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Crystalluria in marathon runners

IV. Black subjects

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Summary. Crystal sizes (scanning electron microscopy) and distributions (Coulter Counter) as well as 24-h urinary sodium (Na) and calcium (Ca) excretions (flame atomic absorption) were determined in a group of black South African runners immediately after a marathon and again 3 weeks later. White runners and black and white control subjects were included in the study. Particle volume-size histograms for black controls and black runners were identical. There was no significant difference in the Na excretion of all the groups. However, while urinary Ca excretion was significantly raised in white runners relative to white controls, Ca excretion in black runners was unchanged relative to their controls. It is postulated that the lower rates of urinary Ca excretion may result from lower rates of Ca resorption from bone in response to the cyclical loading of running in black marathon runners. The results of this study suggest that black marathon runners are not prone to the same increased risk of renal stone formation as are white runners.

Key words: Black runners – Stone formation – Raised urinary calcium

The occurrence of urinary calculi in South African blacks is extremely rare [1, 5, 8]. For example, during the 9-year period 1971–1979, 1 in 510 white patients admitted to Groote Schuur Hospital, Cape Town, had a renal stone as compared with 1 in 44,298 blacks [8]. Studies conducted some years ago showed that South African blacks have relatively low rates of urinary calcium (Ca) excretion, but relatively high rates of sodium (Na) excretion [7]. It was suggested that this provides a natural protective mechanism against Ca renal stone formation as the Na^+ ions compete successfully with Ca^{2+} ions for lattice positions and preferentially form soluble Na salts (e.g. Na oxalate) which are excreted harmlessly in the urine [7]. More recent studies involving ten calculi obtained from black patients over a 5-year period revealed similar ultrastructural features to those observed in stones obtained from white patients [12]. This prompted the authors to suggest that when stone formation *does* occur in black subjects, it results from the same physico-chemical mechanisms as in other race groups.

In previous studies we have shown that white marathon runners may be at increased risk of urinary stone formation [3, 13] and that the mechanisms initiating stone formation and subsequent growth in this group are different from those occuring in "natural" stone formers [14]. In the latter study it was concluded that whereas pathological factors increase the chronic risk of stone formation in sedentary persons, marathon runners may be at acute risk of urinary stone formation as a direct result of factors associated with long distance running itself.

Since most of the elite marathon runners in South Africa are black and hence would be expected to be naturally at low risk of renal stone formation, it is of some interest to establish whether long distance running alters this risk by producing similar urinary risk indicators in black runners as it does in whites.

Materials and methods

Twenty-four-hour urine samples were collected in polythene bottles containing no preservatives from 12 male black control subjects (ages 18–67) and 14 male black marathon runners (ages 19–40) during the period immediately following the completion of a 42-km marathon footrace ("A" subjects). These samples were analysed for Na and Ca using a Varian-1275 (Australia) model flame atomic absorption spectrometer. Similar collections and analyses were conducted on the urine of 16 white controls and 16 white marathon runners.

Nocturnal urine samples from 4 black controls, 2 black marathon runners, 3 white controls and 4 white marathon runners were also collected in pre-heated thermos flasks 2 days after the particular event. These were divided into two fractions. The first was subjected to scanning electron microscopy (SEM). Although sample preparation was as previously described [3], a Cambridge (Cambridge, UK) S200 scanning electron microscope was used in the present study instead of the S180 as before. The former allows specimens to be viewed and photographed only.

