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Crystalluria in marathon runners

III. Stone-forming subjects

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Summary. In order to investigate further the possible relationship between urinary stone formation and marathon running, the crystalluria in seven male, stone forming runners was characterized. Particle size distribution curves (Coulter counter) and crystal number, size and morphology (scanning electron microscopy) were measured. These studies suggest that urinary stone formation may be accelerated in those subjects with previous histories of renal stone formation but that the nature of the crystalluria is favourably affected by an increase in fluid intake. The presence of large quantities of mucoid material in the urine of "natural" stone formers and its absence in the urine of stone-forming runners is cited as evidence for the existence of different aetiological mechanisms in these groups. It is concluded that while natural stone formers may be at chronic risk of stone formation due to pathological factors, marathon runners may be at acute risk due to factors associated with long distance running itself.

Key words: Stone formers – Runners – Fluid intake – Mucoid material

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In previous studies [2, 6] we proposed that marathon runners are at increased risk of urinary stone formation. This proposition was based on the distinctive similarity between the urinary particle size distribution curves recorded for runners and those reported for recurrent idiopathic stone formers. Further evidence in support of this hypothesis was the marked similarity of the morphological features observed in the crystalluria of runners and stone formers.

The present study was undertaken to examine more closely the possible relationship between stone formation and marathon running. By investigating the crystalluria of stone-forming runners, we hoped to identify further features, if any, which might enable us to describe the mechanism of stone formation as it occurs in runners and to establish whether such a mechanism differs in any way from that occurring in renal stone patients who are non-runners.

Subjects, materials and methods

The controls were 15 randomly chosen healthy male members of staff of the Department of Chemistry, University of Cape Town, aged between 21 and 54 years [2]. The seven male marathon runners who participated in the study had all suffered at least one clinically diagnosed episode of renal stone formation. Only one subject was able to provide his stone for analysis. Two subjects had a history of renal stone formation prior to participation in long distance running. The runners' ages varied between 31 and 44 years. Each had been a long distance runner for several years (mean 5.8 years; range 2–16 years) and each had completed at least one marathon (mean 3.3 marathons; range 1–6). Only three subjects were aware of the dangers of dehydration at the time of their first clinical episode. However, all had subsequently increased their daily fluid intakes.

Nocturnal urine samples were collected from controls and runners in preheated thermos flasks. Urinary volumes varied between 65 and 468 cm^3. In the case of runners, the collections were effected 4 days after the completion of a marathon or strenuous training session. Urine samples were subjected to particle size distribution analyses at 37°C within 3 h of voiding. A Model TA II Coulter counter with population accessory unit was used for this purpose [2]. In addition, crystals were examined in a Cambridge S180 scanning electron microscope (SEM) fitted with an energy dispersive X-ray analysis (EDX) facility [2]. The solitary stone was subjected to X-ray powder diffraction (XRD) analysis using a Philips PW 1050/70 automatic X-ray powder diffractometer and CuK_α radiation.

Results

Particle volume-size analysis

The volume-size distribution curve for the crystalluric particles of the seven stone-forming subjects is shown in Fig. 1. The distribution curve for male controls reported in our earlier study [2] is superimposed. The stone formers' curve is trinodal with well-defined peaks occurring at particle diameters of 2.5 and 9 μm and a further

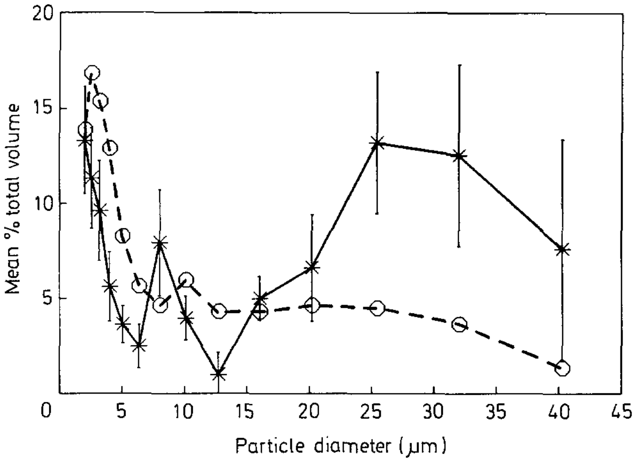


Fig. 1. Mean volume-size distribution curve (+ SEM) for the crystalluric particles in seven male stone-forming marathon runners (*solid line*) and in 15 controls from an earlier study [2] (*dotted line*)

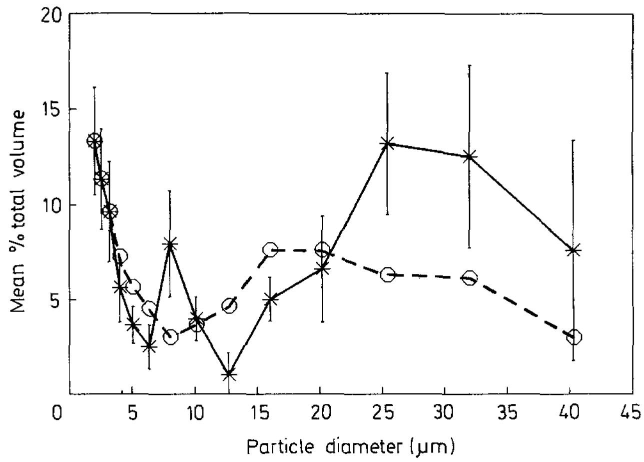


Fig. 2. Mean volume size distribution curve (+ SEM) for the crystalluric particles in seven male stone-forming marathon runners (*solid line*) and in seven male non-stone-forming marathon runners from an earlier study [2] (*dotted line*)

node in the diameter range 25–32 μm. In Fig. 2, the stone formers' curve of the present study is compared with that reported previously for non-stone-forming male marathon runners [2].

