

Congress Report: 6th Stone Symposium of the Series, Bonn-Vienna

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This meeting, up to now held annually once in Bonn and once in Vienna, convened in Bonn during April 13 - 15, 1978. Members are well-known European academic urologists (Vahlensieck, Bonn; Lutzeyer, Aachen; Rutishauser, Basel; Schneider, Jena; Andersson, Stockholm) pathophysiologists/physiologists (Fleisch, Berne; Deetjen, Innsbruck), nephrologists (Amiel, Colombes Cedex), endocrinologists (Bijvoet, Leiden; Schwille, Erlangen), biochemists (Robertson, Leeds; Rose, London; Cifuentes Delatte, Madrid). This team aims to promote scientific investigation by participation, presentation of currently important projects in stone research and stimulation of clinical and experimental research work in order to advance understanding of this disorder. Although contributors originally came from Europe the rapid progress achieved in clinical and basic research, by American and English workers, necessitated the opening of the meeting to overseas' guests on this occasion represented by C. Y. C. Pak (Dallas) and O. Sperling (Tel Aviv).

The programme continued 3 main topics: A. Epidemiology and Pathophysiology; B. Investigative methods; C. New aspects in therapy. A total of 50 papers were presented in English and German, all short communications with the exception of a few lecture-like presentations. The proceedings of the symposium will include all papers and discussions and will appear in "Fortschritte der Urologie und Nephrologie", Steinkopff Verlag, Darmstadt (FRG). The following section gives a very brief insight into the contents of the papers.

A. EPIDEMIOLOGY AND PATHOPHYSIOLOGY

Intake of animal protein (meat, fish) appears strikingly related to stone incidence and not as

much intake of Ca, oxalate, phosphate, Mg, refined carbohydrates, total proteins; it is suggested that the higher risk to form stones arises from a) increased absorption of Ca and oxalate, b) oxalate overproduction, c) uric acid overproduction and overexcretion (Robertson, Leeds). Conversely, urine oxalate in a large population of Ca stone formers and control subjects was found comparable, and there was no higher risk carried by stone formers when this was expressed in terms of physico-chemical activity products under outpatient conditions, i. e. free home diets (Scholz, Erlangen). A major part of enteric oxalate (25%) is absorbed and excreted via the urine suggesting a substantial role of ingested oxalate in determining the risk of stone formation (Bannwarth, Basel). Hautmann (Aachen), in studying distribution spaces, half-life of disappearance and elimination kinetics of oxalate in man concluded that there is no opportunity for the kidney to limit the degree of oxaluria in subjects with hyperoxaluria. Among normocalcaemic hypercalciurics (n = 54) increased bone turnover was found in 38 and normal values in 16, as evidenced by ⁴⁷Ca faecal retention studies (Zechner, Vienna). Pak (Dallas) demonstrated values of serum parathyroid hormone (PTH) and urinary cyclic AMP (cAMP) in absorptive and renal hypercalciuria and their renal response to an oral glucose load in terms of Ca/creatinine ratio; he concluded that in the presence of normal 1, 25-dihydroxycholecalciferol blood levels increased intestinal absorption is the expression of an intrinsic jejuno-segmental defect in absorptive hypercalciuria, whereas thiazides correct elevated metabolite levels and Ca hyperabsorption in renal hypercalciuria. Among inborn errors of metabolism causing purine overproduction and uric acid lithiasis the most important are HGPRT deficiency, PRPP synthetase overactivity and a variety of yet

unconfirmed enzyme abnormalities (glutathione reductase superactivity and glucose-6-phosphatase deficiency) (Sperling, Tel Aviv). Electron microscopy revealed the presence of spheroid apatite (0.02 - 2 μm) in certain growth centres of stones and in random urine samples of potential stone forming subjects suggesting an aetiological role in nidus formation (Blaschke, Münster). Eickenberg (Essen) stated that stone incidence in white people is 2.2 times higher than in black people as based on a US hospital study. Interactions between organic substances (L-aspartic and L-glutamic acid) and hydroxi-apatite (non-stoichiometric) were identified as chemical adsorptive processes through surface ionic competence linking apatite-OH and organic COOH-groups (Carmona, Madrid). Szabo-Földvari (Debrecen) observed increased incidence of urolithiasis during childhood with a relatively short history as most prominent symptom. Ammonium acid urate was frequently found as a component in stones of 10 Turkish children living in Germany, but never in stones of 10 German children (Armbruster, Bochum); this finding was not, however, reflected by differences in ionic composition of serum/urine (Schulte-Vels, Essen). Schäfer (Mainz), using electron microscopy, illustrated the external shape and structural specialities of stones, those in turn allowing speculations upon initial events leading to crystallisation.

