URINARY CALCULI AND SERUM CALCIUM LEVELS IN AFRICANS AND INDIANS

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Among the White, Indian and Coloured people in South Africa the incidence of urinary calculus formation is similar to that in Europe. In the African population the disease is rare; this has been confirmed by several observers.[9-12]

In an analysis of over 1,000,000 records in African mine-workers, Orenstein[12] found only 1 case in which a clinical diagnosis of a renal calculus had been made. Vermooten[16] analysed the admissions to the Johannesburg Non-European Hospital from 1922 - 1935 and found only 4 cases in 91,000 admissions. Only 1 of these was in an African, a woman in whom a ureteral calculus was suspected but never proved.

Lopis and Kaplan[9] recorded the first proved case in 1948 in an African, a Shangaan born in Beira. Muskat[11] recorded 2 further cases in 1951. One was a Rhodesian-born African and the origin of the other patient was not stated.

In 1957 Politzer and Beuchat[13] reported the case of a Shangaan male patient from Portuguese East Africa with vesical calculi. Gelfand,[5] discussing Rhodesian Africans, stated that calculi do occur but gave no clinical details.

It is noteworthy that to date most recorded calculi in Africans have occurred in those originating north of the Union's borders, where calculi appear to be more common.

In King Edward VIII Hospital, Durban, the records of all Africans admitted from 1 January 1951 to 30 June 1959, a period of 8½ years, have been analysed. Of 483,450 admissions there were 7 cases of urinary calculi in locally-born Africans, all men. This represents an incidence of 0·0014%. By way of contrast, out of a total of 9,600 Indian admissions in 1 year, there were 12 cases of proved calculi representing an incidence of 0·125%.

Serum-calcium levels were estimated in control groups of White, African and Indian patients. The method of estimation was that of Bett and Fraser,[1] using the fluorescent dye 'calcein' and titrating with E.D.T.A. The estimations were undertaken by one technician well versed in the technique, and each estimation was duplicated using standard solutions checked before use. Mixed batches of sera from all groups of patients were estimated simultaneously for calcium levels on the particular day, and therefore it is unlikely that any differences are due to differences in technique from day to day.

The serum-calcium levels of the following groups of patients were estimated:

(1) Indian patients with renal or ureteric calculus, (2) three African patients with vesical calculus, (3) Africans recumbent for some weeks for incidental diseases other than renal, and (4) African paraplegics (Table 1).

In addition, serum-mucoprotein levels were estimated using the turbidimetric method of De la Huerga *et al.*[6] in which the entire mucoprotein complex is measured.

The following are the case records of the 7 African males in whom urinary calculi were diagnosed between 1 January 1951 and 30 June 1959.

CASE RECORDS

Case 1

J.Y., African male (Zulu), aged 69 years. Admitted 3 July 1951, complaining of difficulty with micturition for many years and a recent urethral bleeding episode — about a cupful of blood not mixed with urine. Cystoscopy revealed sand-patches of bilharziasis and several small vesical calculi. No analysis of these was done.

Case 2

A.N., African male (Zulu), aged 25 years. Admitted 28 March 1953, having fallen from the roof of a house and sustained compression fractures of D12 and L1 vertebrae with paraplegia. A laminectomy and suprapubic cystostomy were performed with insertion of a de Pezzer catheter.

While in a wheel-chair, 3¼ years later, he was struck by a motor car, sustaining fractures of his pelvis and left femur. The X-ray of the pelvis revealed a large vesical calculus which was subsequently removed by cystostomy on 4 February 1957.

Case 3

M.C., African male (Zulu), aged 37 years. Admitted 4 March 1955, having been run over by a lorry. He was extremely shocked and had bilateral fractures of both horizontal and descending pubic rami and a rupture of the membranous urethra. After resuscitation, a laparotomy was performed and an indwelling urethral catheter and a suprapubic de Pezzer catheter were inserted. On 22 July 1955 a large periurethral abscess was drained.

Four months later he was re-admitted for urethral dilatation and on this occasion a vesical calculus was felt with the end of the urethral dilator. A vesical calculus was removed suprapubically shortly afterwards.

Although advised to return for urethral dilatations, he neglected to do so and his next admission was on 20 May 1958. This was to a medical ward for investigation of a pyrexia of unknown origin. Urine examination revealed pus cells +++++ and a growth of *B.coli* sensitive to polymyxin.