The second fraction was subjected to particle size analysis, but whereas a model TA II Coulter Counter with a population acces-

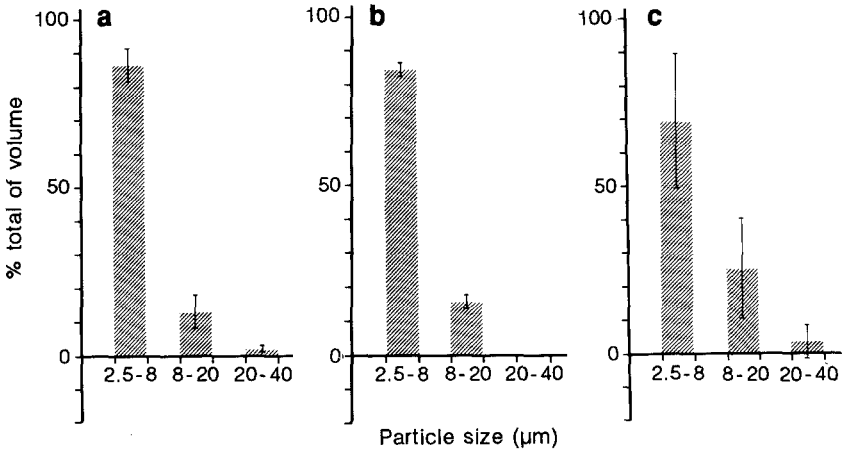


Fig. 1 a-c. Particle volume-size histograms for urines of black subjects. Data from: **a** 4 black controls, **b** 2 black runners recorded 2 days after a marathon and **c** 2 black runners recorded 3 weeks after the marathon

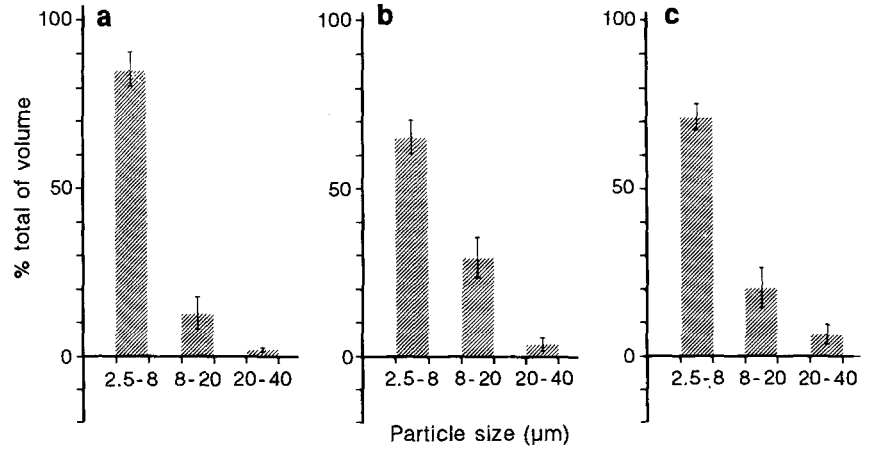


Fig. 2 a-c. Particle volume-size histograms for urines of white subjects. Data from: **a** 3 white controls, **b** 4 white runners recorded 2 days after a marathon and **c** 3 white runners recorded 3 weeks after the marathon

sory unit was used previously [3], a ZM Coulter Counter (Bedfordshire, UK) was used in the present study. This necessitated implementation of a different counting procedure. Particle counting was undertaken in small steps to an upper diameter limit of 25 μm while particles in the range 25–40 μm were determined in one count.

In order to investigate the delayed effect, if any, of marathon running on crystalluria, a follow-up study was conducted 3 weeks after the marathon. Both black and white runners participated ("B" subjects). For the Na and Ca determinations, 12 of the original white and 6 of the original black runners were included, while 3 of the original white and 2 of the original black runners participated in the SEM and Coulter Counter analyses.

Statistical methods were used to analyse the urinary Na and Ca values [15]. Independent groups, [i.e. white and black controls, runners (A) and runners (B)] were compared using two-way analysis of variance. Measurements of groups with repeated observations were subjected to profile analysis. Box-plots were used to depict graphically the distribution of Na and Ca excretion values.

Results

Particle volume-size analysis

The volume-size distribution histograms for black controls (Fig. 1a) and black marathon runners ("A") (Fig. 1b) showed no significant differences. Most particles occurred in the size range 2.5–8.0 μm. The histogram for the follow-up study was very similar except that crystals in the size range 20–40 μm were detected (Fig. 1c). The corresponding histograms obtained for the white runners are shown in Fig. 2.

