Recurrent urinary infections in girls: relation to enuresis

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Summary: Maximum bladder capacities (MBC) have been studied in 89 girls receiving treatment for urinary infections at a time when the infection had been controlled. Fifty-six of the girls had been enuretic when first seen, 40 remained enuretic even when the infection had been cured. The MBC's of the enuretic children were significantly smaller than those who were not or had not been enuretic. The enuresis and small bladder capacities were therefore not usually due to the urinary infection. It is concluded that in girls either enuresis predisposes towards the development of urinary infections, or that a common underlying pathology predisposes to both entities.

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Asymptomatic bacteriuria has been shown by Kunin, Deutscher and Paquin[1] to occur in 1 per cent of schoolgirls in Virginia. This high incidence of unsuspected urinary infection is probably a widespread if not universal phenomenon, for similar incidences have been found in Dundee[2] in Scotland and in Birmingham[3] in England. Urinary infections, if repeated and uncontrolled, may give rise to ureteral reflux, pyelonephritis and even permanent renal damage.[4] The latter may or may not contribute to renal failure in later life.[5] Symptomatic bacteriuria, however, is also common, for many such patients have urgency, frequency, dysuria and fever, and are seen and identified on this account. It seems probable that 5% of all girls have urinary tract infections at some time, though in varying degrees of severity, some having only an occasional episode, while others have repeated urinary infections.[6]

Management of these children is made difficult not only because of the recurrent nature of the disease, but also because it is not known why the disease exists at all. Attempts have been made to find an explanation on anatomical grounds but it is now generally agreed that bladder neck obstruction,[7] urethral stenosis[8,9] and ureteral reflux do not in themselves cause the syndrome, though reflux may complicate it.[10] Nor do poor socio-economic conditions or lack of hygiene appear to contribute to the etiology.[11] Although Kunin, Deutscher and Paquin[1] have not found any evidence that the disease is familial, we have encountered instances in which both the mother and her daughter were affected, and where sisters also had the disease. We therefore decided, when asked to see children with recurrent urinary infections, to study the familial incidence of the disease and in particular to review the sisters of the proband to determine if there is an increased incidence of urinary infections in siblings. In addition we undertook to study functional bladder capacities of children with recurrent urinary infections, suspecting that these might be altered in children with ureteral reflux.

Material and methods

As recurrent urinary infections without obvious anatomical explanation are much commoner in girls than in boys, the study was limited to girls. Ninety-two girls aged 3 to 13 years from 90 families were studied. Two children had been adopted and therefore their family histories were not available. Each child had either a history of previous urinary infections,

confirmed by their attending physician, or the presence of a urinary infection was noted by us when the child was first seen. The majority had had the onset of their disease before their fourth birthday (Fig. 1). In most the repeated nature of the infection was confirmed on more than one occasion during the course of the study. All except two children were subjected to intravenous pyelography and voiding cystourethrography. Seventy were cystoscoped. All were maintained on long-term chemotherapy, usually nitrofurantoin, sometimes a sulphonamide, while the study was in progress. All sisters over the age of 3 years were also examined, and midstream specimens of urine taken for culture and colony count. If a positive culture was obtained the study was repeated.

Bladder capacity studies — When the infection had been controlled the parents were asked to measure and record all specimens of urine passed over the course of a week. If the child had day dribbling or enuresis the parent was asked to record this also. The average bladder capacity (ABC) was taken as the average amount of urine passed at a time during the course of a week. The maximum bladder capacity (MBC) was taken as the largest volume of urine passed at any one time during the same period. As controls, identical studies were carried out on normal girls who were free of urinary symptoms, and who did not pass urine between going to bed and rising in the morning.

Results

Before giving particulars of the incidence of the disease in families and of the bladder capacities, details are given of the radiological and cystoscopic findings, for we believe these indicate that the cases under study do not differ materially from those studied by others and reported in the literature.

