ENDEMIC URINARY LITHIASIS IN TURKISH CHILDREN†*

A CLINICAL STUDY OF 119 CASES

BY

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Endemic urinary lithiasis is a clinical entity with the following characteristics: a high prevalence in boys, a high percentage of bladder stones, uric acid as the usual chemical constituent of the stones, restriction to the lower social and economic classes, a well-marked peak incidence of the disease between 2 and 4 years and a limitation to certain parts of the world.

Civiale (1838) was one of the first to report an extensive series of cases. In Great Britain the disease was common at the end of the last century but disappeared dramatically between 1910 and 1920 (Lett, 1936; Thomas, 1949). Assendelft (1900) reported a series from Russia, Bokay (1912) from Hungary, Račić (1935) from Yugoslavia and Balacesco (1929) from Roumania. Chevalier (1929) and Brown and Brown (1941) reported cases from Syria, Levy and Falk (1957) from Israel and Brun (1933) from Tunisia. The disease has also been reported from China (Thomson, 1921), from Siam (Noble, 1931) and from India (McCarrison, 1931).

Erkun (1935), Taner (1940) and Ozdilek (1946) have reported previous series from Turkey where the disease appears to be commoner than anywhere else.

Whereas detailed analyses of sporadic urinary lithiasis in childhood have been published by Myers (1957) and by Winkel Smith (1944) from Great Britain and Denmark respectively, no such analysis appears to exist for the endemic form of the disease and no extensive series has been reported in the British literature for almost 30 years.

Present Investigation

The series under review covers 119 consecutive cases of urinary lithiasis in children which were seen and diagnosed at the Hacettepe Children's Hospital in Ankara between January 1958 and May 1960, a period of two years and four months. The Hacettepe Children's Hospital is a new children's hospital which is part of Ankara University's Medical School and it is unlikely that any selection of patients has taken place in this series. The steadily increasing number of lithiasis patients seen is in proportion to the increasing number of all surgical cases seen during the time of this study. During the same period about 42,500 new patients were seen in the hospital's out-patient departments and about 6,000 patients were admitted. Urinary lithiasis cases therefore represent approximately one in 350 patients seen and one in 51 patients admitted to the hospital. Operations for calculus disease have accounted for 9% of all surgical procedures carried out by us.

The patients came from all parts of Turkey, but the majority were from the Anatolian plateau; relatively few came from the fertile coastal districts as is shown on the map (Fig. 1). With very few exceptions our patients came from the lower social and economic classes; their fathers being either smallholders or labourers. In no instance was a family history of lithiasis elicited.

The anatomical distribution of the stones is shown in Table 1. Bladder and urethral stones thus accounted for 58%, while stones in the upper urinary tract were present in 42% of patients.

In 23 patients (19%) the stones were in multiple sites (Table 2).

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.
† Part of this material has been used in the thesis of M.D. of Cambridge University.
‡ Present address: The Hospital for Sick Children, Great Ormond Street, London.

Table 1

<table>
<thead>
<tr>
<th>Site</th>
<th>Numbers</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>41 (5)</td>
<td>30</td>
</tr>
<tr>
<td>Ureter</td>
<td>17 (3)</td>
<td>12</td>
</tr>
<tr>
<td>Bladder</td>
<td>55 (1)</td>
<td>42</td>
</tr>
<tr>
<td>Urethra</td>
<td>21 (1)</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>134</td>
<td></td>
</tr>
</tbody>
</table>

Figures in parentheses denote female patients.
Fig. 1.—Map of Turkey showing incidence of stones. The circled figures indicate number of cases.

