur according to whether patients are on their home diet or on controlled diet (1). On the contrary, normal female subjects show a urinary excretion of citrate greater than males and a significant difference can be observed also in females, depending on their menopause state (1).

In 1994 *Pak* (14) proposed a functional definition of hypocitraturia that was a citrate excretion lower than 320 mg/day; this value is universally accepted and it is commonly used in the clinical practice. Hypocitraturia seems to be more frequent in recurrent than in single stone formers. Moreover, male stone formers show a higher incidence of hypocitraturia than post- and pre-menopausal females. Furthermore, when urinary citrate excretion is corrected for glomerular filtration rate (GFR) and normalized to 100 ml of GFR the difference between males and females becomes statistically significant ($p < 0.001$) (15). These data confirm that the behaviour of urinary citrate excretion is similar in stone formers and in healthy subjects when they are considered according to gender (1, 15). Several physiological factors can reduce urinary citrate excretion in patients with calcium lithiasis, even though they are not completely understood. Differences in intestinal handling, serum concentration and filtered load of citrate were not found between kidney stone formers and normal subjects (16-18). On the contrary, several metabolic abnormalities, such as metabolic acidosis (19), hypokalemia (20) and starving (21), seem play a role on the renal handling of citrate. In fact all these factors can decrease urinary citrate excretion, as well as a diet rich in acid-ashes (22). Although several factors can regulate citrate excretion, acid-base status seems to play a pivotal role. Systemic acidosis increases citrate reabsorption from the renal tubules with a consequent lowering of urinary citrate excretion, whereas alkalosis decreases citrate reabsorption thus increasing urinary citrate excretion (23, 24). In acidosis, the increased citrate utilization by the mitochondria in the tricarboxylic acid cycle, lowers citrate intracellular levels and promotes citrate tubular reabsorption, thus reducing its urinary excretion.

However, hypocitraturia has been observed in renal calcium stone formers without other metabolic abnormalities (25). The hypocitraturia of undetermined aetiology or idiopathic hypocitraturia, may be linked both to intrinsic renal defects (impairment of the sodium-citrate cotrasport or alteration of intracellular citrate regulation etc), or to inappropriate intestinal citrate or alkali absorption; finally, hypocitraturia may be a normal response to a high protein intake of meat which has a high acid content and can, therefore, induce a subtle decrease of proximal tubule cells pH, thus reducing citrate excretion. Several studies were performed maintaining patients on controlled diet in order to avoid the influence of diet factors and, still, stone formers showed lower citrate excretion than controls (16, 17, 25).

All these observations suggested that a genetic predispositions, as described above, may be involved in the pathogenesis of idiopathic hypocitraturia in stone formers (26). The main causes of hypocitraturic calcium nephrolithiasis are summarized in Table 2.

Several studies have pointed out the crucial role of a long-

Table 1.

Prevalence of hypocitraturia in patients with stone diseases.

Authors	Year	%
Nicar MJ et al.	1983	55
Hosking DH et al.	1985	29.2
Jaeger PH et al.	1986	8.0
Caudarella R et al.	1986	12.6
Pak CYC et al.	1987	50
Vahlensieck W et al.	1987	47
Akinci et al.	1991	46,56
Höbart K, Hofbauer J	1991	34
Fardella et al.	1994	68,3
Hess B et al.	2002	29
Usui Y et al.	2003	38,4%

Table 2.

Causes of hypocitraturic calcium nephrolithiasis.

1. idiopathic hypocitraturia
2. Distal renal tubular acidosis
3. Chronic diarrheal syndrome
4. Drugs (thiazide, acetazolamide, Topiramato, Zonisamide, etc)
5. High intake of animal protein
6. Gout and gouty diathesis
7. By-pass or ileal resection
8. Inflammatory bowel diseases
9. Medullary sponge kidney
10. Strenuous physical excercise

term selective medical therapy for the prevention of stone formation in recurrent stone formers.

Furthermore, the systematic research of potential risk factors represents a natural and critical step for prescribing a correct treatment. In fact, idiopathic calcium stone disease shows a strong tendency towards stone recurrences. Preminger et al. described that stone formation continued in 39% of the patients during conservative or placebo trials and that 69% of the untreated subjects finally need surgical treatment. In contrast only 2% of patients treated with medical therapy required further surgical treatment (27). *Tiselius et al.* suggested a recurrence probability of 30% for single stone formers treated only with dietary advices and this rate increased up to 70% during a follow-up period of 10 years (28). In contrast *Ettinger et al.* (29), in a three years prospective randomized double-blind trial, found new calculi formation in 63.6% of subjects receiving placebo and in 12.9% of subjects receiving potassium-magnesium citrate. When compared with placebo, the relative risk of treatment failure for potassium-magnesium citrate was 0.16 (95% confidence interval 0.05 to 0.46). *Siener et al.* (30), after two year from the first renal episode, found a recurrence rate of 43% in stone-formers treated with medical therapy. These authors ascribed this relevant recurrence rate to the presence of a particularly active stone disease; they hypothesized also the persistence of residual stone fragments in subjects who underwent shock-wave lithotripsy (ESWL). Furthermore, they proved that both the number of previous ESWL and the history of several recurrence episodes were independent predicting factors for a high risk of new stone formation. Literature data do not supply an accredited tool able to identify the time elapsing between the first stone episode and the successive recurrence. Several factors can hinder the achieving of this outcome, such as the clinical course of stone disease (high recurrence rate), the presence of residual fragments in urinary tract after ESWL and, finally, the absence of biochemical parameters enabling the prevision of recurrence risk. In fact, although high values of urinary supersaturation for calcium oxalate are, generally, associated with a greater risk of stone recurrence, the evaluation of this urinary factor did not supply reliable information about the future course of the disease (31, 32). In the last twenty years the therapy with alkaline salts has been widely used in patients with calcium stone disease that showed, as metabolic alteration, a decreased urinary citrate excretion; furthermore, alkaline salts, namely potassium citrate, were successfully used in calcium stone formers without hypocitraturia as well as in patients with uric acid nephrolithiasis associated or not with calcium stones. Alkali citrates treatment has been proposed for the medical therapy of stone disease because a significant number of stone formers show low urinary citrate excretion and also for the significant role played by citrate on crystallization steps. In fact, urinary citrate after the binding with calcium ions, forms soluble calcium citrate complexes that reduce the urinary supersaturation for both calcium oxalate and phosphate. Moreover, citrate inhibits crystal growth as well as aggregation of calcium oxalate and calcium phosphate crystals (33). Citrate also increases the activity of some urine macromolecules (eg. Tamm-Horsfall protein) that inhibit calcium oxalate aggregation (34) and it seems to be able to reduce the expression of urinary osteopontin, that is a crucial component of the stone protein matrix (35). Furthermore, citrate increases urinary pH that plays a key role in uric acid crystallization and stone formation; in addition, monosodium urate crystallyzation is a well-known risk factor for calcium oxalate stone formation by means of the heterogeneous nucleation. Finally, alkali citrate seems to have a beneficial effect in infection stone disease, delaying the urease induced crystallization (36).