Radiological studies — Reflux was present in the first study in 43 and absent in 47. Reflux appeared to be commoner in those developing their first infection under the age of 2, but the sample is too small for detailed analysis (Table I). Reflux was commoner in those whose voiding cystourethrograms had been carried out at an early age (Table II). Of those aged 7 years and under, 36/64 had reflux, of those aged 8 years or over, 7/26 had reflux. The difference between the two groups is statistically significant ($X^2_{(1)}$ 5.419, $0.01<P<0.25$), suggesting diminishing incidence of reflux with age among girls with recurrent urinary infection. Those with reflux more commonly had radiological evidence of renal parenchymal damage, 15/43, than those who had no reflux, 2/47.

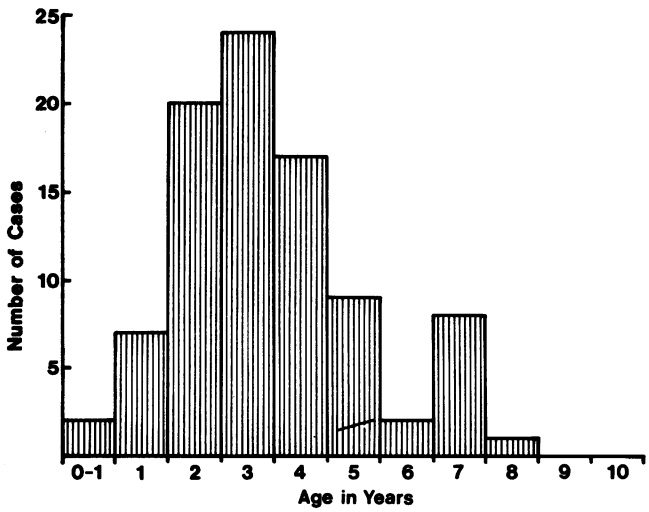

Fig. 1 — Age at onset of first urinary infection.

Repeated voiding cystourethrograms were carried out in 27; in seven the reflux disappeared, in 10 it diminished, in five it remained unchanged, and in five it increased in severity.

Cystoscopic findings — 70 children were cystoscoped on one or more occasions. In only seven were the findings considered normal. In 31 there was obvious cystitis cystica, in seven the bladder was trabeculated, in 29 the urethra was considered by the attending urologist to be stenotic, and urethral dilatation or meatotomy was carried out. The ureteral openings were gaping when gross low-pressure reflux was present.

Bladder wall biopsy — This was carried out in two children with infections that were difficult to control. In both there was conspicuous infiltration of the bladder wall with eosinophils.

Bladder capacity studies — These were carried out in 89 children while on chemotherapy and free from infection. When the results were analyzed it became apparent that many of the children had small bladder capacities, and that most of these when first seen had either diurnal (day dribbling) or nocturnal enuresis. Maximum bladder capacity studies were therefore analyzed in relation to these two symptoms (Table III). There was no correlation between MBC's and reflux; reflux occurred as commonly in children with small as in those with normal bladder capacities. A comparison of the two groups (Table III) — the non-enuretic and enuretic children with urinary infection — with adjustment of the respective means to take into account the disparity in the number of individuals within a specific age group, indicates a highly significant difference between the adjusted means based on 56 with enuresis and 33 without:

$$t_{(87)} = \frac{310.57 - 217.86}{\sqrt{369.70}} = \frac{92.71}{19.23} = 4.82,\ P<0.001.$$

Table I
Reflux related to age at onset of first urinary infection

Age in years	Reflux	No reflux
0-1	2	—
1	5	2
2	9	11
3	13	11
4	8	9
5	4	5
6	—	2
7	2	6
8	—	1
9	—	—
Totals	43	47

Table II
Reflux related to age at first voiding urethrogram

Age in years	Reflux	No reflux
1	1	—
2	3	1
3	7	6
4	8	8
5	4	5
6	6	5
7	7	3
8	4	8
9	1	7
10	—	2
11	—	2
12-13	2	—
Total	43	47

Furthermore, when the group of children whose enuresis subsided on cure of their infection as well as the non-enuretic counterparts are eliminated, a yet more significant difference with their respective mean bladder capacities is obtained.

