Urol Res (1988) 16:89–93

Urological Research

Crystalluria in Marathon Runners

II. Ultra-Marathon – Males and Females

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Accpeted: July 1, 1987

Summary. Particle-volume size distribution curves for the urines of a group of male ultra-marathon runners have been recorded and show the same features as those reported in an earlier study involving standard marathon runners. It is again suggested that these features indicate risk of urinary stone formation although this does not appear to be increased by the more stressful ultra-marathon. Distribution curves obtained for female runners closely resemble those recorded for controls, thus rendering it impossible to assess their risk profile. A commonly observed feature of both the male and female urines was the presence of various urinary salts. Profuse calcium oxalate dihydrate crystals were detected in some samples 11 days after the race. It is suggested that entrapment sites within the urinary tract have a selective specificity for these crystals while urinary salts pass through unhindered.

Key words: Ultramarathon – Crystalluria – Dehydration – Stone formation risk – Entrapment specificity

Introduction

In a previous study [3], we subjected urine samples from a group of male marathon runners to particle counting and sizing in a Coulter Counter. The volume-size distribution curves so obtained were distinctly different to the distribution patterns recorded for control subjects but remarkably similar to those reported for recurrent idiopathic stone formers. Morphological features of the runners' crystalluria were also found to resemble closely those of stone formers. We concluded that marathon runners are at risk of urinary stone formation.

The present study was undertaken to examine this phenomenon further. Because dehydration and urinary tract trauma were cited as possible causative factors [3], we decided to investigate a group of runners participating in an ultramarathon in which these factors were likely to be intensified. Female subjects were also studied. The particular event chosen was the 90 km Comrades Marathon, possibily one of the most gruelling ultra-marathon running events in the world.

Materials and Methods

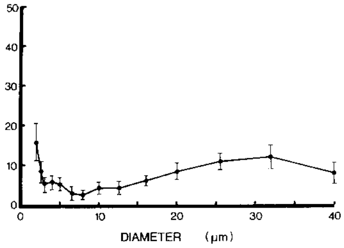
Seven male and four female ultra-marathon runners between the ages of 22 and 40 years volunteerred to participate in the study. None had a history of urolithiasis and all were experienced runners whose training schedule prior to the race involved running 40–160 km per week. Nocturnal urine samples were collected from the male subjects on days –10, –7 and –3 prior to the race and on days +4 and +11 after the race and from the female subjects on days –3, +3 and +11.

All urine specimens were collected in preheated thermos flasks and were subjected to analysis within 3 h of voiding. Particle size-distributions, scanning electron microscopy and statistical analyses were performed as previously described [3].

Results

Particle Volume-Size Analysis

Volume size distribution curves for both groups were obtained by plotting Vd against d where Vd is the volume of crystals of diameter d (μm). The mean distribution profiles (males) for the pre-race (days –10, –7 and –3) and post race (day +11) urines are shown in Figs. 1 and 2 respectively. Both curves are binodal with the first peak occurring at a particle diameter of 2.5 μm. The second node is not as sharp and is spread over a wide diameter range (15–40 μm) in the pre-race urines and over a slightly narrower range in the post-race samples (18–32 μm). Maxima are attained at diameters of 32 and 25 μm respectively. Although the particle size distribution profile for day +4 urines is not presented here, we report that a tri-nodal curve was recorded with peaks occurring at diameters 4, 10 and 25 μm. Despite the appearance of an extra peak in this curve the



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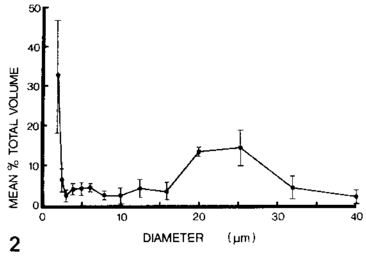

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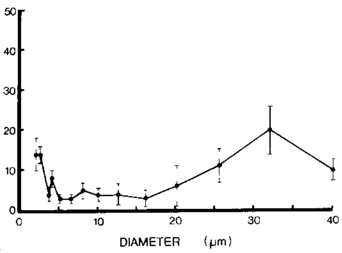

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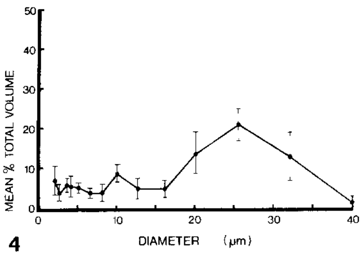

