Evidence of increased oxalate absorption in patients with calcium-containing renal stones

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Summary
1. The possible roles of the diet and of intestinal absorption in the increased excretion of oxalate by patients with renal calcium stones have been studied.
2. Dietary surveys showed that the mean daily intake of oxalic acid by stone-formers was not significantly different from that of non-stone-formers.
3. The mean urinary excretion of oxalate, expressed as an oxalate/creatinine molar ratio, was significantly reduced by fasting, the change being more marked in the stone-formers than in the normal subjects. Moreover, fasting abolished the difference in mean oxalate/creatinine ratios between stone-formers and control subjects.
4. These results are compatible with the hypothesis that the small increases in urinary oxalate excretion which occur in some idiopathic calcium oxalate stone-formers are due to increased absorption of oxalate from the intestine, which may be due to a reduction in intraluminal calcium concentration.

Key words: calcium, diet, intestinal absorption, oxalates, urinary calculi.

Introduction
The cause of renal calcium stones is still not fully understood but a major factor is undoubtedly the tendency to absorb excessive quantities of dietary calcium, leading to hypercalciuria and frequent oversaturation of the urine with respect to calcium and oxalate and calcium phosphate (Nordin, Peacock & Wilkinson, 1972; Robertson, Peacock & Nordin, 1968). Oxalate excretion has received less attention than calcium excretion. A few patients with calcium stones exhibit a marked hyperoxaluria, which is due, in most cases, to intestinal disease (Smith & Hofmann, 1974) or, occasionally, to primary hyperoxaluria (Williams & Smith, 1972), but the majority of patients have a normal or only slightly raised excretion (Elliot, 1968; Yendt, 1970; Thomas, Melon, Thomas, Steg, Desgrez & Albuquer, 1972; Hodgkinson & Williams, 1972). However, it is now recognized that oxalate has a greater relative effect on urine supersaturation than does calcium so that quite small increases in oxalate excretion cause a relatively large increase in urine saturation (Robertson & Nordin, 1968; Finlayson, 1974; Williams, 1976).

This study is concerned with the possible mechanisms that are responsible for the small increases in oxalate excretion in idiopathic calcium stone-formers. Increased oxalate excretion could be due to excessive oxalate intake, increased absorption or increased endogenous synthesis of oxalate. In order to distinguish between these we have examined the dietary intakes of oxalate and calcium by stone-formers and non-stone-formers, and have also determined the effect of fasting on the urinary excretion of oxalate and calcium.

Methods
We studied 98 male patients (aged 26-74, mean 45-6, years) who had a recent history of calcium-containing stone in the upper urinary tract. Patients with intestinal disease, primary hyperoxaluria or "infection" stones, that is, with stones containing...
more than 10% by weight of magnesium ammonium phosphate hexahydrate, were excluded. Measurements were also made on 67 male patients with a mean age of 52-6 years who had a variety of minor disorders but no history of urinary tract calculi, and on 10 healthy male members of the laboratory staff who had a mean age of 38-9 years.

Two studies were carried out: (1) a survey of the dietary intakes of oxalate and calcium by stone-forming and non-stone-forming patients; (2) determination of the effects of fasting on the urinary oxalate/creatinine and calcium/creatinine ratios in stone-forming patients and normal men. Dietary intakes of oxalate and calcium were determined by questioning each patient as to the nature and amount of foods and beverages that he had consumed recently. The oxalic acid and calcium contents of these foods were then calculated from tables (McCance & Widdowson, 1960; Zarembski & Hodgkinson, 1962). Twenty-four-hour urine samples were collected in polythene containers to which 1 ml of 20% (w/v) chlorhexidine gluconate BP (Hibitane) had been added as a preservative. Urine samples were collected between 08.00 and 10.00 hours on the morning after a 12 h overnight fast, both calcium and oxalate excretion being basal after such a fast (Zarembski & Hodgkinson, 1969; Nordin, Peacock & Marshall, 1976).

Calculi were analysed quantitatively (Hodgkinson, 1971), calcium and creatinine being determined by automatic colimetry (Technicon Autoanalyzer methods AA II-03 and II-11 respectively) and oxalic acid by a manual colorimetric method (Hodgkinson & Williams, 1972). Values are given as mean ±SEM. Statistical differences were assessed by unpaired t-tests.

Results

Dietary intakes of oxalic acid and calcium

The mean daily intake of oxalate by 98 patients with stones was 1.21 ± 0.05 mmol/day. This value was slightly higher than that of 67 non-stone-forming patients (1.12 ± 0.07 mmol/day) but the difference was not statistically significant (P > 0.05). The distribution of oxalic acid intakes in the two groups was similar, although a few subjects in each group had exceptionally high values, due mainly to increased intakes of tea or beer, and such individuals were found more frequently among stone-formers than among the control subjects (Fig. 1).