We may conclude, first, that girls with recurrent urinary injections who are enuretic have small MBC's, and secondly that the small MBC is not usually due to the infection, for it often persists when the infection has been cured. As a corollary, not all girls with recurrent urinary infections have small MBC's; urinary infections therefore do not necessarily cause a diminution in MBC. In the group as a whole 56 (63%) of 89 children had nocturnal enuresis; of these 48 (86% of the enuretics) or 54% of the total number of children studied had small bladder capacities and eight did not. This proportion with small bladder capacities compares with our findings in uncomplicated enuretic children, 76% of whom had small bladder capacities. The enuresis cleared in 16 when the urinary infection was eradicated. This favourable response occurred mainly in the older children; 12/18 aged nine and over became dry at night, while only 4/38 under the age of nine became dry when the urinary infection had been controlled.

Familial incidence of recurrent urinary infections and nocturnal enuresis — The incidence of a history of enuresis or urinary infection in the families under review was compared with the findings in 84 normal families studied and reported elsewhere. In both groups some subjects with enuresis had urinary infections and *vice versa.* All those who were enuretic are included in the enuretic group, and all who had urinary infections are similarly included in the group with urinary infections. Children under the age of 4, because many such children are still enuretic, have been excluded from the sibling analysis (Table IV). A comparison of the two groups of families reveals that in families from which a girl presents with a recurrent urinary infection, a history of enuresis and urinary infections in parents and siblings is much commoner than it is in normal families. A more complete comparison which includes the findings in families from which a child presents with enuresis is given in Table V. In the families of enuretics the incidence of enuresis in parents, though not in siblings, is much greater; a history of urinary infections in the parents and sisters, though not in brothers, is also commoner.

Discussion

It is well known that girls with recurrent urinary infections often have nocturnal enuresis[4] and may not infrequently be day dribblers. We ourselves, and this is probably true of most workers in this field, have assumed in the past that the enuresis and day dribbling are symptomatic of the urinary infection. This may be true in some instances, for 16/56 children with urinary infections who were also enuretic became dry when the infection subsided. This explanation, however, cannot apply to the majority, who remain enuretic even when the infection has been cured. In our experience the enuretics with and without urinary infections are identical, apart from the infection. Both groups have small functional bladder capacities and in both the enuresis responds, in approximately one-quarter of the cases, (nine of 40 cases in this series) to the elimination of certain foods from the diet.[12] The enuretics and children with recurrent urinary infections are similar, if not identical, in one other respect, for the incidence of both disorders is greatest in the 3- to 4-year age group, and this incidence falls progressively as the child grows older. Most enuretics for example have become dry by the age of 14,[13] while most girls with recurrent urinary infections have, according to Kunin,[11] grown out of their problem by the time they reach puberty, though urinary infections tend to return with marriage and pregnancy. The many features which these two disorders have in common suggest either that they have a common etiological basis or that enuresis predisposes to the development of recurrent urinary infections. Is the latter suggestion feasible? In enuresis, as we have explained elsewhere,[12] the bladder muscle is in spasm, hence the small functional bladder capacity. Contraction of the detrusor muscle leads to relaxation of the proximal urethra and a tendency to day dribbling; this may allow bacteria to enter the bladder "against the stream", but only in girls, for obvious anatomical reasons. The enuretic girl, particularly if a day dribbler, would, in these circumstances, be as likely to acquire a urinary infection as the child with a neurogenic bladder. We are not sure, however, that this explanation is entirely valid, though it may be true in some instances, for not all enuretic girls with day dribbling acquire urinary infections. Whether the discovery of the cause, followed by the cure of the enuresis, will lead to prevention of further urinary infections is still to be determined. An alternative explanation is that enuresis and recurrent

Table III

Maximum bladder capacities (MBC) in day dribblers, enuretics and non-enuretic girls with urinary infections, and in normal female controls.

