

## Childhood urolithiasis in Britain

S. GHAZALI, T. M. BARRATT, and D. I. WILLIAMS

From The Hospital for Sick Children, Great Ormond Street; The Institute of Child Health; and The St. Peter's Hospitals Group, London

**Ghazali, S., Barratt, T. M., and Williams, D. I. (1973).** *Archives of Disease in Childhood*, 48, 291. **Childhood urolithiasis in Britain.** 120 children with urinary calculi were treated between 1966 and 1971. 75% were male, and the median age of diagnosis was 3 years. In 34 there were associated urological abnormalities and in 8 a metabolic cause of calculi was identified. 12 of 67 children had hypercalciuria. In 95 children the urine was infected on admission to hospital; in 76, particularly the younger children, this was with *Proteus* species. Calculi recurred after surgery in 13 children, and in 9 the only identifiable factor was failure to eradicate the *Proteus* infection.

That there are substantial historical and geographical variations in the incidence of urinary calculi in childhood is well known. The classical endemic calculus disease of children, characterized by a predominance of uric acid bladder stones with sterile urine, ceased to be common in England as long ago as 1920 (Lett, 1936), and is also dying out in many countries around the Mediterranean where it was once extremely common, for instance in Sicily and Lebanon (Andersen, 1969). It is reasonably well established that the factors leading to the disappearance of endemic stone disease are related to improved nutritional standards, in particular to the introduction of a mixed diet rather than one predominantly dependent upon cereal products. It is not always so well recognized that in England and in many parts of Europe we are commonly treating infants with infected mixed phosphate, upper tract stones, yet this type of disease is rare in Scandinavia (Andersen, 1968) and in North America (Thompson, Ross, and McCoy, 1967). The low incidence of calculi in these countries suggests that it might be possible to reduce the incidence in Britain if the aetiology could be elucidated, and with this possibility in mind we have reviewed the identifiable causative factors in a series of children referred to one of us (D.I.W.) at The Hospital for Sick Children, Great Ormond Street and at St. Peter's Hospital, London. 112 children had been referred up to 1966, and were reviewed previously (Williams and Eckstein, 1968). Since then a further 120 children have been treated and are described in this communication.

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### Patients

**Incidence.** 120 children were operated on during the 6-year period 1966 to 1971 inclusive. This number represents a greater annual incidence of referrals than in the previous period and suggests the possibility that the disease is becoming more frequent. However, during the same period 51 children with Wilms' tumours were referred and the relative frequency of the two disorders remains at approximately the same level in the two series.

The age of the children at presentation is shown in Fig. 1: 75% were under 5 years of age. Fig. 1 also

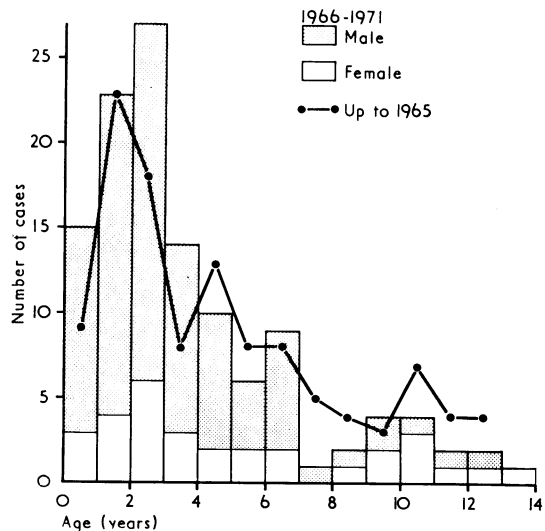


FIG. 1.—Age of children at operation for urinary lithiasis. Similar data from the earlier study (Williams and Eckstein, 1968) are included for comparison.

shows the age distribution for the previous series showing that there has been little change. 89 cases were male and 31 were female; the male preponderance is particularly evident in early life.

The children were from all social classes in the population and from several immigrant groups, but no Negro child was diagnosed as having calculus disease, confirming the common observation of a relative immunity of Negroes to urolithiasis.