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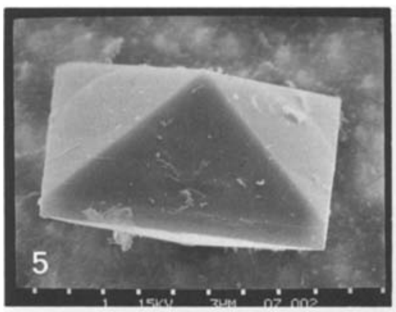
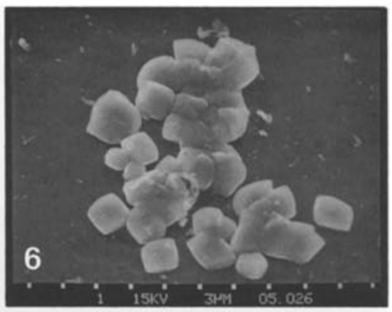
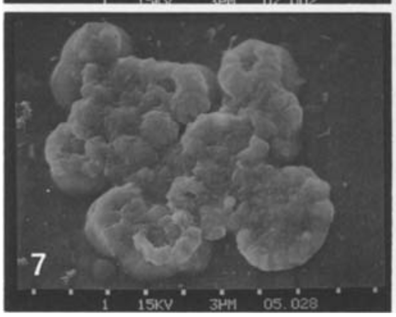
Figs. 1–4. Mean volume-size distribution curve (+ SEM) Fig. 1. For 7 male ultra-marathon runners' urines (days −10, −7 and −3). Fig. 2. For 7 male ultra-marathon runners' urines (day +11). Fig. 3. For 4 female ultra-marathon runners' urines (day −3). Fig. 4. For 4 female ultra-marathon runners' urines (day +3)







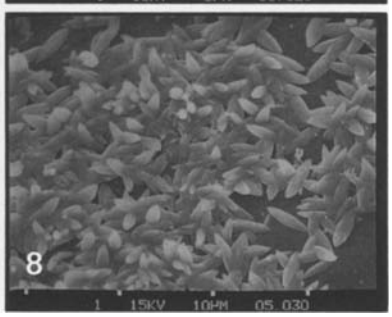


Fig. 5. Large COD crystal occassionally observed in male pre- and post-race specimens (note cross section 25 µm; mag 2,130x)

Fig. 6. Urinary salt deposits typically observed in male runners' urine samples; elemental composition Na, S, K, (Cl) (note small cross section ~3 µm; mag 4,620x)

Fig. 7. Urinary salt deposits and/or epithelial debris typically observed in male runners' urine samples; elemental composition Na, S, K (mag 4,620x)

Fig. 8. Urinary salt deposits typically observed in male runners' urine samples; elemental composition Na, S, K. (note small size of individual entities, ~5 µm; mag 2,130x)

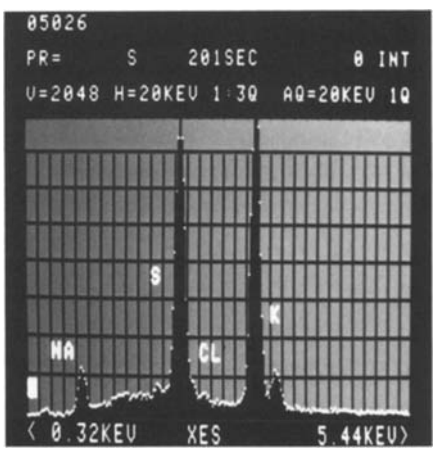


Fig. 9. Energy dispersive X-ray analysis spectrum recorded for the deposits shown in Fig. 6

latter was somewhat flatter than those shown in Figs. 1 and 2 with a more even distribution of particle sizes over the entire diameter range.

The distribution curves for the female pre- (day −3) and post- (day + 3) race urines are shown in Figs. 3 and 4 respectively. Both curves have a major peak in the large diameter range (30 and 25 µm respectively) as well as a smaller one at a diameter of 3–5 µm. In addition, the post race urine curve has a moderate peak at a diameter of 10 µm.