The mean calcium intake was also slightly higher in the stone-formers than in the control subjects (Fig. 2).
Oxalate and kidney stones

Stone-formers than in the control subjects, the difference in mean values between the two groups then being abolished (Fig. 2, Table 1). Similar results were observed for calcium (Fig. 3 and Table 1).

Discussion

These results indicate that the moderate increase in excretion of oxalate observed in some calcium stone-formers is due mainly to an increase in absorption of oxalate. Other evidence, based upon the effect of changes in oxalate intake upon oxalate excretion, supports this view (Zarembski & Hodgkinson, 1969). This study showed that changes in oxalate excretion resulting from changes in oxalate intake and expressed as percentages of the latter, ranged from 2.6% to 4.0% in normal subjects, compared with 6.7%–16.2% in stone-formers.

An excessive intake of oxalate has been implicated in the formation of calcium oxalate stones in some Asian countries (Singh, Kothari, Sharma & Saxena, 1972; Valyasevi & Dhanamitta, 1974) but most of our patients had a normal oxalate intake, the only exceptions being one or two heavy beer and tea drinkers. An increased endogenous synthesis of oxalate likewise appears to be a rare cause of hyperoxaluria among stone-formers, occurring notably in the inherited condition, primary hyperoxaluria (Williams & Smith, 1972). Increased oxalate absorption, associated with hyperoxaluria and calcium oxalate stones, occurs in some gastrointestinal disorders (Smith & Hofmann, 1974) but most patients with calcium stones do not have a history of gastrointestinal disease.

### Table 1. Mean urinary excretion values and significance of differences between different groups

<table>
<thead>
<tr>
<th>Control (n = 10)</th>
<th>Stone-formers (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-fasting (1)</td>
<td>Fasting (2)</td>
</tr>
<tr>
<td>Oxalic acid (mmol/24 h)</td>
<td>0.365 ± 0.034</td>
</tr>
<tr>
<td>Oxalic acid/creatinine</td>
<td>0.025 ± 0.003</td>
</tr>
<tr>
<td>Calcium (mmol/24 h)</td>
<td>6.98 ± 0.85</td>
</tr>
<tr>
<td>Calcium/creatinine</td>
<td>0.480 ± 0.062</td>
</tr>
</tbody>
</table>

**Significance (P)**

<table>
<thead>
<tr>
<th>Group</th>
<th>(1) vs (2)</th>
<th>(1) vs (3)</th>
<th>(1) vs (4)</th>
<th>(2) vs (3)</th>
<th>(2) vs (4)</th>
<th>(3) vs (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxalic acid (mmol/24 h)</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Oxalic acid/creatinine</td>
<td>&lt;0.05</td>
<td>n.s.</td>
<td>&lt;0.001</td>
<td>n.s.</td>
<td>&lt;0.01</td>
<td>n.s.</td>
</tr>
<tr>
<td>Calcium (mmol/24 h)</td>
<td>n.s.</td>
<td>n.s.</td>
<td>&lt;0.001</td>
<td>n.s.</td>
<td>&lt;0.001</td>
<td>n.s.</td>
</tr>
<tr>
<td>Calcium/creatinine</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>n.s.</td>
<td>&lt;0.001</td>
<td>n.s.</td>
<td>&lt;0.001</td>
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</table>
and the most likely cause of the increased absorption in these cases is that it is secondary to the increased calcium absorption.

Oxalate absorption appears to be a passive process (Binder, 1974) that is influenced by the concentration of free calcium in the intestinal lumen. Lowering the concentration of free calcium in the gut by reducing the calcium intake or by feeding with EDTA results in a significant increase in oxalate excretion (Zarembski & Hodgkinson, 1969). The increased absorption of calcium in idiopathic hypercalciuria also results in a reduced concentration of calcium in the intestine, as shown by the reduced faecal excretion of calcium (Edwards & Hodgkinson, 1965). It seems probable therefore that the moderately increased excretion of oxalate in many calcium stone-formers is due to a small increase in oxalate absorption, which in turn is due to a fall in the intraluminal concentration of calcium.

Low-calcium diets are widely used in the treatment of calcium stones but such diets will reduce the intraluminal concentration of calcium still further and lead to a further increase in the absorption and excretion of oxalate. It is necessary therefore to restrict oxalate intake as well as calcium intake in the long-term treatment of patients with calcium stones (Nordin, Hodgkinson, Peacock & Robertson, 1971).

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References