The blood urea was 36 mg. per 100 ml. An intravenous pyelogram (IVP) showed a bilateral hydronephrosis. The urinary infection was treated and, after subsequent admissions, he was transferred to the surgical wards for urethral dilatation. A repeat IVP on 7 October 1958 for upper abdominal pain revealed bilateral staghorn calculi. The blood urea was 45 mg. per 100 ml. On 11 November 1958 the right kidney was explored. The perinephric tissues were adherent and the surface of the kidney was studded with small abscesses. The stone was removed in pieces by pyelolithotomy and nephrolithotomy and the pelvis drained. It is planned to remove the other calculus shortly.

Case 4

M.D., African male (Zulu), aged 76 years. Admitted 5 May 1956 with acute retention of urine for 1 day. Straight X-ray of the pelvis revealed calcification of the bladder wall but, although urine examination revealed pus cells ++, no ova of *S. haematobium* were recovered. The prostate was normal on palpation.

He was re-admitted on 7 September 1957 complaining of dysuria. Straight X-ray of the pelvis revealed calcification of the bladder wall and several dense opacities. Cystoscopy was performed on 12 September 1957 when small vesical calculi were visualized. Some were crushed with a lithotrite and the remainder were removed on 18 September 1957 by suprapubic cystostomy.

Case 5

M.N., African male (Zulu), aged 70 years. Admitted on 28 January 1958 complaining of frequent difficult micturition for 2 months and inability to pass urine for 1 day. Investigations revealed a moderately enlarged prostate. Urine examination showed no pus cells and was sterile. An IVP revealed a

rounded calculus within the left kidney. Transvesical prostatectomy was performed for a fibro-adenomatous hyperplasia of the prostate. The calculus was not removed.

Case 6

Z.D., African male (Zulu), aged 45 years. Admitted on 24 March 1958 complaining of lower abdominal pain, frequency, difficulty with micturition, and perineal pain, for 5 months. When the prostate was palpated he voided urine containing threads of pus. The urine examination revealed pus cells +++ and a moderately heavy growth of *B. proteus* and *Ps. pyocyaneus*. Straight X-ray of the pelvis revealed a large opacity in the bladder. Subsequently a large vesical calculus was removed by suprapubic cystostomy.

Case 7

S.T., African male (Zulu), aged 59 years. This patient was first admitted on 12 October 1956 for investigation of frequency of micturition. On rectal examination the prostate felt normal to palpation. A stricture was found in the bulbous urethra and this was dilated. Cystoscopy revealed only some trabeculation of the bladder.

He was re-admitted on 31 July 1958. He then stated that following the urethral dilatation he was well for several months, but his initial complaints recurred and had increased in severity up to the time of his admission. In addition he had been unable to walk for a week. Examination showed that he had a paraplegia and chronic retention of urine with overflow. Investigation culminated in the removal of an intradural neurilemmoma at the level of D5 - D7. He was discharged, being able to walk again.

His next admission was on 5 May 1959 when he complained of dysuria. An IVP revealed bilateral hydronephrosis and a large filling defect in the bladder consistent with an enlarged prostate.

The blood urea was 24 mg. per 100 ml. Cystoscopy showed a bladder calculus, enlargement of the middle and both lateral lobes of the prostate and marked trabeculation. This was followed by transvesical prostatectomy and removal of the bladder calculus.

The stone was circular in outline and flattened from side to side. It weighed 300 mg. and was a dirty-white colour and firm in consistency.

DISCUSSION

Of the 7 African cases presented here, 1 appears to be a primary urinary calculus (case 6), since no predisposing factors could be found. In 4 of the remaining patients (cases 2, 3, 5 and 7), there was either prolonged recumbency or urinary obstruction, or a combination of both; while in the other two patients (cases 1 and 4), there was associated bilharzial infection of the bladder.

The problems of primary urinary calculi and the complication of recurrent calculus formation therefore seldom occur in the African.

Bilharziasis

The rôle played by bilharzial infection appears, in Africans, at any rate, to be of no major importance. Bilharziasis is endemic in the coastal belts of Natal. Dormer[4] found that 10% of all African school children investigated in Durban have active bilharziasis, which suggests that at any one time the greater part of the local African population is suffering from, or has suffered from, the ravages of this disease. Were it of major significance in calculogenesis more urinary calculi would undoubtedly be found.