Scanning Electron Microscopy (SEM) and Energy Dispersive X-Ray Analysis (EDX)

Very few recognizable crystals were observed in the pre and post-race urines of the male runners. Occasionally large

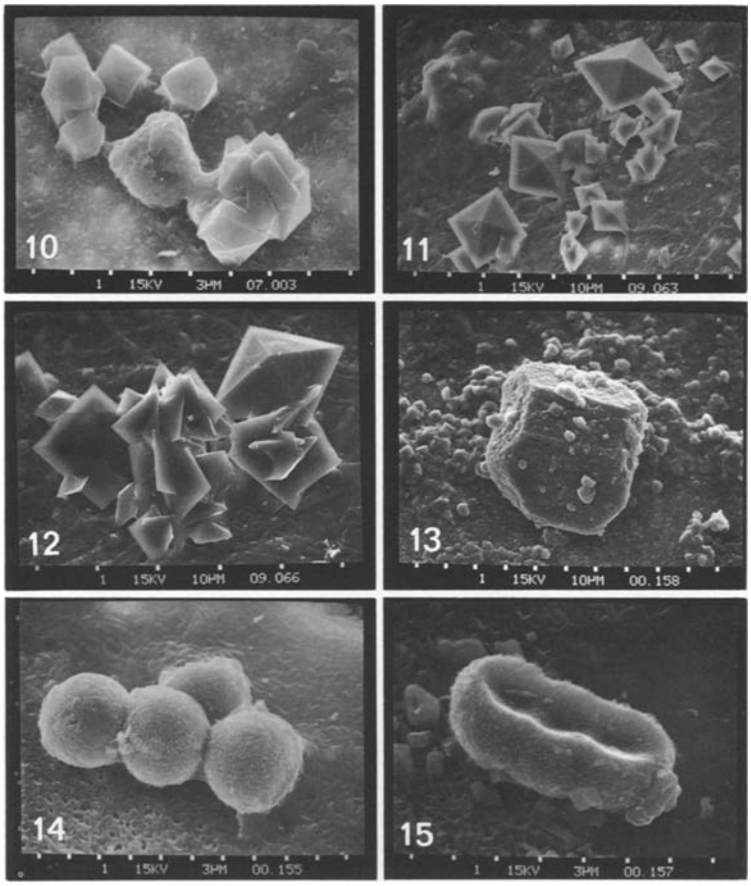


Fig. 10. COD crystals covered in mucoid material containing Si (mag 1,320x)

Fig. 11. COD crystals typically observed in two female ultra-marathon runners' urines on day +11 (note variation in crystal sizes; mag 910x)

Fig. 12. Aggregate of COD crystals typically observed in two female ultra-marathon runners' urines on day +11 (note cross-section ~50 μm; mag 1,320x)

Fig. 13. Large struvite crystal typically observed in the urine of one female ultra-marathon runner (note adhering apatite spherules and tiny COD crystals. Cross section of struvite crystal 55 μm; mag 70x)

Fig. 14. Spherular aggregates of tiny hair-like apatite crystals typically observed in same sample as Fig. 13 (mag 2,380x)

Fig. 15. "Onion-ring" deposit typically observed in same sample as Fig. 13 (mag 3,370x)

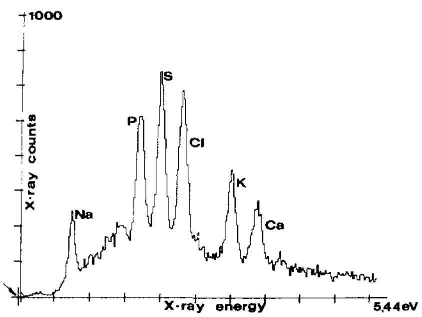


Fig. 16. Energy dispersive X-ray analysis spectrum of deposits shown in Figs. 14 and 15. Ca and P indicates presence of apatite; other elements indicate urinary salts

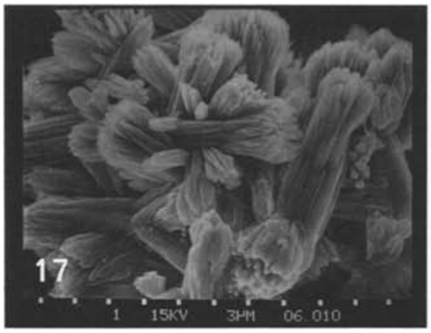
calcium oxalate dihydrate (COD) crystals occurred (Fig. 5) but these were rare. Deposits of epithelial debris and/or urinary salts displaying various morphologies were common. These particles generally contained Na, S and K only, but other elements such as P and Cl were sometimes present as well. Examples are shown in Figs. 6–9. In 2 subjects, Si was detected in mucoid deposits (Fig. 10).

