Covert bacteriuria of childhood

A clinical and epidemiological study

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Savage, D. C. L., Wilson, M. I., McHardy, M., Dewar, D. A. E., and Fee, W. M. (1973). *Archives of Disease in Childhood*, 48, 8. **Covert bacteriuria of childhood: a clinical and epidemiological study.** A 4-year screening programme for covert bacteriuria in Dundee primary schoolgirl entrants showed a prevalence of 1.6% and an annual incidence of 0.9%. Among 109 children with bacteriuria, 70% had symptoms of lower urinary tract infection, 35% had vesico-ureteric reflux, and 23% radiological evidence of pyelonephritis. Both pyuria and a past history of urinary infection were related to radiological evidence of reflux or pyelonephritis.

Covert bacteriuria was found more frequently in children from social classes IV and V; and their housing, home circumstances, and home care were worse than a control group, even when allowance was made for their social class differences. The children appeared generally healthy but were smaller than a control group.

The data suggest that the great majority of these children are not seriously at risk and that there is at present not sufficient evidence to warrant prescriptive screening.

Most publications on urinary tract infection during childhood have been concerned with overt infection, that is infection recognized by the symptoms it has caused. The clinical, laboratory, and radiological findings in this group of children are well known, and the short and long-term prognoses are now more clearly understood (Smellie and Normand, 1968; MacGregor, 1970; Savage, 1971).

Recently there has been interest in asymptomatic bacteriuria, that is significant bacteriuria detected during screening programmes. In these surveys many of those found to have bacteriuria had symptoms referable to the lower urinary tract, and we believe the description asymptomatic to be inappropriate and have preferred the term 'covert'. Covert bacteriuria, therefore, is defined as significant bacteriuria detected during a screening programme. Though adult populations, particularly during pregnancy, have been extensively investigated, there is little information about covert bacteriuria during childhood.

In the only large survey during childhood (Kunin, Deutscher, and Paquin, 1964) the rate of infection and radiological abnormalities was

higher in the younger Caucasian girls, and for this reason we decided in Dundee to screen primary schoolgirl entrants (Savage *et al.*, 1969). This study has continued and the present report details the clinical, laboratory, bacteriological, and radiological findings. The epidemiological aspects are discussed and the case for *prescriptive* screening* for covert bacteriuria of childhood is appraised.

Material and method

Study area. Dundee is an industrial city in Eastern Scotland. The population of about 182,000 consists largely of native-born Scots, and the main industries are jute and light engineering.

Study population. From 1967 to 1970 the majority of 5-year-old girls entering the Dundee Education Authority primary schools were screened for covert bacteriuria (Table I). Those screened in 1967 were reported in a pilot study (Savage *et al.*, 1969). During 1968 and 1969 almost all the schoolgirls had their urine examined, but in 1970 a smaller number were examined primarily to collect more cases for a random-

*Defined as a screening programme which has as its primary aim a direct contribution to the health of the individual (McKeown, 1968).

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TABLE I
Covert bacteriuria in Dundee schoolgirl entrants

Prevalence 5-year-old Girls					
Year	Examined	Children available (%)	1st specimen positive (%)	Covert bacteriuria	Covert bacteriuria (%)
1967	943*	89	3.9	20	2.1
1968	1601	96	4.4	23	1.4
1969	1683	96	7.4	28	1.7
1970	990*	77	6.3	15	1.2
Incidence (1968 cohort re-examined)					
1969	1443	99	3.3	8	0.6
1970	1323	99	3.1	16	1.2
Prevalence 13-year-old girls					
1969	1455*	82	2.8	10	0.7

*Not all schools included.

ized control trial of therapy. The incidence of covert bacteriuria in the 1968 cohort was determined by rescreeing them in 1969 and 1970.

During 1969, 1455 13- to 14-year-old schoolgirls (Table I) had their urine examined to determine the prevalence of bacteriuria in an older age group.