The most commonly prescribed alkaline salts are potassium citrate, sodium-potassium citrate, potassium-magnesium citrate and calcium citrate (1). Calcium citrate is usually prescribed for osteoporosis treatment and it increases urinaryexcretion both of citrate and calcium; nevertheless, since this salt provides an alkali load, the increased calcium excretion is counterbalanced and the risk of stone formation is not increased (1). Therapy with potassium citrate or magnesium potassium citrate is commonly prescribed in clinical practice in order to increase urinary citrate and to reduce stone formation rates in patients with idiopathic calcium lithiasis, with or without hypocitraturia (1, 37). The increase in urinary citrate excretion was observed and described by our group during the follow-up of our stone forming patients (1).

In 2006, at a *Congress on Urolithiasis* (38), we presented data showing a statistically significant increasing trend of urinarycitrate excretion in a follow up period of 10 years ($p < 0.00001$) with the highest values being observed after 5 years of therapy (Figure 1).

Furthermore, the same results were obtained also when urinary citrate excretion was normalized at 100 ml/min of GFR ($p < 0.001$). Gastrointestinal alkali absorption showed an increasing trend during follow up that was very similar to that of citrate (Figure 2). As previously observed, the initial value of urinary citrate excretion seems to influence the behaviour of citrate in urine; patients with a basal value lower than 320 mg/day showed, during the follow up, a lower pronounced increase of citrate excretion than subjects with higher basal values (Figure 3). This observation confirms our previous results that only 20 per cent of patients with true hypocitraturia can reach the mean value of urinary citrate excretion observed stone former group (1).

Mattle and Hess (37) make a critical review of the liter-

Figure 1.

Trend of urinary citrate excretion in patients treated with potassium citrate. (Values are expressed as mean; vertical bars represent the 95% confidence interval) (38).

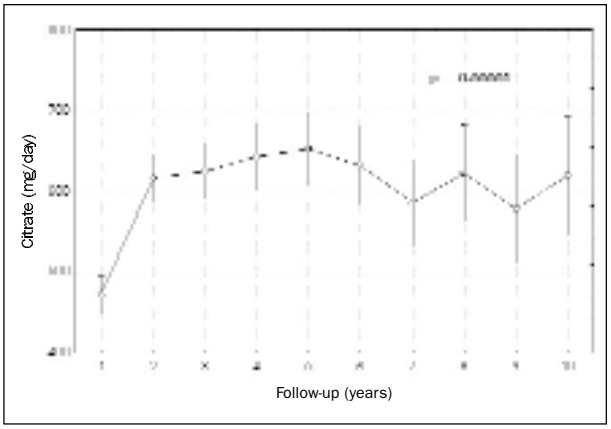


Figure 2.

Trend of gastrointestinal alkali absorption in patients treated with potassium citrate. (Values are expressed as mean; vertical bars represent the 95% confidence interval) (38).

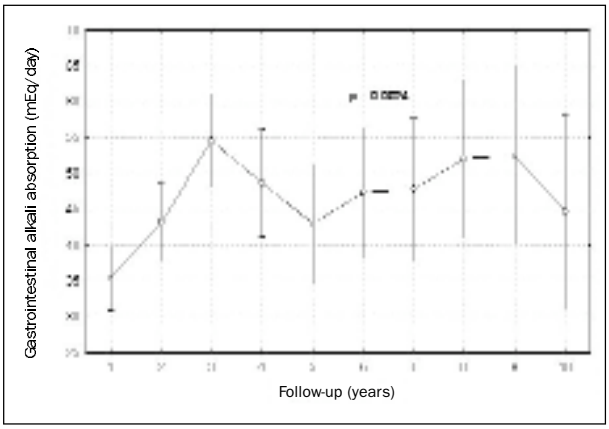
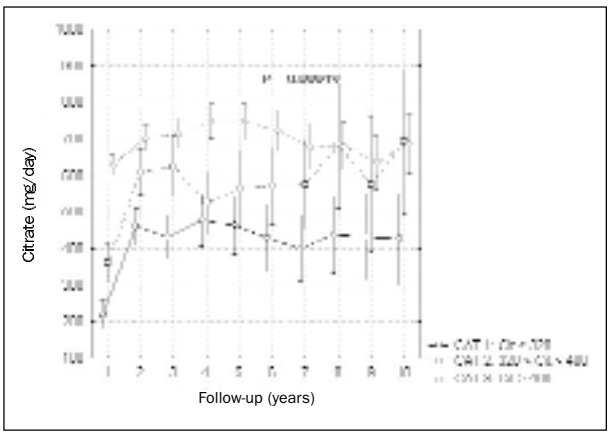


Figure 3.