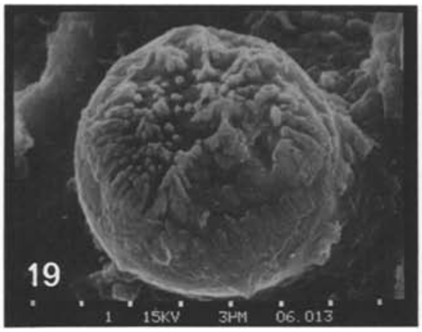
Profuse deposits of single and aggregated COD crystals were observed in 2 of the female subjects 11 days after the race. The single crystals were typically of diameter 20–25 μm (Fig. 11) but crystals in the smaller size ranges also occurred. Aggregates and clusters had cross-section dimensions of 40–50 μm (Fig. 12). Deposits containing Si were also observed in one of these urine samples.

Our third female subject had several very large struvite crystals in the 30–80 μm size range (Fig. 13). In addition, two morphologically distinct deposits were also observed in the urine samples of this runner. The first of these are the spherical bodies shown in Fig. 14. These concretions were of diameter 8–12 μm and occurred in clusters measuring approximately 25 μm in cross-section. Single, "unclustered" entities were not observed. An example of the second type of unique-looking deposit is shown in Fig. 15. These had an onion-ring appearance and measured about 18 μm in diameter. Both kinds of deposit were found to have the same elemental composition – Na, P, S. Cl, K, Ca (Fig. 16).

The urine samples of the fourth female subject were generally featureless. Non-descript, epithelial debris was observed but there were no crystals.

It is of some interest to note that the nature of the crystalluria in the two female subjects who had profuse COD deposits on day +11, was distinctly different on day +4. COD crystals were absent in urine samples collected on this day. Instead, deposits rich in K and S (with trace amounts of Na) were commonly observed (Figs. 17 and 18). In addition, spherules also having this elemental composition were observed (Fig. 19). Deposits as shown in Fig. 20 were also common. The block-like entities were found to contain





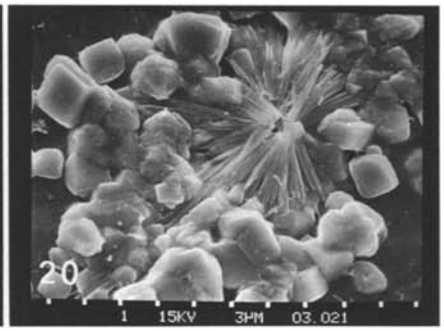


Fig. 17. Deposits observed in female ultra-marathon runners' urine on day +4 (mag 1,480x)

Fig. 18. Energy dispersive X-ray analysis spectrum of deposits shown in Fig. 17 (note trace amount of Na)

Fig. 19. Spherular deposit observed in female ultra-marathon runners' urine on day +4; same elemental composition as deposits shown in Fig. 17 (mag 3,330x)

Fig. 20. Block-like and "spiky" crystals observed in female ultra-marathon runners' urine on day +4. Both types contain Na, K and S but latter contains Ca as well (mag 3,330x)

K, S and Na (the latter in somewhat higher concentrations than in Figs. 17 and 19) while the elemental content of the spiky deposits (Fig. 20) was identified as K, S, Na *and* Ca.

Discussion

The particle volume-size distribution curves for the male ultra-marathon runners display the same features (binodal, peaks at 2, 5 and in the range 25–35 μm) as those of the standard marathon runners [3]. As has been highlighted in our earlier paper [3], such distributions are characteristic of idiopathic stone formers. The present study using a new group of subjects under different race conditions has therefore confirmed our earlier results. Moreover, it appears that the intensified effects of dehydration and urinary tract trauma experienced by runners during the ultra-marathon race do not produce any significant changes in the nature of their crystalluria relative to those recorded after the standard marathon. Since our hypothesis of urinary stone risk is based on these features, the results of the present study suggest that there is no greater risk associated with participation in the more gruelling ultra-maraton.