On the other hand, urinary bilharziasis is as frequently seen, if not more so, in Indians. The incidence of primary urinary stone in these patients is not very different from that in White patients, while secondary stone formation, particularly ureteric calculus, associated with stricture of the ureter, is one of the commonest urinary diseases encountered.

Predisposing Causes

When calculi do occur in Africans the important predisposing factors are urinary obstruction and infection, and prolonged recumbency, usually due to paraplegia. It should be stressed, however, that all these conditions are common in the African surgical wards, yet urinary calculi are rarely found.

It is unlikely that the rarity of calculus in the African is due to any racial immunity; the American Negro, who springs from the same stock, displays no such immunity,[3] although there is a lower incidence in Negroes than in White Americans. The US Negro has been shown to have a higher level of protective urinary colloids than the White, and Butt has reported an inverse proportion between the incidence of stone and the level of urinary colloids.[2]

Vermooten[17] examined 1,060 pairs of kidneys at the medico-legal laboratories in Johannesburg and found Randall's plaques in 4·3% of Africans, in none of whom calculi were present. The Caucasian incidence of Randall's plaques was 17·2%. This high incidence of Randall's plaques in Africans associated with so small an incidence of calculus, suggests that factors in addition to these plaques are necessary for calculus formation.

Of the environmental factors associated with calculus formation, diet is probably the most significant. Not only are the types of diet and the dietary deficiencies important, but equally so are the secondary metabolic changes induced by such deficiencies. These may be discussed under the following headings:

1. *Calcium Intake*

The majority of urinary calculi are calcium-containing stones. The African's intake is ½ - ⅓rd of the European's and this apparently produces no harmful effects.[17]

2. *Calcium Absorption*

Not only is the intake of calcium lower but in addition absorption may be lessened by 2 factors: (*a*) Vitamin-D deficiency, and (*b*) intestinal hurry. Studies on faecal excretion show that the faecal bulk in Africans is 4 times that of the European and its rate of passage through the alimentary tract is twice as fast.[17]

3. *Urinary Output*

Metabolic studies have shown that the average urinary output of the African is considerably greater than that of the European. This is not a racial characteristic but occurs also in Europeans on a high carbohydrate diet.[18]

4. *Acid-ash Diet*

Vermooten[16] believes that the acid-ash residue produced by a high carbohydrate diet favours the low incidence of urinary calculi in the African.

5. *Vitamin-A Deficiency*

This has been quoted as a factor in the aetiology of urinary calculi.[10] Whether or not this is of any importance, biochemical studies have shown that the blood-levels of vitamin A in the African are within the limits[5] of normal for White patients.

6. *Citrate Theory*

Citrate combines with calcium to form a soluble complex and a reduction in citrate excretion has been suggested as a factor in the production of calculi. Muskat[11] pro-

pounded an interesting theory which suggested that the low incidence of calculi may be related to nutritional liver damage, which is common in the African. This view is based on the observation that oestrogens enhance citrate excretion in the urine and that a damaged liver fails to metabolize circulating oestrogen completely.

7. *Serum Proteins and Serum Calcium*

The serum-calcium level is independent of the dietary intake; it is, however, partly dependent on the level of the serum proteins. Each gram of albumin and globulin binds approximately 0·84 mg. of calcium as a proteinate.[7] The level of serum proteins is generally found to be lower in the African than in the European[14] and Walker *et al.*[19] showed that the serum-calcium level is, on the average, 1 mg. per 100 ml. lower in the African than in the European and the urinary calcium is considerably less.

Table I shows the mean values of serum calcium obtained for Whites and Indians, which are very similar,

TABLE I. SERUM CALCIUM (MG. PER 100 ML.)

Group	No. of cases	Mean	S.D.	p*
Indian control	34	10·5	0·86	<·05
African control	30	9·9	1·24	
Indian control	34	10·5	0·86	<·05
Indian calculus	30	11·1	1·24	
African control	30	9·9	1·24	<·01
African paraplegics	10	11·1	0·84	
African control	30	9·9	1·24	<·07
African recumbents	18	10·01	0·63	

* t-test

and that for Africans, which is 0·6 mg. less than the Indian level. This difference is probably significant and tends to confirm Walker's findings.[19] The difference between the Indian control and Indian calculus group (0·6 mg.), is probably statistically significant; the difference between the African control and African paraplegics (1·2 mg.), is likewise significant, while the difference between the African controls and African recumbent patients (0·11 mg.), is not significant (Table I). Fig. 1 shows the distribution of serum-calcium levels in these groups.