Urinary citrate excretion in patients treated with potassium citrate. Patients have been subdivided in 3 groups according the basal value of citraturia. (Values are expressed as mean; vertical bars represent the 95% confidence interval) (38).



ature regarding the preventive treatment of renal stones with alkali citrate. In all the papers examined, the authors found that some metabolic modifications, such as urinary citrate and potassium increase together with pH augmentation, induced by alkali treatment, were constantly reported. Still, our results confirm these data (Figure 4 and 5). A general agreement about the modifications of other risk factors following citrate therapy was not found. For example, same authors found a decrease of calcium urinary excretion while other authors did not find this result. In some papers urinary supersaturation was evaluated (measured as formation product ratios) showing an opposite trend for calcium oxalate and calcium phosphate; in fact, the majority of stone formers treated with potassium citrate showed a decrease of calcium oxalate and an increase of calcium phosphate supersaturation. Our data confirm that supersaturation for calcium oxalate (calculated as activity product of calcium oxalate) decreases during the fol-

Figure 4.

Trend of urinary pH in patients treated with potassium citrate. (Values are expressed as mean; vertical bars represent the 95% confidence interval) (38).

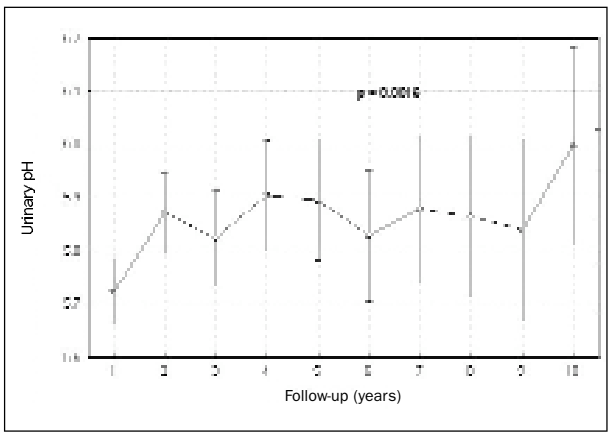


Figure 5.

Trend of urinary potassium excretion in patients treated with potassium citrate. (Values are expressed as mean; vertical bars represent the 95% confidence interval) (38).

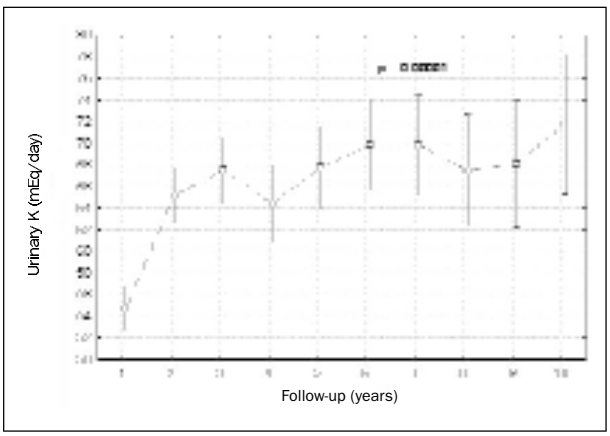


Figure 6.

Trend of urinary supersaturation for CaOx in patients treated with potassium citrate. (Values are expressed as mean; vertical bars represent the 95% confidence interval) (38).

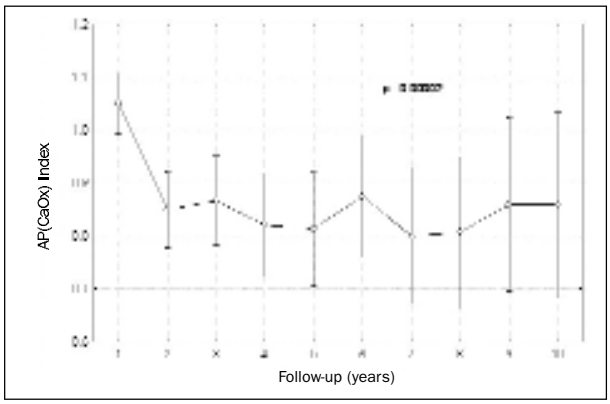


Figure 7.

Prevalence of recurrent stone formers (RSF) before and after the therapy with potassium citrate. Mean duration of stone disease was similar before and after the therapy (38).

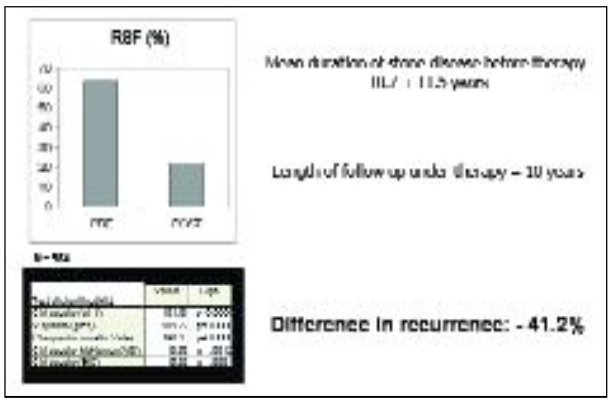
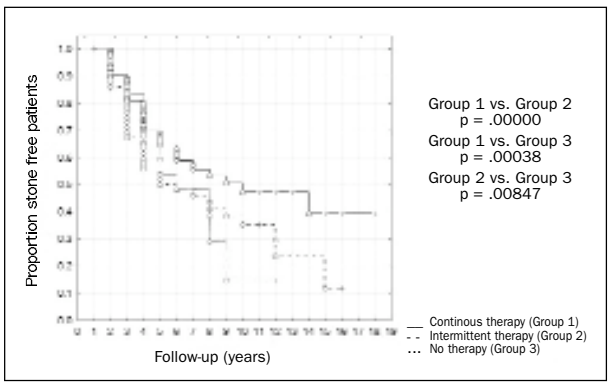


Figure 8.