	A						B					
	A_1			A_2			B_1			B_2		
Age intervals in years	MBC in day dribblers with urinary infections			MBC in enuretics with urinary infections			MBC in non-enuretics with urinary infections			MBC in normal female controls		
	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.
3	9	118.89	70.92	7	120.00	78.53	5	165.00	61.89	11	187.72	48.19
4-5	7	176.43	56.77	8	174.38	52.88	6	229.83	69.76	21	239.63	65.2
6-7	14	220.00	78.59	15	196.33	64.10	7	300.29	83.22	30	305.2	76.06
8-9	7	254.29	63.41	12	252.92	74.94	9	382.22	84.52	23	346.38	115.81
10-13	10	240.40	114.63	14	284.64	128.53	6	417.17	136.98	51	422.63	104.22
Total number of individuals and their adjusted means	47	202.83		56	217.86		33	310.57		136	336.57	

There is a significant difference between those in group A and those in group B ($P < 0.001$).
The differences between A_1 and A_2 are not significant, nor are those between B_1 and B_2.

urinary infections are manifestations of a common underlying disorder. In either case the discovery of the cause of enuresis is essential for the proper understanding not only of enuresis in both sexes, but also of recurrent urinary infections in girls.

In all series of enuretics there appears to be a preponderance of males; the ratio of boys to girls is 3:1 in our own series. This is not because girls become dry at an earlier age than boys, but because nearly two-thirds of the enuretic girls are found to have urinary infections and on this account are excluded from any enuretic series. The enuretic girls with urinary infections in our experience constitute between 44% and 63% of the girls with recurrent urinary infections, 44% of the enuretics who remain enuretic after infection has been cured, and 63% of the girls with recurrent urinary infections when they presented initially. Whatever disorder causes nocturnal enuresis, therefore, manifests itself in boys and in about one-third of the affected girls as uncomplicated enuresis with or without day dribbling. In nearly two-thirds of the girls it manifests itself as a recurrent urinary infection with enuresis, again with or without day dribbling. Enuresis is not, however, associated with or related to all recurrent urinary infections in girls, for approximately a third of such children in our experience have not been enuretic. Whether the urinary infections in this group of children have a different etiology, or whether all have the same basic underlying cause, whether immunological, genetic or allergic, must remain at the present time a matter for conjecture.

With regard to radiological studies in these children, we believe that any girl with a urinary infection requires thorough investigation, and this includes an intravenous pyelogram as well as a voiding cystourethrogram. However, we consider that children with uncomplicated enuresis do not require these studies and should not be exposed to unnecessary x-radiation.

Table IV

Percentage incidence of enuresis and urinary infections in families (UI) when the child presented with a urinary infection, and in normal families (C).

	Fathers		Mothers		Siblings			
					Boys		Girls	
	C	UI	C	UI	C	UI	C	UI
Number	84	88	84	88	124	113	109	110
History of Enuresis %	3.6	11	4.8	11.4	11.3	18.0	6.4	12.5
History of Urinary Infections	0	3	21.4	30.7	1.6	2.0	11.9	16.3

C—control family.
UI—urinary infection family.

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Résumé

Les infections urinaires récidivantes chez les filles: leur relation avec l'énurésie

La capacité vésicale maximum (CVM) a été étudiée chez 89 filles traitées pour infections urinaires, à une période où l'infection urinaire était enrayée. De ces 89 filles, 56 avaient souffert d'incontinence urinaire au moment de leur première visite et 40 souffraient encore d'énurésie, même après la disparition de l'infection. La CVM des enfants souffrant d'énurésie était nettement plus faible que chez celles qui n'étaient pas ou n'avaient jamais été victimes d'énurésie. Il s'ensuit que l'énurésie et la faible capacité vésicale n'étaient pas généralement attribuables à l'infection urinaire. Les auteurs concluent que l'énurésie chez les filles les prédispose à l'infection urinaire ou estiment qu'une pathologie profonde commune les prédispose aux deux pathologies.

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Table V

Incidence of enuresis and urinary infections in parents and siblings when child presents either with enuresis (E) or urinary infection (UI) compared with normals (C).

	Fathers			Mothers			Siblings					
							Boys			Girls		
	C	E	UI	C	E	UI	C	E	UI	C	E	UI
Number	84	84	88	84	84	88	124	95	113	109	123	110
History of enuresis %	3.6	28.6	11.0	4.8	26.2	11.4	11.3	15.7	18.0	6.4	12.2	12.5
History of urinary infections %	0	7.1	3.0	21.4	31.0	30.7	1.6	0.9	2.0	11.9	9.4	16.3

C - control family. E - enuretic family. UI - urinary infection family.