### Results

**Site.** 110 children had calculi in the upper urinary tract and in only 10 cases were the stones confined to the bladder (Fig. 2). Of the children

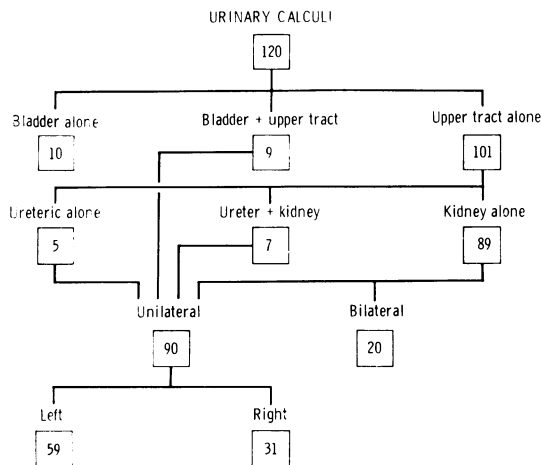


FIG. 2.—The site of calculi in 120 children with urolithiasis.

with the upper tract calculi, 9 also had bladder involvement, 5 were confined to the ureter, 89 to the kidney, and 7 had stones in both kidney and ureter. 20 of the calculi were bilateral, and of the unilateral upper tract calculi 59 were left-sided and 31 right-sided. The pattern of upper tract involvement strongly contrasts with the classical form of endemic stone disease of childhood.

### Aetiology.

**Metabolic disorder.** A definite metabolic cause for calculus formation was recognized in only 5 children: cystinuria (2), oxaluria, distal renal tubular acidosis, and hyperadrenocorticism. 3 further children had been immobilized for long periods shortly before their presentation with stones (burns, osteomyelitis, and fracture).

**Urinary tract anomaly.** In 34 children there were associated urological anomalies (Table I). In 8 of these the stone was apparently formed in sterile urine and in these, stasis alone may have

TABLE I  
*Urological abnormalities in 120 children with urinary calculi*

	No. of children
Pelviureteric junction obstruction	8
Abnormalities of fusion or rotation	8
Severe ureteric reflux	5
Neurogenic bladder	3
Epispadias	3
Duplex system	2
Ureteric stenosis or valve	2
Bladder neck obstruction	1
Rectovaginal fistula	1
Ectopic ureterocoele	1
<b>Total</b>	<b>34</b>

been responsible for its formation, but in 26 cases the urine was infected and the anomalies might have predisposed to the infection. For the purposes of this retrospective survey, pelviureteric junction obstruction was deemed to have existed in those cases treated by pyeloplasty, and severe ureteric reflux in those treated by ureteric reimplantation. Transient reflux and persistent reflux of lesser degree occurred in other cases, but still only in about half of the children with infected stones, so that there was no clear-cut association between reflux and stone formation.

**Infection.** In 95 children the urine was infected on admission to hospital (Fig. 3): 76 of these,

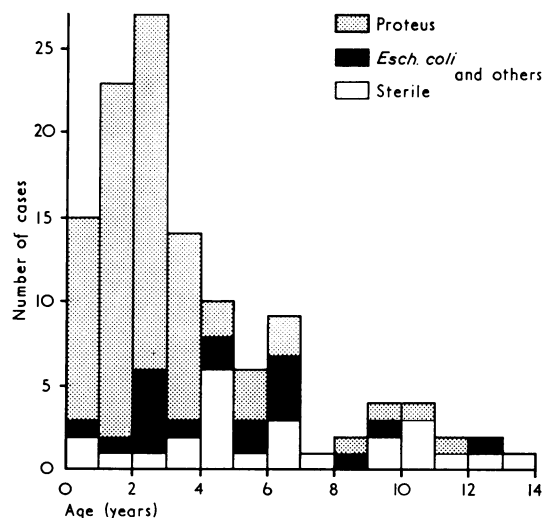


FIG. 3.—The incidence of *Proteus* and other infections in children with urolithiasis.