Proportion of stone free patients according to the therapeutical compliance (38).



low-up (Figure 6): on the contrary, calcium phosphate activity product did not show this trend. These results can be due to pH modification that increases citrate complexation of calcium but increases pH-dependent dissociation of phosphate. Thus, in clinical practice, urinary pH should be measured regularly to maintain its value between 6.5 and 7.0.

Mattle and Hess (37) found 21 uncontrolled studies that having stone recurrence as the primary endpoint: these studies included about 1000 patients treated with alkali therapy and showed a decrease in stone forming rate ranging between 47% and 100%. Four randomized controlled trials, including 227 patients, when analyzed on an intention-to-treat basis, showed that more than 50% of alkali treated patients remain stone free after 1 year of treatment, whereas only 35% of subjects receiving placebo was stone free ($p < 0.0005$). Similar results were obtained in two randomized placebo-controlled trials that having as primary endpoint the clearance or the dissolution of residual stone fragments; 66% of patients became stone free after one year of therapy while only 27.5% of subjects receiving placebo resulted stone free ($p < 0.0005$). Our results showed, during a follow up of ten years, a 41.2% decrease recurrence rate in patients treated with potassium citrate (Figure 7). A further supporting evidence of the efficacy of potassium citrate therapy, derives from the observation of *Kaplan-Mayer* curve suggesting that treated patients show a lower rate of recurrence than subjects who dropped-out from treatment; patients with an inconstant citrate assumption showed an intermediate behaviour (Figure 8).

The drop-out rate in stone formers treated with alkali citrate is very high; in fact, *Mattle* and *Hesse* observed that about one third of alkali citrate treated patients, left the studies. The drop-out rate was higher when stone formers assumed magnesium-potassium citrate that seem to have a greater efficacy in stone prevention than potassium citrate. In our observational study the compliance and adherence to the therapy were indirectly suggested by the persistent increase of citrate and potassium urinary excretion as well as by the pH values. The drop-out rate was due to adverse effects at gastrointestinal level.

In conclusion all literature data, as well our observations, confirm the efficacy of potassium alkali citrate therapy, that is able not only to ameliorate urine parameters and calcium oxalate supersaturation level, but allows the clinical achievement of a reduction in stone recurrence rates. Another important role of alkali citrate therapy comes from the observation that the clearance of dissolution of pre-existing stones or fragments is significantly improved in patients undergoing ESWL. The treatment with alkali citrate seem to be a safe and efficient tool for the prevention of calcium stone disease in subject both with or without hypocitraturia and also in those with other metabolic abnormalities. Last but not the least, a growing evidence is pointing out the protective role of alkali citrate in preserving bone mass in stone formers as well as in non stone forming osteopenic subjects.

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ORIGINAL PAPER

Dissolution of radiolucent renal stones by oral alkalinization with potassium citrate/potassium bicarbonate.

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Summary

Aim: Uric acid stone disease is dependent on three pathogenetic factors: acid urine pH, low urine volume, and hyperuricosuria. However, the most important factor for uric acid stone formation is persistently acidic urine that represents a prerequisite for uric acid stone formation and growth. Urinary alkalization with alkali administration has been advocated for dissolution of stones on the basis of estabilished clinical experience. The aim of this study was to evaluate the clinical efficacy of therapy with potassium citrate/ potassium bicarbonate for dissolution of radiolucent stones.

Patients and Methods: A total of 8 patients with radiolucent stones (< or = 15 mm) in functioning kidneys were enrolled (4 M, 4 F; mean age 66+/-2 years) Ultrasonography (or computed tomography scan) was done to confirm stone presence and burden and plain X-ray to exclude calcified stones. At basal a blood sample was drawn for glucose, creatinine and uric acid measurement and a 24 hour urine sample was collected for evaluation of daily uric acid excretion. Urine cultures were also performed in order rule out urinary tract infection. All patients at presentation and weekly during the study period filled out urinary pH and volume diaries. Each study day three samples of urine were collected for pH and volume measurement (morning from 8 AM to 2 PM; afternoon from 2 PM to 8 PM, and night from 8 PM to 8 AM). Two study periods were considered: during the first 6 week period a daily water intake of 1500 ml was suggested whereas in the following 6 week period the same water intake plus potassium citrate 40 mEq and potassium bicarbonate 20 mEq (divided in two doses). Potassium alkali were chosen in order to reduce the risk of calcium precipitation because of their calcium-lowering effect. The effects of treatment on stone dissolution was evaluated by ultrasonography after each study period (6 weeks and 12 weeks).

Results: During the first period of treatment stone burden remained unchanged in all patients. On the contrary after 6 weeks of potassium citrate/bicarbonate treatment, complete stone dissolution was found in three of the patients. In the other five cases a partial dissolution was observed and in two of them complete dissolution of the stone was achieved after prolongation of the treatment for 4 and 6 month respectively. Mean urinary volumes were unchanged during all the two study periods. Mean urinary pH was significantly higher during the potassium citrate/bicarbonate treatment period in comparison to the first study period (morning 6.60+/1.06 vs 5.53+/-0.51, p = 0.030; afternoon 6.53+/-0.70 vs 5.63+/-0.41, p = 0.007; night 6.57+/-0.51 vs 5.98+/-0.80, p = 0.092). Tolerance of the drug was good, and no serious effects were observed sufficient to interrupt treatment. None of the patients required subsequent interventions for stone treatment.