Scanning electron microscopy, energy dispersive X-ray analysis and X-ray powder diffraction

Very few crystals of any type were observed in the urines of the five subjects who had no history of urolithiasis prior to participation in marathon running. Occasionally calcium oxalate dihydrate (COD) deposits of less than 10 μm cross section were detected. On the other hand, the urines of other two subjects were characterized by profuse deposits of both calcium oxalate monohydrate (COM) and COD (Figs. 3, 4). Typical sizes were in the ranges 10–15 μm for COM and 20–30 μm for COD. In addition, many large aggregates were observed (Fig. 5). These subjects were advised to increase their fluid intakes, after which the nature of their crystalluria changed as observed in SEM studies. There were fewer crystals and no aggregates; COD crystals were generally smaller than previously observed (cross section 10–20 μm); very few COM deposits were detected (Fig. 6).

XRD analysis of the single urinary stone identified COM and COD as the only constituents. A cleaved surface of the stone is shown in the SEM micrograph (Fig. 7). Elemental analysis using EDX revealed the presence of calcium only, confirming oxalate as the stone type. Figures 8 and 9 show the entrapment of crystals in urinary mucoid material.

Discussion

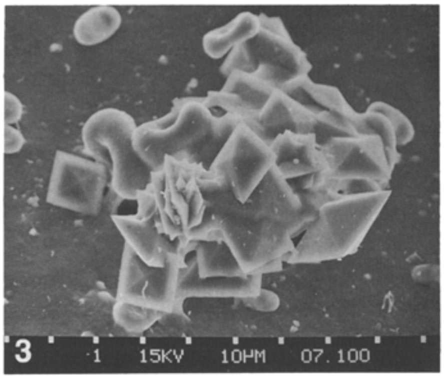
The volume-size distribution curve for the stone-forming runners is different from that obtained for controls (Fig. 1) in that the former shows the presence of particles in the diameter range 20–40 μm. This is in agreement with the findings of Robertson and co-workers in their studies of the crystalluria of recurrent idiopathic stone formers and controls [4]. In the present study, an additional peak corresponding to a particle diameter of 9 μm was observed. While it is noted that such a peak was reported for non-stone-forming runners participating in an ultramarathon [6], we are not sure of its significance, if any.

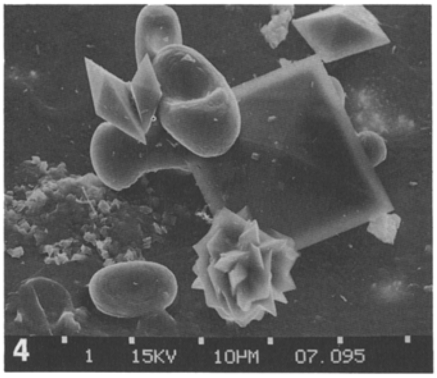
Comparison of the curves for the stone-forming and non-stone-forming runners (Fig. 2) shows that both display the characteristic distribution of recurrent idiopathic stone formers as reported by Robertson et al. [4], i.e. a binodal curve. This confirms our earlier finding that "normal" marathon runners may be at increased risk of stone formation [2, 6]. Figure 2 shows that the stone-forming runners have an even greater number of particles in the large diameter range. Therefore the possibility exists that these high-risk subjects increase their risk still further by strenuous long distance running.

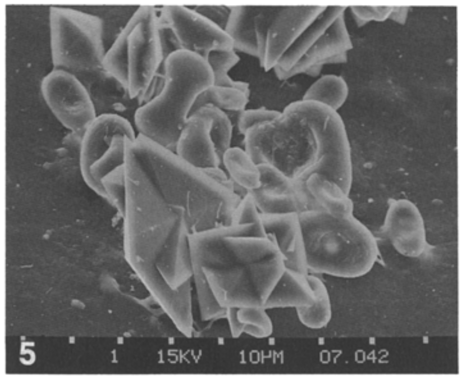
The profuse crystalluria observed in the two subjects with prior histories of renal stone formation, as opposed to the almost complete absence of such deposits in the other five subjects, indicates that different aetiological factors are operative in the two subgroups. It is obvious that marathon running could not have played any role in causing the original stone episodes in these subjects but that some undefined pathology is implicated. However, it is likely that running may have accelerated subsequent stone formation, as suggested in the preceding paragraph. Indeed, the presence of extensive crystalluria in these subjects points to urines with relatively high stone-forming potentials.