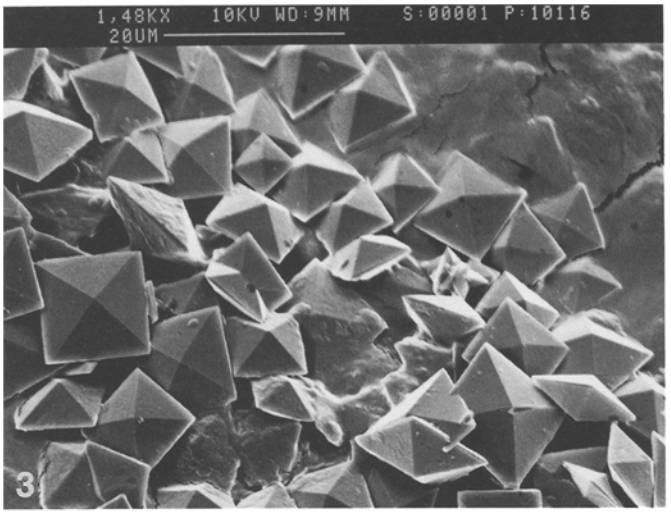
Scanning electron microscopy

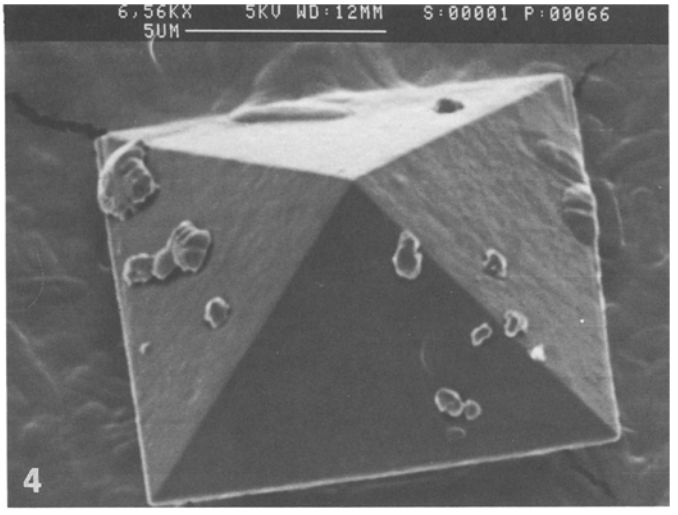
Of the 4 black controls whose urines were examined by SEM, 2 showed the presence of Ca oxalate dihydrate (COD) crystals, one such sample having profuse deposits of average size approximately equal to 10 μm (Fig. 3), while the other was less populated and had much smaller crystals in the size range 3–5 μm.

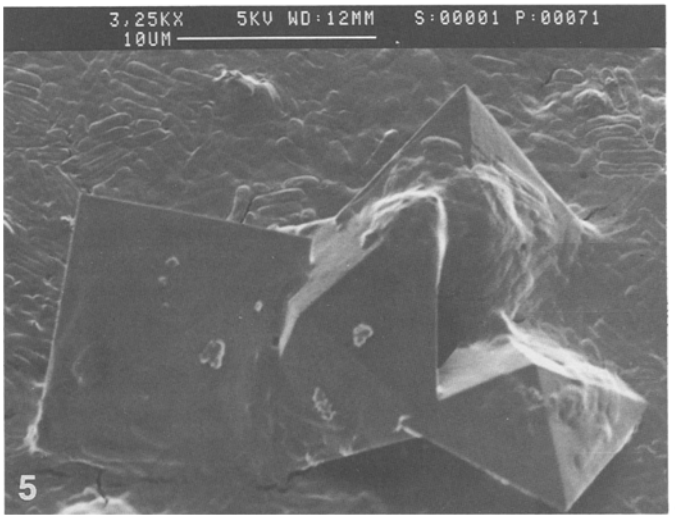
The urines from the black marathon runners displayed varying amounts of COD deposits. In the first group of urines collected 2 days after the marathon, the typical size of single COD crystals was approximately equal to 10 μm (Fig. 4) but aggregates in the size range 10–20 μm were also observed (Fig. 5). In one sample, COD crystals displaying prismatic morphology were detected (Fig. 6). A coating of unknown nature was observed on these deposits. In the follow-up study, 3 weeks after the marathon, larger COD crystals (cross-section approx 30 μm) were observed (Fig. 7).