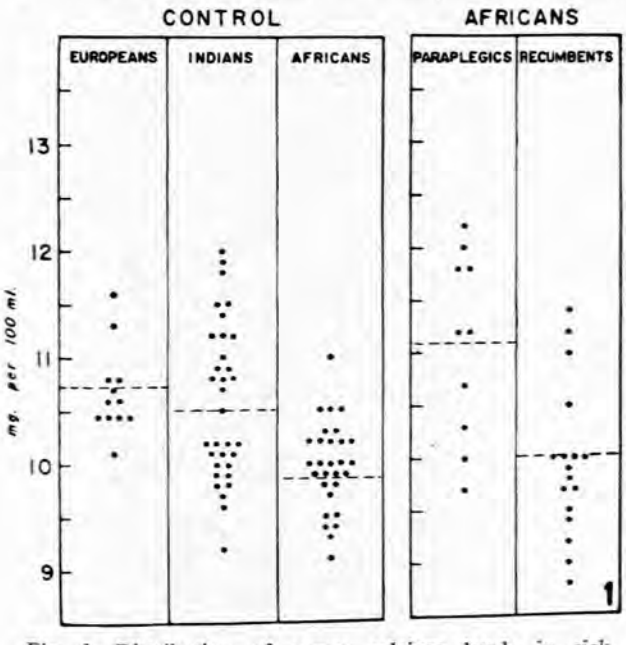

Fig. 1. Distribution of serum calcium levels in sick Africans and control groups. Horizontal dotted lines indicate mean levels in these groups.

In the Indian calculus group, 7 patients had serum-calcium levels above 11·5 mg. per 100 ml. Two of these patients had a serum-calcium level, a year after operative removal of urinary calculi, of 10·8 mg. and 10·2 mg. per 100 ml. respectively. A possible cause for the drop in calcium level in these 2 patients was investigated by comparing samples drawn from a control series at different periods of the same day (Table II). These patients were in hospital for investigation of diseases other than calculus or urinary conditions. There appears to be a significant decrease in calcium levels taken in the middle of the day,

TABLE II. SERUM-CALCIUM LEVELS AT DIFFERENT PERIODS OF THE DAY IN 19 CONTROL PATIENTS WITHOUT CALCULUS OR URINARY DISEASE

	Serum calcium (mg. per 100 ml.)		
Case no.	*Before breakfast*	*1 hour after lunch (1 p.m.)*	*3 - 4 hours after lunch (5 p.m.)*
1	11·5	10·2	11·4
2	10·8	10·6	10·6
3	10·6	10·0	11·1
4	11·2	10·0	10·5
5	10·4	10·6	10·7
6	11·2	11·0	11·4
7	10·7	10·3	10·4
8	10·4	10·7	10·1
9	10·7	10·4	10·5
10	10·0	9·5	10·7
11	10·4	10·5	11·3
12	10·8	10·6	10·7
13	10·4	10·4	10·4
14	11·2	10·7	11·0
15	10·7	10·8	10·9
16	10·4	10·9	11·0
17	10·7	10·4	11·0
18	10·5	10·4	10·3
19	11·0	10·5	10·5
Mean	10·72	10·45*	10·76
SD	0·20	0·25	0·45
SE	0·05	0·06	0·11

SD = Standard deviation, and SE = Standard error.

* Friedman 2-way analysis of variance[15] shows P < ·02.

after lunch, compared with the fasting morning and late afternoon levels, the mean drop being 0·3 mg. per 100 ml. (with a range up to 1·3 mg. per 100 ml. difference). This may in part explain the drop in these 2 patients on whom repeat estimations were done as out-patients in the middle of the day, their first samples having been taken in hospital in the early morning. The possibility of hyperparathyroidism is still being investigated in the remaining 5 patients.

Serum-mucoprotein levels were estimated in both Indian and African control groups by the turbidimetric method of De la Huerga *et al.*[6] in which the entire mucoprotein complex is measured. The values obtained are shown in Table III. The difference between the Indian and African control figures are not statistically significant (Mann-Whitney U-test and t-test[15]). However the difference between the Indian control and the normal US male levels

TABLE III. SERUM MUCOPROTEIN (MG. PER 100 ML.)