TABLE II  
Hypercalciuria (> 6 mg/kg per 24 hr) in children with urinary calculi

Age (yr)	Sex	Site of calculi	Infection	Urine Ca (mg/kg per 24 hr)	Urine Ca/creatinine ratio (mg/mg)	Diagnosis
0.7	M	Renal	Sterile	9.5	0.72	Idiopathic
1.2	F	Renal	<i>Proteus</i>	9.8	0.73	Idiopathic
1.3	M	Renal and ureteric	<i>Proteus</i>	6.5	—	Idiopathic
1.6	M	Renal	<i>Proteus</i>	9.3	0.33	Idiopathic
2.3	M	Ureteric	<i>Proteus</i>	13.5	—	Distal renal tubular acidosis
2.7	M	Renal	<i>Proteus</i>	12.5	0.43	Idiopathic
2.8	M	Renal	<i>Esch. coli</i>	9.4	—	Congenital adrenal hyperplasia
3.3	M	Vesical	<i>Proteus</i>	8.5	0.48	Bladder neck obstruction
6.0	F	Renal and ureteric	Sterile	7.1	—	Cystinuria
7.0	F	Renal	<i>Proteus</i>	7.6	—	Neurogenic bladder
8.5	F	Vesical	<i>Esch. coli</i>	10.2	—	Immobilization (burns)
12.3	M	Vesical	<i>Esch. coli</i>	9.1	—	Epispadias

particularly the younger children, were infected with a *Proteus* species and this group largely accounted for the peak of incidence in the first few years of life. The age at presentation of children with infections other than *Proteus* (predominantly *Esch. coli*) or with sterile urine was more evenly distributed throughout childhood. 26 of the 34 patients with urological anomalies had infected urine, and again *Proteus* was the most common organism. The ratio of infected stones (*Proteus* and *Esch. coli*) to sterile stones was about 4 to 1, similar to that in the earlier series. Thus infected stones in an otherwise normal urinary tract was the commonest form of the disease.

**Hypercalciuria.** The 24-hour urinary calcium estimation was measured preoperatively in 67 children (Fig. 4). In 12 (Table II) it was found to exceed 6 mg/kg per 24 hr, which was suggested by Royer (1961) as the upper limit of normal in children. As confirmation, the 24-hour urinary calcium:creatinine concentration ratio is given in cases where both were measured on the same sample. The upper limit of normal of this ratio is 0.28 (Nordin, 1959), and is exceeded in all the apparently hypercalciuric children in this series in whom data were available for calculation.

The hypercalciuric group is quite heterogeneous. There were two children with a recognized cause for excessive calcium excretion: distal renal tubular acidosis, and congenital adrenal hyperplasia on moderately large doses of cortisone. There was also a child who had been recently immobilized for burns. 3 children had urological abnormalities: epispadias, bladder neck obstruction, and neurogenic bladder. 1 child had cystinuria as well as hypercalciuria, and it is of interest that her calculi consisted of calcium and phosphate but not cystine.

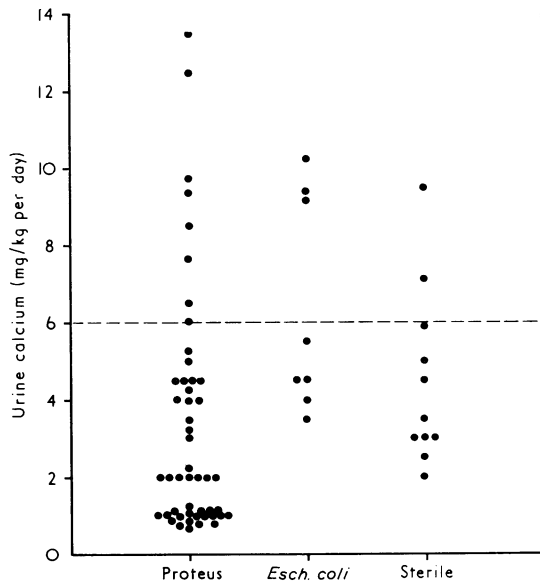


FIG. 4.—Urinary calcium excretion in children with urolithiasis related to infection. The upper limit of normal is taken to be 6 mg/kg per 24 hr (Royer, 1961).

The 5 hypercalciuric children with *Proteus* infection but without urological or metabolic abnormality were indistinguishable from the rest of the children with *Proteus* infection (Fig. 4). The median urine calcium excretion in both the sterile and the *Esch. coli* infection groups was significantly higher ( $P < 0.05$ ; rank sum test) than in children with *Proteus* infection, but as the age distribution differs the groups are not strictly comparable.