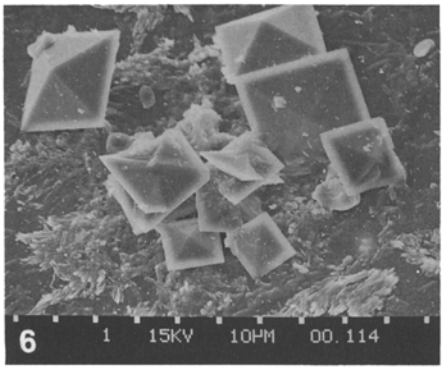
The observation that a significant increase in fluid intake produces favourable changes in crystalluria supports the widely accepted view that stone formers should drink relatively large fluid volumes to reduce their risk profile [3, 7]. Indeed, the same advice is valid for marathon runners.

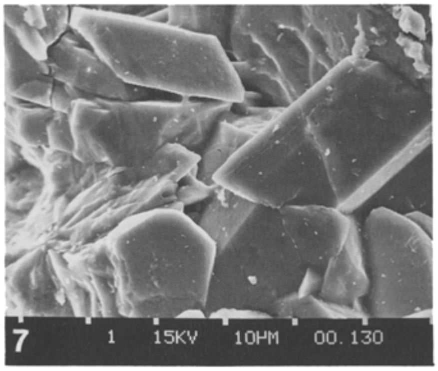
Another feature observed in the crystalluria of subjects with prior histories of stone formation was the presence of large quantities of organic mucoid material which was

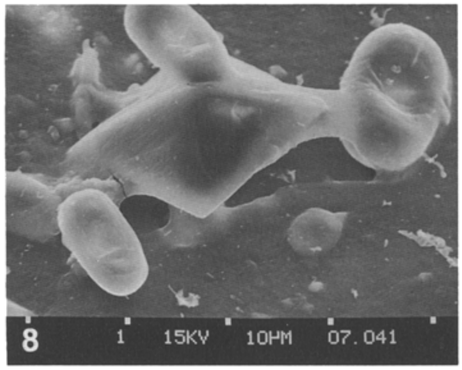












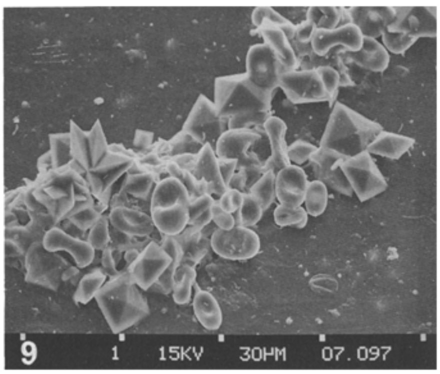


Fig. 3. Profuse deposits of COM (oval and dumb-bell shaped) and COD (octahedral or "envelope" shaped) crystals, typically observed in the urines of subjects with histories of renal stone formation prior to marathon running. Magnification ×750

Fig. 4. COM and COD crystals typically observed in the urines of subjects with histories of stone formation prior to marathon running. Note cross section of large COD crystal approx. 25 µm while cross section of COM crystals approx. 12 µm. Magnification ×1,750

Fig. 5. Large aggregate of COM and COD crystals typically observed in the urines of subjects with histories of stone formation prior to marathon running. Cross section 50–60 µm. Magnification ×1,300

Fig. 6. Single COD crystals observed in the urines of subjects with prior histories of stone formation who had been advised to increase their fluid intakes. Note the relatively small size of the crystals (cross sections 10–20 µm) and the absence of COM deposits as well as crystal aggregates. Magnification ×1,060

Fig. 7. Cleaved surface of the solitary stone available for analysis. EDX showed the presence of calcium only, indicating oxalate as the stone type. Magnification ×1,750

Fig. 8. COM and COD crystals entrapped in urinary mucoid material. Magnification ×2,500

Fig. 9. Large aggregate (cross section 65 µm) of COM and COD crystals held together by urinary mucoid material. Magnification ×1,250

seen to bind crystals into small conglomerates (Fig. 8) or gigantic aggregates (Fig. 9). A similar binding role has been proposed for the organic matrix observed in urinary and other calculi [1, 5]. Mucoid deposits were not detected in the urines of the other five subjects, nor have they been a common observation in our studies of the urine of marathon runners. This again is indicative of different stone-forming mechanisms within these two groups. Thus, while it is reasonable to hypothesize that stone formers may produce mucoidal substances with strong crystal binding characteristics and that these substances play a key role in crystal aggregation, it seems unlikely that this occurs in marathon runners as well. The increased risk of stone formation in the latter is possibly due to other factors such as dehydration and physical trauma, as expounded in our earlier papers [2, 6]. Neither of these factors appears to produce significant quantities of mucoid material. Thus, although we have not examined the urines of any of our subjects after a period of sedentary (i.e. non-training) activity, intergroup comparison of the above-mentioned crystalluric features in both the non-stone-forming and the stone-forming runners *as well as in the controls,* nevertheless shows important differences. Therefore, it seems reasonable to suggest that whereas stone formers may be at *chronic* risk due to pathological factors, marathon runners may be subject to *acute* risk of stone formation due to factors associated with long distance running per se.

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