Presentation of programme to the community. This has been detailed in a previous publication (Savage *et al.*, 1969). We have found no difficulty in obtaining the fullest co-operation from the schools, medical personnel, and parents. Evidently a programme intended to improve the health of the children in a community has found general acceptance.

Urine collections. Urine was collected at school either by the school nurses or one of us (M.McH.). There was no previous cleansing of the external genitals nor were the labia spread. The urine was not a mid-stream specimen and was collected in a disposable sterile aluminium bowl which had been placed in the child's pot. The urine was then poured into a disposable sterile polythene container which was sealed and placed in an insulated standard portable blood transfusion box maintained at between 4 to 6 °C by a water-filled container which had been frozen overnight. The urine was transported back to the laboratory within 3 hours of collection.

Bacteriological methods. On arrival at the laboratory the specimens of urine were placed in a refrigerator maintained at 6 °C and examined within 1 hour. The urine was cultured by the swab method described by Bradley, Crowley, and Darrell (1967). A pure, or nearly pure, and confluent, or semiconfluent, growth was indicative of bacteriuria. Any child with

a positive urine culture by this screening method had further urine specimens examined by the plating-out method used for colony counts in a diagnostic laboratory (Urquhart and Gould, 1965). Horse blood agar and McConkey agar plates were seeded with a standard loopful of urine (0.01 ml) from well-mixed but uncentrifuged urine samples. The bacterial colony count was expressed as the number of viable organisms per ml urine after the plates had been incubated at 37 °C overnight.

Criteria for establishment of a case. 100,000 or more viable bacteria per ml urine on three consecutive occasions was regarded as indicating significant bacteriuria.

Dip-slide culture. Specimens of urine from the final 300 schoolgirls aged 5 years were examined by the Uricult* dip-slide method in parallel with the swab method used in this screening survey. Any specimen that gave a positive result, i.e. confluent or semi-confluent growth, with either the dip-slide or swab culture, or both, was examined again by (1) Uricult dip-slide, (2) the swab method of plating out, (3) the standard loop method of plating out, and (4) pour plate culture.

Urological investigation. Children whose first urine specimen was positive had 2 further midstream specimens of urine collected under the supervision of a nurse. Initially if these contained a significant number of bacteria the child was admitted for investigation of renal function. Over the last 2 years, however, the children have been investigated as outpatients.

The plasma urea, creatinine, electrolytes, and the

*Bristol Laboratories, Stamford House, Langley, England.

serum calcium, phosphate, alkaline phosphatase, and proteins were determined, and the ESR, haemoglobin, and blood film were routinely examined. The children had an intravenous pyelogram, micturating cystogram, a chest x-ray, and a left wrist x-ray for determination of bone age.

Intravenous pyelography (IVP) included tomography of the kidneys in those children in whom the renal cortical outline could not be clearly defined on the routine films. During micturating cystography there was no screening and three films only were taken. The first followed bladder filling, the second was taken after 20 minutes' delay with push-back into the catheter which was connected to a reservoir, and the third was a micturating film. Children with significant urological abnormalities were examined by cystoscopy.

Results

Participation. During 1968 and 1969, 96% of the Dundee primary schoolgirl entrants had their urine examined. 99% of the available 1968 cohort of schoolgirls had their urine re-examined in 1969 and again in 1970 (Table I).

Screening level for significant bacteriuria. Those children with semiconfluent or confluent growth had a repeat urine examination, and with these criteria approximately 4% were recalled for further specimens (Table I).

Dip-slides (300 specimens examined). Among 300 dip-slide tests there were 13 urine specimens which required further investigation. 5, by each of the 4 methods of culture, had a significant bacterial growth and in each case the child was found to have covert bacteriuria. There were 8 false positive results on the dip-slide and 5 false positive results using the swab method. The pour plates and standard loop results showed good correlation; 5 in each method gave positive result.

Prevalence and incidence of covert bacteriuria. As shown in Table I, approximately 1.6% of the primary schoolgirl entrants were found to have covert bacteriuria, and 0.7% of the 13-year-old girls. The incidence of new cases of covert bacteriuria in the 1968 cohort re-examined at 6 years of age, was 0.6%, and when re-examined at 7 years of age 1.2%.