Conclusion: Urinary alkalization with potassium citrate/bicarbonate is a well tolerated and highly effective treatment, resulting in dissolution of nonobstructing uric acid stones.

KEY WORDS: *Urinary calculi; Uric acid; Urinary pH; Alkalinization; Potassium bicarbonate.*

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Introduction

Uric acid calculi account for a significant percentage of urinary stones, although their incidence varies between countries and accounts for 5% to 40% of all urinary calculi (1-3).

Uric acid stone disease is dependent on three pathogenetic factors: acid urine pH, low urine volume, and hyperuricosuria. Patients with medical conditions involving severe hyperuricosuria, such as chronic diarrheal states, myeloproliferative disorders, insulin resistance (including diabetes mellitus) and monogenic metabolic disorders (*Lesch-Nyhan syndrome*, etc.), are at high risk of developing uric acid calculi. However, the most important factor for uric acid stone formation is persistently acidic urine that has to be considered a prerequisite for uric acid stone formation and growth. Consequently the management of nonobstructing uric acid calculi should include maintenance of an alkaline urine, an increase in urine volume, and reduction in urinary uric acid excretion

Urinary alkalization with potassium citrate or sodium bicarbonate has been advocated for dissolution of stones on the basis of estabilished clinical experience (4-6). The aim of this study was to evaluate the clinical efficacy of therapy with a potassium citrate/potassium bicarbonate preparation for dissolution of radiolucent stones.

Patients and methods

A total of 8 patients with radiolucent stones (< or = 15 mm) in functioning kidneys were enrolled (4 M, 4 F; mean age 66+/-2 years). Ultrasonography (or computed tomography scan) was done to confirm stone presence and burden At basal a blood sample was drawn for glucose, creatinine and uric acid measurement and a 24 hour urine sample was collected for evaluation of daily uric acid excretion. Urine cultures were also performed in order rule out urinary tract infection. All patients at presentation and weekly during the study period filled out urinary pH and volume diaries. Each study day three samples of urine were collected for pH and volume measurement (morning from 8 AM to 2 PM; afternoon from 2 PM to 8 PM, and night from 8 PM to 8 AM). Two study periods were considered: during the first 6 week period a daily water intake of 1500 ml was suggested whereas in the following 6 week period the same water intake plus potassium citrate 40 mEq and potassium bicarbonate 20 mEq (divided in two doses). Potassium alkali were chosen in order to reduce the risk of calcium precipitation because of their calcium-lowering effect. The effects of treatment on stone dissolution was evaluated by ultrasonography at 6 weeks and 12 weeks after each study period.

Table 1.

Basal characteristics of the patients.

M/F	4/4
Age (years)	66+/-2
Glucose (mg/dl)	110+/-12
Uric Acid (mg/dl)	5.58+/-0.67
Creatinine (mg/dl)	1.14+/0.32
Urinary uric acid (mg/24 h)	410+/-199

Table 2.

Stone dissolution (main diameter in mm) after potassium citrate/potassium bicarbonate (KCKB) treatment.

Patient	Basal	Water	Water + KCKB	Prolongation
n. 1	12	12	8	0
n. 2	11	11	7	0
n. 3	20	20	5	
n. 4	21	21	0	-
n. 5	12	12	0	-
n. 6	11	11	9	
n. 7	7	7	0	-
n. 8	10	10	9	

Results

During the first period of treatment stone burden remained unchanged in all patients. On the contrary after 6 weeks of potassium citrate/potassium bicarbonate treatment, complete stone dissolution was found in three of the patients. In the other five cases a partial dissolution was observed and in two of them complete dissolution of the stone was achieved after prolongation of the treatment for 4 and 6 month respectively.

Mean urinary volumes were unchanged during all the two study periods (Table 3 - Figure 1).

Mean urinary pH was significantly higher during the potassium citrate/bicarbonate treatment period in comparison to the first study period (morning 6.60+/1.06 vs 5.53+/-0.51, p = 0.030; afternoon 6.53+/-0.70 vs 5.63+/-0.41, p = 0.007; night 6.57+/-0.51 vs 5.98 +/-0.80, p = 0.092) (Table 3 – Figure 2).

Tolerance of the drug was good, and no serious effects were observed sufficient to interrupt treatment. None of the patients required subsequent interventions for stone treatment.

Discussion

Except in cases in which there is severe obstruction or infection of the urinary tract, progressive renal insufficiency, or unremitting pain, the initial treatment of patients with uric acid nephrolithiasis should be medical dissolution therapy by urinary alkalinization

Different alkali formulations have been administered for uric acid stone dissolution, although potassium alkali should be preferred because they may avoid the complication of calcium salt precipiation (1).

Accurate selection of the patients is crucial for successful treatment and patients with calcified stones or insufficient function in the kidney should be excluded (7).

Dissolution of stones can require a prolonged treatment up to six months.

Compliance of the patient and effective fol-

Table 3.

Urinary pH and volume during the study period.