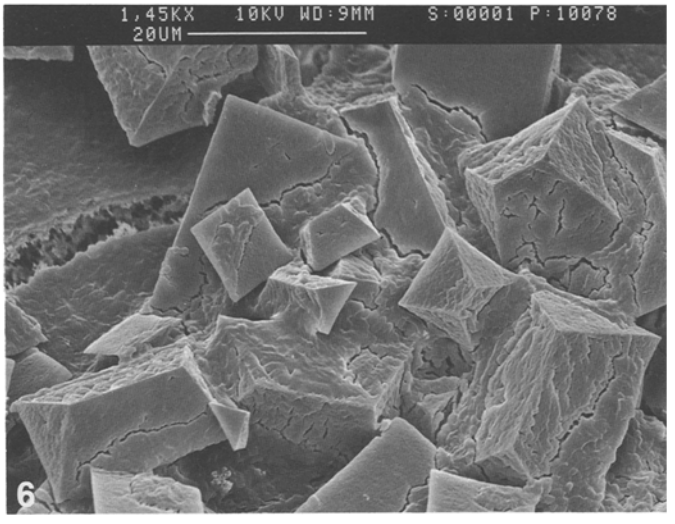
Statistical analysis of urinary Na and Ca excretion

The descriptive statistics for the rates of Na and Ca excretion (mmol/24 h) are given in Tables 1 and 2 respect-









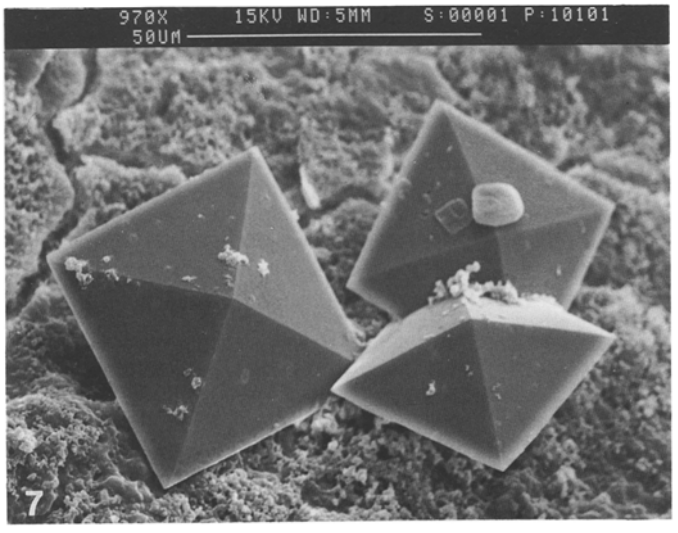


Fig. 3. Ca oxalate dihydrate (COD) crystals observed in the urine of one of the black controls. (Note average size approx. 10 μm)

Fig. 4. Typical COD crystal observed in the urine of black runners 2 days after a marathon. (Size approx. 10 μm)

Fig. 5. Typical aggregate of COD crystals observed in the urine of black runners 2 days after a marathon. (Size approx. 20 μm)

Fig. 6. Prismatic COD crystals observed in the urine of one black runner 2 days after the completion of a marathon. Note that the crystal faces are not "clean" but are covered with an unknown coating