B. INVESTIGATIVE METHODS

Measurement of blood (plasma, serum) ionised Ca requires rigidly controlled standardised conditions in order to yield reliable results (Ulshöfer, Marburg). A set of standardised investigations is proposed for diagnosing hyperparathyroidism among stone formers (Frick, Salzburg). Differences in response (urinary cAMP, serum PTH) to PTH, i.v. Ca were sought among Ca stone patients (Dunzendorfer, Frankfurt/Heidelberg). Inadequately low urinary cAMP in stone patients in response to PTH injection was found by Lilienfeld-Toal (Bonn). Tschöpe (Heidelberg) presented epidemiological data on stone formers with regard to 25-hydroxycholecalciferol, urine Ca and serum PTH. Cifuentes Delatte (Madrid), in searching for brushite stones, verified it in 0.7% (21 of 2851 total analyses) leaving open the question as to its role as a primary nidus. Substitution of phosphate (PO_4^{3-}) by citrate on apatite crystal surface and citrate-calcium-hydroxyapatite bonds were found by Cifuentes (Madrid) using chemical and spectroscopic analysis. Response to oral purine load as a means of evaluating differences in renal uric acid excretion in stone formers was studied by Pflüger (Vienna). Asper (Zürich) presented a method for simultaneous determination of urinary cysteine and cystine, potentially helpful in follow-up of cystinuric patients treated with thiol containing drugs.

Spheroid aggregates of apatite besides cystine crystalluria but no cystine aggregates were detected in a patient with cystine lithiasis (Alken, Mainz). Acid metabolites in urine and serum (oxalate, citrate, hippurate etc.) appear accessible to rapid simultaneous determination by gas chromatography (Dosch, Mainz). Plasma oxalate concentration, presently a matter of debate, was found to range from 0.83 - 2.11 $\mu\text{mol/l}$ (enzymatic, isotopic methods), corresponding to an oxalate/creatinine clearance ratio of 0.99 - 1.9 (Constable, London). Urinary oxalate in normals and stone formers was 21 and 17 mg/day resp., using the enzymatic method (Bichler, Tübingen). A model for studying Ca oxalate crystal growth and its inhibition by EHDP at variable pH and combined with other inhibitors was presented by Bijvoet (Leiden). In vitro flushing of apatite, oxalate and uric acid with alkaline urine and urines with low Mg content of the same patient always yielded struvite apposition (Bastian, Bonn).

C. NEW ASPECTS IN STONE THERAPY

Hering (Aachen) studied correlations between total and ionised serum Ca in hypercalciuric patients and the proper influence of hypocalciuric agents (cationic exchange resins; thiazides). In rats fed a Ca binding cationic exchange resin a very high urinary cAMP and severely altered Ca kinetics (miscible pool, bone accretion/resorption) was observed suggesting development of secondary hyperparathyroidism (Hagmaier, Basel). Uric acid data from a balneological and rehabilitation centre were reported by Baltzer (Marburg), confirming normal serum concentrations in 341 calcium stone patients as compared with controls. Although stone recurrence rate seemed to depend on urinary oxalate in patients ingesting a standard hospital diet, excretion was found to be normal in the majority of cases and did not further respond to allopurinol or succinimide (Bach, Bonn). Finding unchanged urinary oxalate following oral oxalate load in normals and stone formers Butz (Berlin) concluded that restriction of dietary oxalate might be of minor importance in stone prophylaxis. Pyridoxine treatment in endstage renal function arising from primary hyperoxaluria (1 case) was found highly effective in that serum creatinine fell steadily and probably dissolved renal calcium oxalate deposits (Harrison, London). In vitro studies showed that oxalate binds effectively to sulphates (Ca, Sr salts) suggesting usefulness of such drugs in stone prophylaxis (Leskovar, Munich). Effects of Mg-oxide and -citrate on crystalluria in stone patients were studied by electron microscopy (Joost, Innsbruck). From the presence of Mg in apatite calculi and its inability to participate in

apatite lattice a competition between Ca and Mg for sites with negative charge in the crystalline surfaces is deduced and Mg considered an inhibitor for apatite crystal growth (Gonzales-Diaz, Madrid). Aluminium-oxy-sulphate-hydrate was found to effectively bind (in vitro, in vivo) inorganic phosphate and considered a promising agent for lowering the Ca phosphate product below the solubility product (Dulce, Berlin). Comparative results on urinary uric acid and electrolytes during treatment with allopurinol/brenzbromaronum were reported by Braun (Bamberg). A hitherto unknown syndrome of xanthine oxidase deficiency with undetectable serum uric acid and xanthine stone formation was observed by Sperling (Tel Aviv). Different surgical techniques and their consequences for renal function and morphology were studied in animal models by Frang (Pecs).

CONCLUSION

The number of investigators concerned with problems related to urinary tract stones has increased steadily in Europe and is pushing the capacity of this symposium towards its limits. The predominant impression of this last convention was that activities of the Advisory Board members had helped greatly in creating a stimulating programme and both critical and productive discussions.

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