While the pre- and post-race distribution curves have the same general shape, they are nevertheless different. The small and large particle peaks are better defined in the latter, the pre-race curve displaying a somewhat flatter distribution. These differences probably arise from the fact that the pre-race urine samples were collected during the rest period following several months of intensive training while the post race urines were collected in the rest period following the more gruelling race itself. Since the running of the ultra-marathon is likely to have imposed far greater stress on the subjects than the training, it is not unreasonable that different curves are obtained. The distribution features noted under *Results* for day +4 probably reflect an intermediate stage in the voiding of crystalluric particles, a process which appears to continue for at least 11 days after the event itself.

Attention has already been drawn to the remarkable difference in particle distribution curves recorded for control males and females [6]. Since the female control curves are characterized by a large peak at 25 μm [6], it is obvious that the risk criterion for stone formation as formulated both by Robertson in his study of *male* idiopathic stone formers [5] and by ourselves in our study of *male* marathon runners [3] cannot be applied to female subjects. Nevertheless, the curves obtained for our female runners deserve comment. The post-race distribution closely resembles that reported for female controls [6]. However, while the pre-race curve has the same general shape, its large peak occurs at a diameter of 32 μm (as opposed to 25 μm in controls and post-race samples). We are unable to comment as to whether this is singificant or not. However the results of the present study show that marathon running has no effect on the size distribution of crystalluric particles in female runners as it does in males. Obviously, the question of stone forming risk in female marathon runners can only be properly addressed when size-distribution curves for female idiophatic stone formers are available for comparison.

SEM investigations of the ultra-marathon runners' urines did not reveal as many crystals as were observed in our previous study [3], although when present (Fig. 5) these were of similar dimensions. The deposits shown in Figs. 6 to 8 could be epithelial debris and/or urinary salts. Entities having similar elemental compositions were reported in our earlier paper [3].

The observation of profuse single and aggregated COD crystals in two of our female runner's urines 11 days after the race is significant. In an earlier study involving white female control subjects [6], crystals were rare. It therefore appears that the presence of these crystals is a consequence of the marathon. That the crystals were absent on day +4 indicates some type of delay in their voiding, possibly due to their being temporarily trapped at various sites within the urinary tract. Such sites probably arise as a result of epithelial sloughing during the race itself.

We believe that the presence of struvite crystalluria in one of our female subjects is unrelated to the marathon. Crystals of this type are commonly associated with urinary tract infection [1]. It is therefore likely that such an infection arose in the subject shortly before or just after the race. The spherical bodies observed in this specimen (Fig. 14) are probalbly conglomerates of tiny hair-like apatite crystals. Apatite is invariable present in struvite calculi where it occurs as spherular aggregates of diameter 2–10 μ [7]. In the present study, elemental analysis indicates contamination of these spherules by various urinary salts. The onion-ring entity (Fig. 15) might be a partially formed aggregate of these spherules. Indeed, it closely resembles a similar looking apatite structure reported by Werness [9].

The presence of Si in the urinary depostis of several subjects could arise from either of two possible sources. Firstly, since urine contains silicate (as SiO_2, mean excretion 17 mg/24 h) [8], dehydration could lead to its deposition. Secondly, long term magnesium trisilicate ingestion (for esophagitis or indigestion) has been reported as a cause of Si calculi [2, 4], thereby suggesting that our subjects might have been treating themselves with such preparations.

A commonly observed feature of the male and female urines was the presence of various urinary salts (Figs. 6–8, 17, 19, 20). It is tempting to suggest that this is indicative of dehydration in the subjects concerned. However, the absence of well known, low solubility, urinary crystals (e.g. COD) in such samples appears to contradict this idea. A possible explanation might lie with the crystal entrapment theory which we discussed in our previous paper [3]. We now suggest that calcium oxalate and other crystals become attached at various sites in the urinary tract, only to become dislodged and voided at a later stage. Urinary salts on the other hand pass through the tract unhindered, perhaps because of their relatively smaller sizes. It is therefore suggested that entrapment sites might have a preferential specificity for calcium oxalate urinary crystals.

Acknowledgments. We wish to record our thanks to the University of Cape Town and South African Medical Research Council for the award of research grants. We are extremely grateful to the Plant Protection Research Institute (Stellenbosch) for the loan of the Coulter Counter as well as Coulter Electronics SA (Pty) Ltd through whose good offices the loan of the instrument was made possible. All SEM studies were conducted in the Electron Microscope Unit of the University of Cape Town.

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