Fig. 7. Typical COD crystals observed in the urines of black runners 3 weeks after the marathon. Note that crystal sizes (approx. 30 μm) are larger than those occurring 2 days after the race (Fig. 4)

ively. These data are graphically depicted in the box-plots shown in Figs. 8 and 9 respectively. In a two-way analysis of variance with marathon running and ethnic group as the two factors, there were no significant effects for Na values ($P = 0.7446$). However, there was a significant interaction between marathon running and ethnic group for Ca values ($P = 0.0197$). This is shown in Fig. 9. White controls have significantly higher rates of Ca excretion than black controls with an estimated difference of 2.07 mmol/24 h (SE = 0.79, $P = 0.0086$). The same is true for white runners compared to black runners; here the estimated difference is 4.60 mmol/24 h (SE = 0.76,

Table 1. Descriptive statistics for Na excretion (mmol/24 h)

Group	*n*	Mean	Standard deviation	Minimum value	Maximum value
Black controls	12	96.41	70.01	16.60	192.60
White controls	16	125.69	85.56	23.00	258.70
Black runners	14	109.52	72.76	28.10	242.30
White runners	16	122.02	73.31	45.10	313.20

No significant differences between groups

Table 2. Descriptive statistics for Ca excretion (mmol/24 h)

Group	*n*	Mean	Standard deviation	Minimum value	Maximum value
Black controls	12	1.75	1.49	0.19	4.16
White controls	16	3.82*	2.78	0.46	8.25
Black runners	14	1.70**	0.95	0.14	4.35
White runners	16	6.29	2.02	3.80	10.00

* $P < 0.01$ for black controls versus white controls; ** $P < 0.001$ for black runners versus white runners

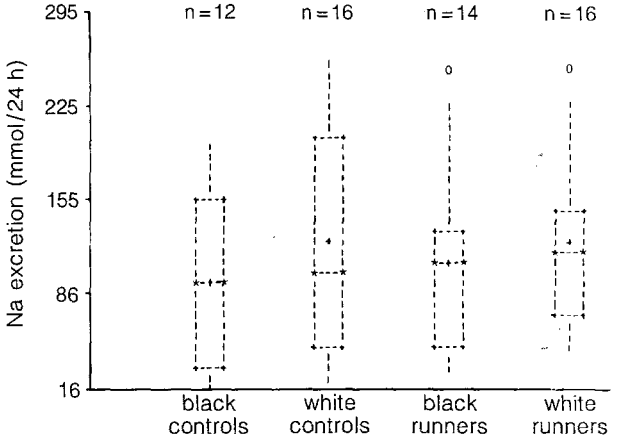


Fig. 8. Box-plots for 24-h urinary Na excretion

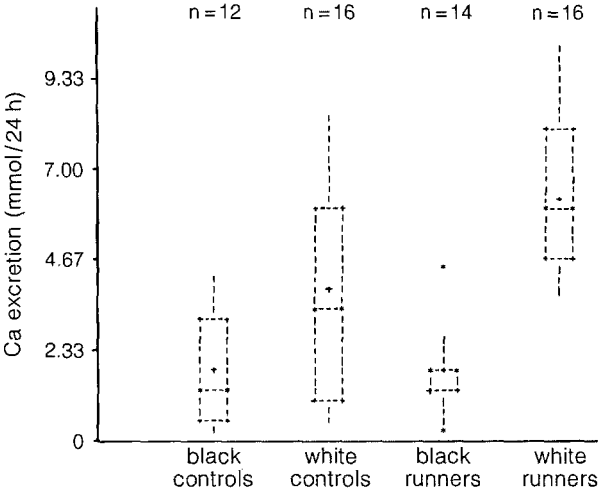


Fig. 9. Box-plots for 24-h urinary Ca excretion

$P = 0.0001$). The comparison of white controls versus white runners shows a significant increase in the mean rate of Ca excretion for the latter group (estimated increase = 2.48 mmol/24 h, SE = 0.74, $P = 0.0052$), whereas in the black groups there was no significant difference between runners and controls (estimated difference = −0.05 mmol/24 h, SE = 0.82, $P = 0.9484$).