Group	*No. of cases*	*Mean*	*SD*
Indian control	19	51·7	14·8
Indian calculus	22	60·2	36·2
African control	16	68·4	31·7
African paraplegics ..	8	89·8	31·6
Normal US male ..	40	81·2±18·2*	
Normal US female ..	30	77 ±14	

* Normal American figures (De la Heurga *et al.*[6]).

and between the African control and the normal US male levels are both significant at the 0·1% level (t-test).

Further studies are required to elucidate the rôle, if any, of the serum-mucoprotein level in the genesis of renal calculus.

CONCLUSIONS

The explanation for the rarity of primary calculus formation in Africans is not readily available. Calcium intake is lower and faecal calcium output is higher in the African, who usually partakes of a high carbohydrate diet. This, together with a high rate of citrate excretion associated with the liver dysfunction found in chronic malnutrition, may be part of the explanation. It is noteworthy however that, considering the high incidence of urinary infection, obstruction and urinary bilharziasis, secondary stone formation seldom occurs in Africans while it is frequent in Indians.

SUMMARY

1. Seven cases of urinary calculus in Africans are presented.

2. The incidence of urinary calculus in Africans at the King Edward VIII Hospital supports the view that urinary stones seldom occur in this racial group. The problems of primary renal calculus and recurrent calculus formation rarely arise in the African.

3. When calculus does occur in Africans there is nearly always some obvious predisposing factor such as urinary obstruction, bacterial infection and recumbency.

4. Predisposing factors to secondary urinary calculus formation, viz. bilharziasis, long-standing chronic infection, and urinary obstruction are equally common in Indian and African patients. Yet the incidence of both primary and secondary calculus formation is high in the Indian (0·125%) compared to the African (0·0014%).

5. Some of the metabolic factors responsible for calculus formation are discussed.

6. Serum-calcium levels in an African control group show a mean value of 0·6 mg. per 100 ml. less than in Indian controls, a finding similar to that reported between Africans and Whites.

7. A significant variation has been noted in serum-calcium levels taken at varying intervals in relation to meals; in comparing serum-calcium levels, estimations should be done on samples taken at the same time each day bearing in mind that midday samples show a significantly lower level.

8. There appears to be a significant difference between serum-mucoprotein levels in African and Indian control groups and those in US normal males.

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REFERENCES

1. Bett, I. M. and Fraser, C. P. (1958): Biochem. J., **68**, 13.
2. Butt, A. J., Hauser, E. A., Seifter, J. and Perry, J. Q. (1952): Sth. Med. J., **45**, 381.
3. Dodson, A. I. and Clark, J. R. (1946): J. Amer. Med. Assoc., **132**, 1063.
4. Dormer, B. A. (1942): S. Afr. Med. J., **16**, 353.
5. Gelfand, M. (1943): *The Sick African*. Cape Town: Stewart.
6. Huerga, J., De la, Dubin, A., Kushner, D. S., Dyniewicz, H. A. and Popper, H. (1956): J. Lab. Clin. Med., **47**, 403.
7. Irving, J. T. (1957): *Calcium Metabolism*. London: Methuen.
8. Kinnear, A. A. (1956): S. Afr. J. Lab. Clin. Med., **2**, 263.
9. Lopis, S. and Kaplan, S. A. (1948): Clin. Proc., **7**, 103.
10. McCarrison, R. (1931): Brit. Med. J., **1**, 1009.
11. Muskat, D. A. (1951): S. Afr. J. Clin. Sci., **2**, 18.
12. Orenstein, A. J. (1937): Quoted by Vermooten, V. *loc. cit.*[16]
13. Politzer, W. M. and Beuchat, A. (1957): S. Afr. Med. J., **31**, 311.
14. Powell, S. J. (1958): S. Afr. J. Lab. Clin. Med., **4**, 273.
15. Siegel, S. (1956): *Nonparametric Statistics for the Behavorial Sciences*, p. 116. New York: McGraw Hill.
16. Vermooten, V. (1937): J. Amer. Med. Assoc., **109**, 857.
17. *Idem* (1941): J. Urol., **46**, 193.
18. Walker, A. R. P. (1956): Nutr. Rev., **14**, 321.
19. Walker, A. R. P., Arvidsson, U. B. and Politzer, W. M. (1954): S. Afr. Med. J., **28**, 48