Children with covert bacteriuria. 7 of the children found to have bacteriuria during the screening programme were not included since they were already under treatment for urinary infection.

A total of 110 girls aged 5 to 7 years with covert bacteriuria were detected in this screening pro-

gramme. One child's parents refused to allow her to attend the clinic and she has not been included in the data except as one of the total with covert bacteriuria. The parents of 3 children refused radiological investigation in their child and 2 cystograms were not completed for technical reasons. Therefore 106 children are detailed with the result of their intravenous pyelogram but only 104 children had a micturating cystogram completed satisfactorily.

Further data on the 10 girls aged 13 years are detailed separately.

Primary schoolgirl entrants

History and symptoms in children with covert bacteriuria. There was a past history of urinary infection in 20% of the children. Urinary infection had been diagnosed in 1 child during infancy, in 8 in their third year, in 5 in their fourth year, and in the remainder (8) in the year before primary school entry. None of these children was regarded by her parents or general practitioners as having a urinary infection at the time of screening nor were any on therapy.

In over a quarter of the children there was a family history of urinary infection. In 7 this involved sibs, 4 of whom were diagnosed during the survey. In 3 pairs of sibs, including identical twins, there was in each child vesicoureteric reflux or pyelonephritis. A maternal history of urinary infection was common, usually a cystitis of pregnancy.

The symptoms of urinary infection in these children are detailed in Table II. In nearly all the children the parents reported the child to be in good health. Over a third of the children had

TABLE II
History and symptoms in 109 children with covert bacteriuria

	No.	%
Past history of urinary infection	22	20
Family history of urinary infection	31	28
Good health	106	97
Never completely dry day or night	40	37
Nocturnal enuresis	56	51
Diurnal enuresis	51	47
Urgency of micturition	59	54
Frequency of micturition	58	53
Dysuria	14	13
Unexplained fevers	8	7
Loin pain	4	4
Nocturia	4	4
Haematuria	0	0
Symptoms (excluding nocturnal enuresis)	76	70

TABLE III

Heights and weights of children with covert bacteriuria compared with controls

	Covert bacteriuria	Pyelonephritis/ reflux	No radiological abnormality
No. of cases	92	37	48
<i>Height</i>			
Mean difference from controls	-2.02 cm	-2.06 cm	-1.88 cm
SD	5.06	4.66	5.42
P	<0.001	<0.05	<0.05
<i>Weight</i>			
Mean difference from controls	-0.94 kg	-1.24 kg	-0.77 kg
SD	2.27	2.02	2.39
P	<0.001	<0.01	<0.05

never been completely dry by day and night and about half of them wet their pants during the day. Enuresis was present in 60%. The most frequent symptoms were urgency and frequency of micturition. These symptoms are difficult to define in this age group, but when directly asked, the mother was usually certain as to their presence or absence. Urgency was diagnosed when the child regularly ran to the lavatory, and frequency when she micturated more than other children. 63% of the children had one or other of these symptoms. Other symptoms were uncommon and dysuria was usually intermittent and isolated. Some of these less common symptoms were often found in children with pyelonephritis. In half of the children with dysuria, 6 of the 8 with unexplained fevers, and 3 of the 4 with nocturia, pyelonephritis was present. 3 of the 4 children with loin pain had renal disease (pyelonephritis, hydronephrosis, staghorn calculus).

Even when nocturnal enuresis was excluded, 70% of the children had symptoms that are recognized as being frequently associated with lower urinary tract infection. In only 25% were there no symptoms whatsoever.

Clinical examination. In nearly every case the child appeared healthy and general examination was in most cases normal though 3 children appeared listless and unwell, almost certainly due to their bacteriuria. None of the children examined was found to have serious co-existent disease and the blood pressure was normal in all cases. 5 children had mild vulvitis.