In order to establish whether marathon running had any delayed effects on urinary Na or Ca excretion and, if so, whether the effects within the two ethnic groups were different, a repeated measures analysis was performed using rates of urinary Na and Ca excretion determined immediately after and 3 weeks after participation in a marathon. The analysis was limited to those runners for whom data were available for both time periods. The descriptive statistics for the rates of Na and Ca excretion are given in Tables 3 and 4 respectively, while the box-plots in Figs. 10 and 11 depict the data graphically. The analysis showed that there was no significant interaction between ethnic group and time for Na excretion rate ($P = 0.6127$), i.e. the effect of time on the mean Na excretion rate was identical in both groups. Since the profiles are parallel, the actual effect of time was tested using all the Na excretion rates irrespective of ethnic group and was found to be non-significant ($P = 0.8780$), indicating that the time delay of 3 weeks did not affect the mean Na excretion rate in either group. Similar results were obtained for Ca, i.e. there was no significant interaction between ethnic group and time ($P = 0.1579$), nor did significant changes occur within either group over the 3-week period ($P = 0.3441$). As fas as ethnic group comparisons are concerned, the mean Na excretion rate

Table 3. Descriptive statistics for Na excretion (mmol/24 h) immediately after (A) and 3 weeks after (B) participation in a marathon

Group	*n*	Mean	Standard deviation	Minimum value	Maximum value
Black runners (A)	6	130.70	77.79	44.90	219.00
Black runners (B)	6	123.88	82.76	62.70	268.90
White runners (A)	12	132.58	81.40	45.10	313.20
White runners (B)	12	145.30	72.28	53.00	271.60

No significant differences between groups or over time

Table 4. Descriptive statistics for Ca excretion (mmol/24 h) immediately after (A) and 3 weeks after (B) participation in a marathon

Group	*n*	Mean	Standard deviation	Minimum value	Maximum value
Black runners (A)	6	2.10	1.22	0.71	4.35
Black runners (B)	6	2.36	1.45	0.75	4.98
White runners (A)	12	6.25*	1.89	4.02	9.06
White runners (B)	12	4.99*	1.97	1.91	7.72

No significant time effect; *, $P < 0.001$ for white runners versus black runners

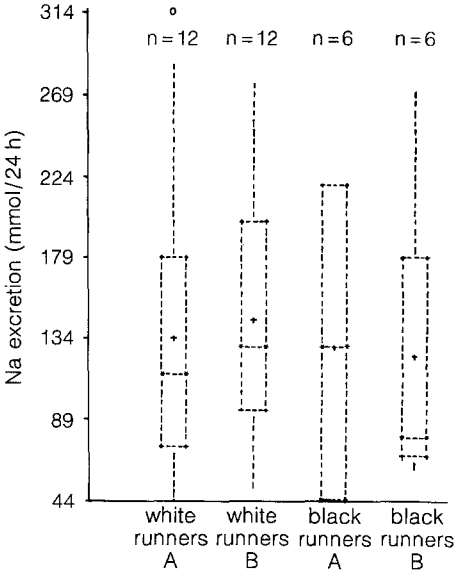


Fig. 10. Box-plots for 24-h urinary Na excretion immediately after (*A*) and 3 weeks after (*B*) a marathon