**Treatment.** Pyelolithotomy was the commonest operation performed. Occasionally considerable

TABLE III  
 Recurrence of urinary lithiasis after surgery

Age (yr)		Infection		Urological malformation	Urine calcium (mg/kg per 24 hr)
At first operation	At recurrence	Before operation	After operation		
0·7	1·1	<i>Proteus</i>	<i>Proteus</i>	None	0·8
1·6	1·9	<i>Proteus</i>	<i>Proteus</i>	None	1·0
1·6	2·9	<i>Proteus</i>	<i>Proteus</i>	None	9·3
1·9	2·9	<i>Proteus</i>	Mixed	None	0·9
2·3	5·3	<i>Proteus</i>	<i>Proteus</i>	None	4·0
2·4	2·7	<i>Proteus</i>	<i>Proteus</i>	Pelviureteric obstruction	1·8
2·7	4·5	<i>Proteus</i>	<i>Proteus</i>	None	12·5
2·8	3·5	<i>Proteus</i>	<i>Proteus</i>	None	1·2
3·6	4·6	<i>Proteus</i>	Mixed	None	—
4·0	4·6	<i>Proteus</i>	<i>Proteus</i>	None	—
5·5	7·1	<i>Esch. coli</i>	Mixed	Pelviureteric obstruction	—
5·9	7·9	<i>Proteus</i>	<i>Proteus</i>	None	4·2
7·0	10·0	<i>Proteus</i>	<i>Esch. coli</i>	Neurogenic bladder	7·6

destruction of renal tissue followed pyonephrosis and nephroureterectomy (8 cases) or partial nephrectomy (4 cases) was undertaken.

**Recurrence.** Calculi recurred after surgical removal in 13 of the 120 children (Table III). The major factor, and the only identifiable one in 9 children, appeared to be persistence of *Proteus* infection after removal of calculi leading to early recurrence. 3 children with recurrence also had hypercalciuria and 3 had urological abnormalities. No child in this series suffered a recurrence after surgical removal of calculi for the second time.

#### Discussion

The data presented indicate that childhood urolithiasis remains a substantial clinical problem, but they failed to define a clear-cut causative factor, or to explain the difference between the incidence in Britain and in North America. The infected calculi seen in Britain have, in common with the classical endemic calculi, the peak of age incidence in the second and third years of life as well as the low recurrence rate; but in contrast, upper tract stones are much commoner and all the children in our series appeared to be receiving an adequate mixed diet. About a quarter of our cases had some urological malformation which may have played some part in the genesis of calculi, but only a small number had a metabolic cause. Much the most frequent aetiological factor appeared to be a *Proteus* infection, which is relatively rare in uncomplicated urinary infections in childhood, but there must presumably be some other as yet unidentified factor which causes an infant during the first few years of life to form a stone when infected with a *Proteus* organism.

It is important that those who treat children with urinary tract infection are aware of this relation between *Proteus* infection and stone. As these calculi are often not very dense, their radiological exclusion necessitates close examination of the plain abdominal x-ray and intravenous pyelogram. The calculi which form in infected urine consist of organic matrix in which is deposited struvite (magnesium ammonium phosphate) and apatite (basic calcium phosphate). The principal factor in their genesis is the urease activity of the infecting organism: the high ammonium ion concentration leads to the precipitation of struvite and, by raising the pH, favours the precipitation of apatite. The effect of alteration of calcium concentration on this system is marginal (Robertson and Nordin, 1969), and the relevance of the observation of hypercalciuria in a few of these children in this series is unclear.

Standards for urinary calcium excretion in healthy children are not well established: the upper limit of 6 mg/kg per 24 hr (Royer, 1961) was determined in French children and may not be applicable to the United Kingdom, since, for example, national habits of prescription of vitamin D differ. Nevertheless, it is of interest that hypercalciuria as thus defined was observed in 12 children. It was unexpected (Table II) to observe hypercalciuria in 3 children with urological abnormalities, serving as a reminder that the aetiology of calculi may be multifactorial. No child was hypercalcaemic and in only 3 children was the cause of hypercalciuria evident. Hypercalciuria is ordinarily observed in about one-third of adult patients with renal calculi (Hodgkinson and Pyrah, 1958) so that its incidence in children is lower, suggesting that the infective cause is more important.

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Correspondence to Dr. T. M. Barratt, Department of Immunology, Institute of Child Health, 30 Guilford Street, London W.C.1.

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#### New journal for syndrome identification

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