Table 2
DISTRIBUTION OF STONES IN MULTIPLE SITES

<table>
<thead>
<tr>
<th>Multiple Sites</th>
<th>No. of Stones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both kidneys</td>
<td>8</td>
</tr>
<tr>
<td>Bladder and kidney</td>
<td>6</td>
</tr>
<tr>
<td>Bladder and ureter</td>
<td>2</td>
</tr>
<tr>
<td>Bladder and urethra</td>
<td>1</td>
</tr>
<tr>
<td>Urethra and kidney</td>
<td>1</td>
</tr>
<tr>
<td>Urethra and ureter</td>
<td>2</td>
</tr>
<tr>
<td>Kidney and ureter</td>
<td>1</td>
</tr>
<tr>
<td>Urethra, ureter and kidney</td>
<td>1</td>
</tr>
<tr>
<td>Both kidneys and both ureters</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>23</strong></td>
</tr>
</tbody>
</table>

Table 3
SIDE OF KIDNEY OR URETER INVOLVED

<table>
<thead>
<tr>
<th>Kidney</th>
<th>Ureter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left</td>
<td>18</td>
</tr>
<tr>
<td>Right</td>
<td>14</td>
</tr>
<tr>
<td>Bilateral</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 4
PRESENTING SYMPTOMS

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Nos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysuria</td>
<td>55</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>20</td>
</tr>
<tr>
<td>Retention of urine</td>
<td>11</td>
</tr>
<tr>
<td>Haematuria</td>
<td>10</td>
</tr>
<tr>
<td>Passing stones</td>
<td>5</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>5</td>
</tr>
<tr>
<td>Anuria</td>
<td>3</td>
</tr>
<tr>
<td>Oedema</td>
<td>1</td>
</tr>
<tr>
<td>Ascites (abdominal swelling)</td>
<td>1</td>
</tr>
<tr>
<td>No symptoms</td>
<td>7</td>
</tr>
</tbody>
</table>

Fig. 2.—Age distribution of patients.
Although kidney stones were often multiple, stones in the bladder were almost always solitary.

The side affected in cases of upper urinary tract disease is shown in Table 3.

The age distribution of the patients is shown in Fig. 2. This shows a well-marked peak incidence between the ages of 2 and 4 years. However, when the cases are broken down into the different anatomical sites of the stone it becomes clear that the marked peak incidence applies only to stones in the bladder and urethra, while cases with upper urinary tract stones are evenly distributed throughout the years (Fig. 3).

There were 10 girls in this series (8.5%); five with kidney stones, three with ureteric stones and one each with a bladder and a urethral stone.

The presenting symptoms were recorded in 108 of the patients and are shown in Table 4. No fewer than seven patients had no symptoms referable to the stone, this being a chance finding during investigations for unrelated medical conditions. In eight of the children symptoms began while the child was still being breast fed.

The laboratory investigations carried out on the first 100 cases are shown in Figs. 4, 5 and 6. These show that the majority of the patients had normal haemoglobin values and that the non-protein-nitrogen (N.P.N.) was within normal limits in most of the uncomplicated cases. The serum calcium, phosphorus and alkaline phosphatase were usually normal. The urine was acid in about 75% of cases, but in some of these the reaction changed to alkaline.
on repeated examinations. However, the pH of the urine at the time the stone is diagnosed may not be closely related to that at the time of stone formation. Microscopy of the urine usually showed epithelial cells, leucocytes and crystals of uric acid or oxalates.

All patients had an abdominal radiograph and in only four of these were the stones not opaque to X rays. We have made a point of using a large enough film to include the whole abdomen in all cases; in a number of these a silent kidney stone was found when the symptoms were referable to a bladder stone. Excretion urograms were carried out in 70 of the patients and in all but two of the cases the diagnosis was made or confirmed radiologically. Ureteric catheters were not available during most of this study.

The complications which were encountered are shown in Table 5. It will be seen that no less than 72 patients (61%) had a complication which could be attributed directly to the stone. Urinary infection was present in 25 patients and the organisms isolated from the urine are shown in Table 6. The more unusual complications encountered have been reported on previous occasions (Eckstein, 1960a; Eckstein, Oral and Dogramaci, 1958; Eckstein, 1960b; Eckstein, Marulyali and Tatman, 1959; Eckstein and Kenanoglu, 1961).

The treatment of the patients is summarized in Table 7. It has been our policy to remove all stones which were considered to be too large to be passed spontaneously (Campbell, 1951; Williams, 1958). Only two patients were suitable for conservative therapy, one case of ureteric stone and one of bladder stone and in six cases the spontaneous expulsion of a urethral stone occurred. In three patients no treatment was advised because of other disease (metastatic neuroblastoma of orbit, encephalitis and osteomyelitis with rheumatic carditis). In 78 patients (66%) surgical removal of the stone was carried out. Several children had more than one operation and a total of 98 surgical procedures was performed (Table 8).