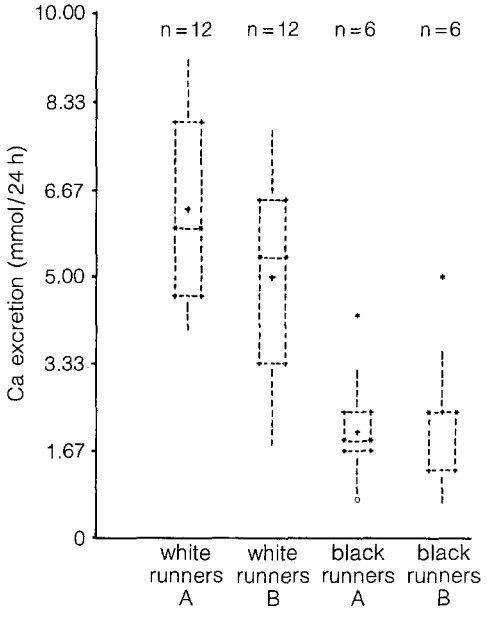


Fig. 11. Box-plots for 24-h urinary Ca excretion immediately after (*A*) and 3 weeks after (*B*) a marathon

was not significantly different ($P = 0.5466$), while differences in the Ca excretion rate were highly significant ($P = 0.0001$).

Discussion

The particle volume-size histogram for black controls (Fig. 1a) and its resemblance to that for white controls (Fig. 2a) is in agreement with the distribution curves reported by Rodgers and De Klerk [12]. In earlier studies we showed that the distribution curves for white controls and white runners were significantly different [3, 13]. As the runners' distribution curve resembled that for recurrent stone formers, it was concluded that runners may be at increased risk of renal stone formation.

In the present study, comparison of the histogram shown in Fig. 2a (white controls) with those presented in Fig. 2b and c (white runners) again shows significant differences. However, the volume-size histograms for black controls and black runners are not different (Fig. 1a and b, respectively). This suggests that black runners may not be prone to the same risk of renal stone formation as are white marathon runners. The detection of relatively

large particles in the follow-up studies of both black and white runners (Fig. 1c and 2c, respectively) might be indicative of a delayed effect in the voiding of such particles after a marathon. In our earlier study we suggested that crystals or debris or both could become entrapped at various sites in the urinary tract [3]. It seems reasonable to suggest that these particles might reside for long periods before being voided.

The SEM observation of COD crystals in the urines of black controls is surprising as it is contrary to the finding of Rodgers and De Klerk [12]. The crystals observed in the present study were in the size ranges 3–5μm and 8–12μm. This correlates well with the size distribution histogram of the present study (Fig. 1a), as well as with the size distribution curve reported by Rodgers and De Klerk [12] despite their failure to find crystals using SEM.

Although the particle size histograms for black controls and black runners were identical, SEM investigation showed differences with respect to crystal size. In particular, SEM revealed the presence of larger particles in the runners' urines. Since large COD crystals were not observed in the controls' urines, it seems likely that such crystals are a consequence of marathon running.

The unusual morphology of COD crystals observed in some urines deserves comment (Fig. 6). The commonly observed crystal habit of COD is bipyramidal (octahedral), as shown in Fig. 3. Prismatic morphology arises as a result of unequal growth rates of some of the faces. Slower growth rates might possibly be due to surface contaminants or certain special components in the urine which might inhibit growth along a certain axial direction, or both. Indeed, Fig. 6 shows an unidentified coating on prismatic COD crystals. Rodgers and De Klerk [12] have drawn attention to the presence of large amounts of deposited urinary salts in the crystalluria of black subjects and have suggested that these salts may play an inhibitory or protective role. It is suggested that the coating observed in Fig. 6 might be salt-like in nature and might have influenced the resultant morphology of the COD crystals.

The mean 24-h rates of urinary Na excretion in whites and blacks (runners and controls) are not significantly different and, with the exception of the value for black controls, fall within the "normal" range as reported by Hesse and co-workers [2]. This finding contradicts the result of Modlin [7], who reported significantly higher rates of Na excretion in blacks relative to whites. As the Na content of the extracellular compartment is tightly regulated, Na cannot be stored to any great extent in the body; thus the higher rates of urinary Na excretion in the black subjects studied by Modlin [7] would indicate only a higher daily dietary Na intake. As such, this would not represent a true racial difference in renal Na handling or whole body Na metabolism and therefore would not be expected to be present in all groups of black South Africans.