	Urinary pH (mean+/-SD)					
	Morning	**Sig vs w1**	**Afternoon**	**Sig vs w1**	**Night**	**Sig vs w1**
Week 1	5.53+/-0.51		5.63+/-0.41		5.98+/-0.80	
Week 2	4.83+/-1.94	0.36	5.12+/-1.97	0.50	5.78+/-0.47	0.45
Week 3	5.90+/-0.63	0.21	6.31+/-0.87	0.09	6.05+/-0.78	0.85
Week 4	5.43+/-2.15	0.90	6.05+/-0.67	0.14	6.01+/-0.66	0.91
Week 5	4.57+/-2.66	0.29	6.05+/-0.62	0.12	5.97+/-0.62	0.95
Week 6	5.46+/-2.02	0.91	6.00+/-0.52	0.14	6.13+/-0.65	0.57
Week 7	6.60+/-1.06	0.03	6.53+/-0.70	0.007	6.57+/-0.51	0.092
Week 8	6.48+/-0.70	0.005	6.25+/-0.82	0.027	6.62+/-0.85	0.226
Week 9	5.91+/-2.40	0.68	6.58+/-0.86	0.007	6.80+/-0.67	0.043
Week 10	6.76+/-1.20	0.028	6.67+/-0.79	0.007	6.76+/-0.78	0.157
Week 11	6.81+/-0.92	0.012	6.26+/-0.82	0.036	6.78+/-0.72	0.081
Week 12	6.83+/-1.07	0.013	6.72+/-0.85	0.005	7.18+/-0.65	0.012
	Urinary Volume (Mean+-SD)					
Week 1	560+/-200		595+/-233		806+7-411	
Week 2	497+/-267	0.36	547+/-243	0.64	993+/-470	0.25
Week 3	640+/-254	0.30	506+/-161	0.27	1090+/-431	0.12
Week 4	627+/-253	0.34	597+/-244	0.97	925+/-459	0.31
Week 5	568+/-232	0.86	566+/-193	0.75	932+/-517	0.29
Week 6	628+/-294	0.45	541+/-160	0.60	896+/-451	0.33
Week 7	593+/-225	0.56	585+/-105	0.89	1043+/-348	0.053
Week 8	593+/-229	0.73	581+7-226	0.88	1031+/-359	0.102
Week 9	558+/-245	0.98	588+/-222	0.94	1052+/-363	0.047
Week 10	575+/-220	0.72	575+/-217	0.83	1031+/-398	0.072
Week 11	562+/-258	0.97	631+/-237	0.69	1051+/-434	0.045
Week 12	562+/-221	0.95	647+/-215	0.58	1062+/-423	0.044

low up are mandatory in order to obtain dissolution of the stones (8).

Urinary alkalinisation could also be used as complement of extracorporeal lithotripsy (SWL) for the non-invasive treatment of uric acid renal calculi. Using the combination of ESWL and oral urinary alkalinisation, about 80% of patients were rendered stone free at 3-month follow-up (9). A recent study confirmed that combined ESWL and dissolution therapy accelerated clearance and delayed recurrence of radiolucent renal stones in children (10).

More rapid dissolution may be accomplished with intravenous alkalinization or direct irrigation of the stone with an alkaline solution.

Rapid alkalinization of the urine to pH 8 can be achieved and maintained after intavenous infusion of 1/6 molar lactate with fast relief of obstruction and dissolution of urinary calculi (11-13). The success of this therapy is believed to be related to the sustained urinary alkalization in comparison to intermittent alkalization obtained with oral agents. The mechanism of action of lactate is oxidative conversion to bicarbonate with consequent urine alkalinization. Monitoring of serum electrolytes, blood pressure, and fluid balance has been recommended particularly in cardiac-compromised patients.

Sodium bicarbonate, acetylcysteine, tris(hydroxymethyl) aminomethane and tris(hydroxymethyl)aminomethane-E are the preferred agents for dissolving uric acid calculi in patients who require irrigation (14).

Sadi et al evaluated the efficacy of the different irrigating solutions utilized for local dissolution of uric acid stones demonstrating that tris-hydroxymethylaminomethane (THAM) was several times faster than sodium bicarbonate in dissolving uric acid calculi. Sodium bicarbonate should only be used in solutions at pH below 9 to avoid coating of the stones with hard shells of sodium urate, that is impossible to dissolve (15).

Only a few patients with acutely symptomatic stones opt for endourologic therapies that are difficult to plan due to the radiolucent nature of the stones. Computed tomography without injection of contrast material can provide a definitive diagnosis and it is the modality of choice to identify stone locations and size in these patients. In contrast to the lucent appearance on conventional urography the stones are dense on computer-

Figure 1.

Urinary volumes during the study period.

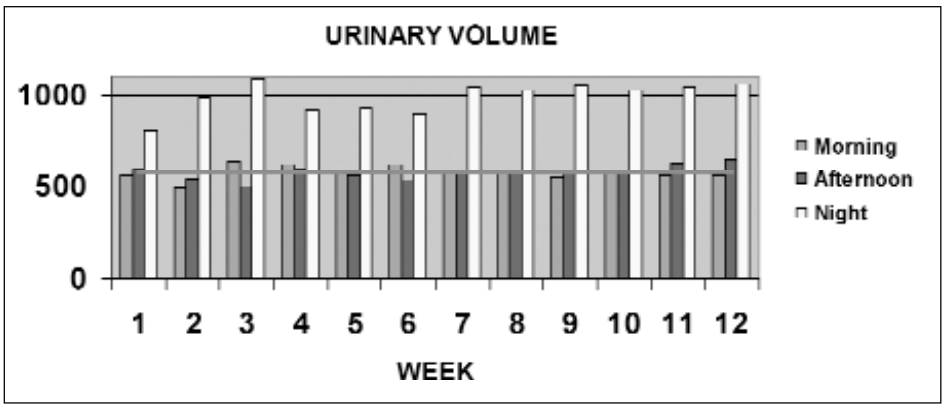
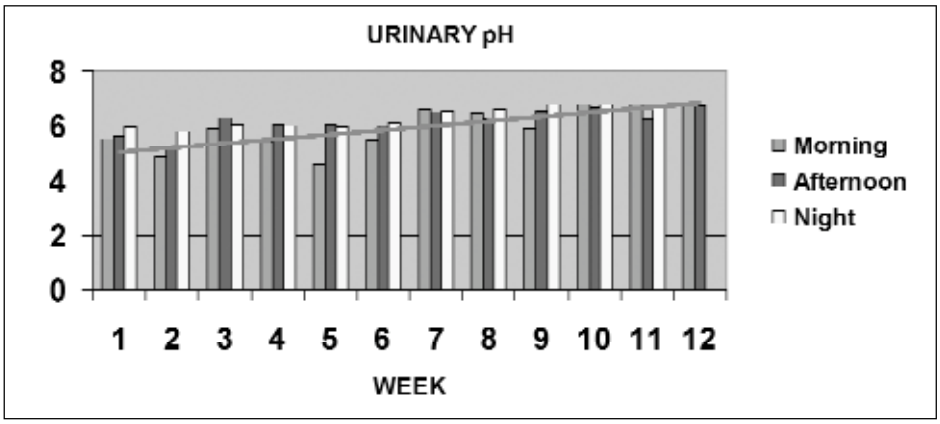


Figure 2.