We have not carried out instrumental removal of
ENDEMIC URINARY LITHIASIS IN TURKISH CHILDREN

Fig. 5.—Non-protein-nitrogen levels in first 100 cases.

ureteric calculi nor performed lithotritry and agree with Grob (1957) and most other writers that, in children, surgical removal of the stone is to be preferred. Only Keegan (1900) and Winsbury-White (1954) advocate litholapaxy in boys. Impacted

<table>
<thead>
<tr>
<th>Complication</th>
<th>Nos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary infection</td>
<td>25</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>21</td>
</tr>
<tr>
<td>Retention of urine</td>
<td>12</td>
</tr>
<tr>
<td>Pyonephrosis</td>
<td>4</td>
</tr>
<tr>
<td>Anuria</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Extravasation of urine</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Renal atrophy</td>
<td>2</td>
</tr>
<tr>
<td>Ureteric stricture</td>
<td>1</td>
</tr>
<tr>
<td>Perinephric abscess</td>
<td>1</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>72</strong></td>
</tr>
</tbody>
</table>

Figures in parentheses denote fatal outcome.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Nos.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em></td>
<td>12</td>
</tr>
<tr>
<td><em>Proteus</em></td>
<td>10</td>
</tr>
<tr>
<td><em>A. aerogenes</em></td>
<td>3</td>
</tr>
<tr>
<td><em>Ps. pyocyanea</em></td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases operated on</td>
<td>78 (66%)</td>
</tr>
<tr>
<td>Conservative treatment</td>
<td>2</td>
</tr>
<tr>
<td>Spontaneous expulsion (urethra)</td>
<td>6</td>
</tr>
<tr>
<td>No treatment (concomitant disease)</td>
<td>3</td>
</tr>
<tr>
<td>Referred for surgery elsewhere</td>
<td>7</td>
</tr>
<tr>
<td>Refused treatment</td>
<td>23 (19%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>119</strong></td>
</tr>
</tbody>
</table>
urethral calculi were removed by urethrotomy unless extraction with forceps could be carried out without traumatizing the urethra.

One child suffering from calculus anuria and one with perforation of the urethra and extravasation of urine died and there were two further deaths, probably from septicaemia, after simple cystolithotomy. There have been very few postoperative complications although one child required nephrectomy for secondary haemorrhage after pyelolithotomy.

The stones showed considerable variations in size and shape and were usually laminated. Fifty of the stones removed were analysed qualitatively and the chemical findings are summarized in Fig. 7 and in Table 9. Thus uric acid was present in 38 of the stones while phosphates and carbonates were uncommon findings. There was no significant

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**Table 8**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Nos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder:</td>
<td></td>
</tr>
<tr>
<td>Cystotomy</td>
<td>37</td>
</tr>
<tr>
<td>Cystoscopy only</td>
<td>1</td>
</tr>
<tr>
<td>Urethra:</td>
<td></td>
</tr>
<tr>
<td>Cystotomy</td>
<td>4</td>
</tr>
<tr>
<td>Perineal urethrotomy</td>
<td>5</td>
</tr>
<tr>
<td>Stone extracted</td>
<td>4</td>
</tr>
<tr>
<td>Suprapubic drainage</td>
<td>3</td>
</tr>
<tr>
<td>Kidney:</td>
<td></td>
</tr>
<tr>
<td>Pyelotomy</td>
<td>20</td>
</tr>
<tr>
<td>Nephrotomy</td>
<td>7</td>
</tr>
<tr>
<td>Nephrectomy</td>
<td>7</td>
</tr>
<tr>
<td>Partial nephrectomy</td>
<td>3</td>
</tr>
<tr>
<td>Nephrostomy</td>
<td>1</td>
</tr>
<tr>
<td>Ureter:</td>
<td></td>
</tr>
<tr>
<td>Ureterolithotomy</td>
<td>5</td>
</tr>
<tr>
<td>Ureteronecystotomy</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
</tr>
</tbody>
</table>

---

**Fig. 6.—**Calcium, phosphorus, and alkaline phosphatase levels in first 100 cases.
difference in the chemical composition of bladder and kidney stones. Epprech and Schinz (1950) have shown that the uric acid in the endemic type of stone is present as ammonium urate and as a mixture of two forms of calcium urate.