On the other hand, rates of Ca excretion, which also fall within the "normal" range [2], were significantly lower in the black subjects. McDonald and co-workers [6] have reported that exercise increases the rate of urinary Ca excretion. Our results for white marathon runners agree with this observation, but the effect is not apparent in black runners. Since elevated urinary Ca excretion is regarded as a risk factor for renal stone formation [11], the present values indicate that while white runners are at increased risk of urinary stone formation the same may not be true for black runners.

There are three possible explanations for the finding of low and unaltered rates of urinary Ca excretion in black marathon runners. Firstly, urine collection may have been suboptimal in black runners so that complete 24-h samples were not collected; secondly, the different rates of urinary Ca excretion between racial groups may be the result of different habitual dietary Ca intakes; thirdly, there may be racial differences in Ca metabolism, possibly originating in different responses of bone to the cyclical loading imposed by running.

With regard to the first possibility, this could have been resolved by determination of renal creatinine clearance in all subjects. These were not obtained, partly because many subjects were unwilling to permit the drawing of venous blood samples necessary for determination of serum creatinine concentration.

However, an alternative cross-reference parameter might be the rates of urinary Na excretion. Since there were no significant differences in these rates for any of the groups, either before or after the marathon, it seems probable that the 24-h urine samples were complete in all groups. This question is currently being addressed.

The second possibility, namely that habitual dietary Ca intake differs between racial groups, can be determined by analysis of dietary patterns. But it seems unlikely that changes in habitual dietary Ca intake could explain the different urinary Ca excretion rates in white runners immediately after the marathon and 3 weeks later (Fig. 11). Indeed, dietary Ca intake in white runners has not been found to be increased and may be low especially in those with bone injuries [9, 10]. Rather, it would seem more probable that the marathon per se and chronic training increases urinary Ca excretion in white runners, but that this is without effect in black runners.

Therefore, the third possibility is that there are inherent racial differences in the response of bone to the cyclical loading imposed by training for and running in the marathon. Indeed, for some time there has been interest in the possibility that there may be subtle racial differences in bone metabolism [4]. For example, it is believed that the incidence of bone stress fractures as a result of physical activity is less in blacks than in whites [4]. The lower risk for the development of such fractures among blacks has been related to their relatively higher bone densities in conjunction with different activity levels or inherent racial traits, or both [4]. Thus it seems possible that black runners might have a higher bone mass which does not increase its rate of turnover in response to running. This intriguing possibility requires further study.

In contrast, it appears that a daily dietary Ca intake of up to 50% greater than the recommended daily allowance of 800 mg/day may be necessary to prevent bone injuries in physically active white males and females [9]. This would be compatible with an effect of exercise increasing bone Ca turnover selectively in whites.

The fact that the rates of urinary Ca and Na excretion determined immediately after the marathon were not significantly different to those recorded 3 weeks later is not surprising since most long distance runners are likely to maintain at least a minimum level of activity in the period immediately after a marathon and are likely to have resumed heavier training 3 weeks later. This point can be demonstrated by consideration of the results of McDonald and co-workers [6]. Their mean urinary Ca excretion rate in a group of controls was 163.3 ± 30.4 mg/day (4.1 ± 0.8 mmol/day) while that in a group of resting tri-athletes *prior* to exercise was 245.8 ± 93.0 mg/day (6.1 ± 2.3 mmol/day).

In conclusion, our previous studies showed that white male marathon runners may be at increased risk of renal stone formation [3, 13]. Two causal factors were postulated - dehydration and physical trauma to the urinary tract. In the present study, we have identified a third factor which is likely to increase the overall risk in white runners, that is habitually increased rates of urinary Ca excretion. In addition, the present study has also provided evidence that black runners are not prone to the same increased risk of renal stone formation as are white runners. Whilst the mechanisms explaining this finding are presently unknown, this observation highlights the apparent phenomenon of increased immunity to renal stone disease enjoyed by black South Africans.

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