Urinary pH during the study period.



ized tomography (16). Additionally, stone dissolution can be monitored with sequential computerized tomography studies. Our data demonstrate that urinary alkalization with oral potassium citrate/potassium bicarbonate is a well tolerated and highly effective treatment, resulting in dissolution of nonobstructing uric acid stones.

In conclusion medical management with urinary alkalization for stone dissolution and prevention of recurrence is effective and should be the cornerstone of treatment.

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REVIEW

Indications for a medium mineral high bicarbonate water (Cerelia®) in urology.

Alessandro Bertaccini, Marco Borghesi

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Summary

To increase water intake is an useful prophylactic treatment for many urologic diseases, such as urolithiasis or urinary tract infection.
An high water intake increases urinary volume with a dilutional effect that involves a consequent decrease of the concentrations of urinary solutes and a reduction of the levels of the salts involved in the lithogenic process. Furthermore the increased flow of urine in the urinary tract also improves the elimination of debris, gravel and bacteria.
The intake of a water (Cerelia®) with medium mineral (calcium 119.7 mg/l) and high bicarbonate (412 mg/l) content can cause specific changes of urinary composition that can be beneficial for the prevention of stone formation. The bicarbonate load has an alkalinizing effect that increase the urinary pH values and the urinary citrate excretion. This can be helpful to prevent both uric acid lithiasis, as a consequence of the increase of urinary pH (and of the solubility of uric acid), and calcium lithiasis, as a consequence of the increase of urinary citrate (and of inhibition of formation and aggregation of calcium crystals).
Experimental studies demonstrated that the administration of a medium mineral high bicarbonate water induced a significant decrease of serum uric acid levels by increasing the urinary excretion of uric acid without risk of stone formation due to the increase of urinary volumes, urinary pH and citrate excretion.

KEY WORDS: *Water; Urinary calculi; Uric acid, medium mineral, Cerelia*

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HISTORICAL BACKGROUND

The Cerelia spring flows through the Appennino Bolognese, located seven hundred meters above sea level, in Cerelio, a smiling and sunny small town, near Vergato, 48 kilometers from Bologna. According to several historical papers local water was really appreciated and well-known by residents for its beneficial properties, nevertheless there is no information about its therapeutic use until XIX century. During the cholera epidemic in 1855, Cerelio was recognized for its notably low mortality-rate, which was pointed out by chroniclers of that age, who supposed that its weather and water had healthy and protective effects.
In 1902, following the suggestion of Bologna's health county office, the water was chemically, physically and bacteriologically tested. The positive results of these assays brought to the realization, about in the 50's , of several structures to enhance Cerelio's water, until the construction of the present bottling system (Figure 1). Today the production cycle is divided into two separate bottling lines (with both glass or polyethylene terephthalate bottles) that convoy water through stainless steel pipes from the springs to the bottles with minimal air contact. *Federici et al.* (1) demonstrated the absence of chemical-physical variations and the persistence of the eumetabol-

Figure 1.
Panoramic view of Cereglio's bottling system.

ic activity of the water even after a long bottling period (> 120 days). The plant has been certified by EMAS (*Eco-Management and Audit Scheme*) and EPD (*Enviromental Product Declaration*).

Chemical and physical properties

From the chemical and physical analyses carried out by the *Regional Agency for Prevention of Environment* (ARPA) in Emilia Romagna (Table 1), it comes out that Cerelia water is a medium- mineral bicarbonate-alkaline-earthy water with low nitrate and nitrite values.

Table 1.
Chemical and physical tests ARPA (September 2007).

Water temperature	8°C
Conductivity at 20°C	599 μS/cm
PH	7,4
Chemical evaluations	
Fixed waste at 180°C	378 mg/L
Dissolved substances for liter	
Na^+	6,3 mg/L
K^+	0,57 mg/L
Ca^{++}	119,7 mg/L
NO_2	< 0,01 mg/L
NO_3^-	0,9 mg/L
Cl^-	4,4 mg/L
F^-	0,11 mg/L
HCO_3^-	412 mg/L
SO_4^{--}	6,0 mg/L
SiO_2	4,80 mg/L

The bacteriological analysis, carried out on a water sample which was directly taken from the spring and afterwards sowed in agar plates with a 48 hours incubation period, showed complete absence of *Colibacteria*, *Streptococchus faecalis*, *Pseudomonas aeruginosa* and *Staphilococcus aureus* with a microbic charge at 20° less then 8 CFU/ml. According to these results Cerelia water has to be considered bacteriologically safe.