Although an adequate follow-up study has unfortunately not been possible in our cases it is my impression that recurrences in the endemic form of urinary lithiasis are very uncommon.

**Discussion**

We have been unable, as yet, to carry out any complex biochemical studies to elicit the cause of endemic urinary lithiasis. However, the diet of Turkish children appears to be grossly deficient in protein and in vitamin D. Turkish children are breast fed much longer than British children and details about breast feeding are available in 45 of our cases. No less than 44 of these were breast fed, 28 (61%) for one year or more. Generally speaking cow's milk is not consumed by the village population and eggs and meat are eaten on rare occasions only. The staple diet is 'bulgur', a boiled wheat product, vegetables and fruit. Although rickets are very common in Turkey it has been an unusual finding in our cases suggesting that a vitamin D deficiency is not involved in the aetiology. Malnutrition is common in Turkish children and Dogramaci and Wray (1958) have shown that 41% of unselected out-patients were malnourished. The weights of our patients under the age of 6 years have been plotted on a graph produced from figures given by Gomez, Galvan, Cravioto and Frenk (1955) from Mexico where the standard of living is, to some extent, comparable with that in Turkey (Fig. 8). This shows that malnutrition is no more frequently seen in cases of urinary lithiasis than in the average hospital population. Severe vitamin A or C deficiencies are extremely rare and it is likely that a protein deficiency is closely related to the aetiology of endemic urinary lithiasis.

The incidence of upper urinary tract stones in this series is higher than in most of the previous ones reported in the past. Improved radiological facilities no doubt account for some of this difference, but probably some other factor is involved. Two recent reports on endemic lithiasis from Italy (Montinari and Torraco, 1956) and from India (Anderson, 1959) also quote an incidence of upper urinary tract stones of about 50%.

The male predominance has, in the past, been explained by the fact that the female urethra being shorter and wider than that of the male allows small stones to pass which would be held up in a boy's urethra. This theory may apply to bladder and urethral stones but cannot account for the similar sex difference in cases of upper urinary tract stones. It is therefore possible that a sex hormone is in some way involved in the complex aetiology of endemic urinary calculus formation.

The fact that the disease has disappeared in Great Britain within living memory, that it is virtually restricted to the lower social and economic classes and that it is at present endemic in those countries with a relatively low standard of living, especially where the lower social classes are concerned, strongly suggests that endemic urinary lithiasis can be prevented by an improved standard of living. It is possible therefore that this interesting condition

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**Table 9**

<table>
<thead>
<tr>
<th>Composition</th>
<th>No. of Stones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid only</td>
<td>18</td>
</tr>
<tr>
<td>Calcium oxalate only</td>
<td>7</td>
</tr>
<tr>
<td>Uric acid and calcium oxalate</td>
<td>15</td>
</tr>
<tr>
<td>Mixed (phosphates and carbonates)</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
</tr>
</tbody>
</table>

---

**Fig. 7.**—Chemical composition of stones.
will disappear before we have been able to work out its aetiological mechanism.

Summary

Endemic urinary lithiasis is a clinical entity with certain well-defined characteristics. A series of 119 consecutive cases which were seen at the Hacettepe Children's Hospital in Ankara have been reported and discussed. The aetiology of the disease is not known, but it is likely that a protein deficiency is the most important factor in a complex mechanism of stone formation. As the standard of living rises the disease will probably disappear.

References

ENDEMIC URINARY LITHIASIS IN TURKISH CHILDREN


Endemic Urinary Lithiasis in Turkish Children: A Clinical Study of 119 Cases
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Arch Dis Child 1961 36: 137-145
doi: 10.1136/adc.36.186.137

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