Medical use

The medical treatment of nephrolithiasis aims to avoid the growth or to enhance dissolution or spontaneous passage of pre-existing stones and to prevent formation of new recurrent stones. This can be obtained by both dietary measures or pharmacological treatment although the increased water intake remains the pivotal measure for the treatment of all type of stones.
The positive effect of the increased water intake in medical treatment of renal stones has been recently revised (2) confirming that a water intake to increase the urine volume > 2 liters is effective in preventing stone recurrence through the dilution of urinary solutes.
Zanasi and Fatone (3) compared the effect of the administration of 1 liter of medium mineral high bicarbonate water (Cerelia®) to 20 healthy subjects during a time period of 30 minutes after overnight fasting with the effect of the administration of tap water with the same modality to 20 controls. The administration of medium mineral high bicarbonate water significantly ($p < 0.05$) decreased urine density, nitrogen excretion and uric acid excretion whereas urine volume increased significantly (710 mL after 2 hours and 890 after 4 hours). On the contrary no significant variation was observed after administration of tap water (urinary volume after 2 and 4 hours was respectively 400 mL and 675 mL).Finally creatinine clearances were higher after Cerelia® in comparison to tap water.
Zucchelli et al. (4) previously reported a statistically significant decrease of mean serum uric acid level (5.17 mg/dl vs. 6.34 mg/dl), increase of daily uric acid excretion (497 mg/die vs. 458 mg/die) and consequently an increase of uric acid clearance after the assumption of 200 ml a day of Cerelia water (fasting) for 30 days.
The long term intake of a water with medium mineral and high bicarbonate content can also cause other specific changes of urinary composition that can be beneficial for the prevention of stone formation. In fact the bicarbonate load has an alkalinizing effect that increase the urinary pH values and the urinary citrate excretion. This can be helpful to prevent both uric acid lithiasis as a consequence of the increase of urinary pH (and of the solubility of uric acid) and calcium lithiasis as a consequence of the increase of urinary citrate (and of inhibition of formation and aggregation of calcium crystals).
A medium mineral high bicarbonate water can also ensure beneficial effects in patients suffering from infections of the low urinary tract (lower UTI) and in those with LUTS (lower urinary tract symptoms) by the wash out effect of water that allows for a precocious relief from the symptoms in relation to the elimination of bacteria.

Conclusions

In conclusion according to experimental studies the administration of a medium mineral high bicarbonate content water (Cerelia®) can have a beneficial effect in patients with urological diseases.
It could be suitable for the treatment of uric acid metabolic diseases, both primary (gout) or secondary (tumours, antiblastic therapies, chronic flogosis, autoimmunitary diseases) and for preventing associated diseases (uric acid urolithiasis, urate-related nephropathy).
In particular Cerelia® water is particularly suitable for the uro-oncologic patient (expecially the older one) that often presents disturbances of uric acid metabolism (with increased uric acid excretion expecially during and after specific treatments). The intake of medium mineral high bicarbonate water is advisable in this group of patients (that are characterised by disturbances of uric acid metabolism but also by an high risk of urinary tract infection) in order to decrease the risk of lithiasic complications and dysuric symptoms of the low urinary tract and to increase general well-being and improve quality of life.

Acknowledgements

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torical documentation and *Dr. Silvia Vallecoccia* for the editorial support in the realization of the paper.

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IMAGING IN UROLOGY

Trieste, Italy, 30-31 October 2009

Programma

Venerdì 30 ottobre 2009 – 14.00-18.00 Round Table – International Session

3D/4D Ultrasound of the pelvic floor *M.F. Coelho*
Computer guided ultrasound. Clinical utility of C-TRUS/ANNA "next generation" *T. Loch*
Imaging and urologic treatment in pregnancy *P. Geavlete, R. Multescu*
Comparison between MRI and elastography regarding the diagnostic value in prostate cancer *J. Walz*
The MR spectroscopy of prostate cancer after HIFU treatment *I. Romics*
Contrast enhanced ultrasound of the prostate *H. Wijkstra*
Contrast enhanced ultrasound of the kidney *M. Bertolotto*
Final remarks *C. Trombetta*

Sabato 31 ottobre 2009 – 9.00-13.00 Sessione SIEUN

Moderatori: E. Belgrano, C. Trombetta

Presentazione del corso *P. Martino*
Novità nell'imaging ecografico della prostata *P. Consonni, P. Martino*
Update nella biopsia prostatica *V. Scattoni*
La MR spettroscopia della prostata: stato dell'arte *G. D'Eramo*
Trattamenti eco guidati nel carcinoma prostatico: prospettive attuali e future *A. Galosi*
Update in ecografia andrologica *G. Liguori*
La biopsia renale: attualità e prospettive *S. Palazzo*
Update in ecografia nefrologica *F. Petrarulo*
Studio ecodinamico delle vie urinarie superiori ed inferiori: indicazioni e stato dell'arte *P. Rosi, M. Del Zingaro*
Ecografia ed incontinenza urinaria *R. Gunelli*
Comunicazione su invito: Ruolo dell'elastografia e del power doppler prostatico con mezzo di contrasto ecografico ed inibitori delle 5-fosfodiesterasi nella re-biopsy di pazienti con PSA elevato *G. Morelli*
Discussione

I PUNTI SIEUN

(una possibilità di incontro tra Soci SIEUN e di contatto con altri specialisti)
Presso i punti SIEUN i nostri soci potranno essere continuamente informati su tutte le attività e le iniziative della Società e rinnovare il pagamento della quota associativa.

I PROSSIMI APPUNTAMENTI SIEUN

XVI Congresso Nazionale AURO.it *(Verona, 23-26 settembre 2009)* nell'ambito del quale si terrà la Lettura SIEUN "**Diagnostica delle piccole masse renali**" *(giovedì 24 settembre – ore 16.00-18.00)*
82° Congresso Nazionale SIU*(Rimini, 4-7 ottobre 2009)*
International ESUI Meeting "Imaging in Urology" *(30-31 ottobre 2009)*
XXI Congresso Nazionale SIUMB *(Roma, 14-18 novembre 2009) nell'ambito del quale si terrà il Face to Face* ***"Inquadramento clinico dell'ematuria - diagnostica per immagini"*** *(domenica 15 novembre 2009 - ore 19.00-19.30)*

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