Height and weight. The height and weight of 92 children with covert bacteriuria were compared with those of 1600 schoolgirl entrants to the Dundee primary schools in 1968. The heights and weights of both groups were those recorded

at the routine school examination. A mean figure for these parameters was obtained for children varying from 4 years 9 months to 6 years, and was compared with that of the group with covert bacteriuria and subgroups of those children with and without radiological abnormality. These findings are shown in Table III. The mean difference in height of the children with bacteriuria from the control group was -2 cm (0.79) and in weight was -0.94 kg (2.06 lb). Both the differences are significant at the 0.001 level. No significant difference exists between the children with pyelonephritis and/or reflux and those without radiological abnormality (mean difference in height 0.18 cm, weight 0.47 kg), but both these groups individually are significantly different from the control group of children.

Height and weight were re-examined with the children subdivided into social classes I to III and IV and V. The control children in social classes IV and V were smaller than those in social classes I to III ($P < 0.01$), but there was no difference between these groups in children with covert bacteriuria. Within these social groups the bacteriuric children were significantly smaller than the controls (social classes I to III: $P < 0.01$; social classes IV and V: $P < 0.05$).

Pyuria and bacteriuria. At the first outpatient attendance a fresh unspun midstream specimen of urine was examined, and in nearly every case the urine was slightly opaque. Proteinuria (Albustix) was absent except for a few cases which had a trace amount present (< 30 mg/100 ml). Pyuria, defined as more than 25 leucocytes per mm^3 of unspun urine was seen on this first occasion in 65% of the children, and bacteria were seen on direct microscopy in 102 of the 109 children.

TABLE IV

Mean Hb, total leucocytes, and erythrocyte sedimentation rate

Estimation	Normal x-rays n = 44	Pyelonephritis n = 20	Reflux n = 36	P
Hb (g/100 ml)	12.41	11.65	11.84	<0.05
WBC (per mm ³)	7845	7160	7377	NS
ESR (mm/hr)	12	27	21	See text
Urea (mg/100 ml)	29	32	30	NS

Note: n, number of children; NS, not significant; P, probability.

The presence or absence of a significant number of pus cells was inconsistent in any one child during episodes of reinfection, but the correlation of a significant growth on culture and bacteriuria diagnosed on microscopy was 95%.

Haematological and laboratory investigations. The results have been examined in the whole group and comparison has been made between children with normal and abnormal renal tracts. The results are seen in Table IV.

Initially, plasma calcium, phosphate, alkaline phosphatase, total protein, and protein albumin and globulin fractions were measured. However, even with the radiological evidence of renal damage these estimations were within normal limits and were not therefore continued as a routine investigation. Plasma creatinine was persistently raised in only 1 child with bilateral atrophic pyelonephritis. Urea levels were not significantly different in the various groups and, apart from the 1 child with persistently raised values, they were not raised.

In no child was the total white cell count raised ($>15,000 \text{ mm}^3$) nor was there significant difference in the levels among the various groups of children. However, Hb less than 10.5 g/100 ml was found in 7 children with pyelonephritis or reflux, and the mean value for Hb in these groups of children was significantly lower than in those with normal renal tracts ($P < 0.05$).

An erythrocyte sedimentation rate (Westergren) greater than 20 mm/hr was found significantly more frequently in children with pyelonephritis ($P < 0.005$), reflux ($P < 0.01$), or radiological abnormality ($P < 0.05$). The mean ESR was also higher in these groups but because of the wide range (1–115 mm/hr) compared with that in children with normal renal tracts (0–26 mm/hr), the mean values are not comparable statistically.

Radiological studies. These are summarized in Table V. In half of the children the intravenous pyelogram and the cystogram were normal.

Radiological evidence of pyelonephritis (Hodson, 1959) was seen in the IVP in 23% of the children and in the great majority this was limited to the upper or lower pole of one kidney. In 4 children one kidney was more than 1 cm shorter than the other. In 2 this was probably due to an anatomical difference, but in the 2 others this was not so and there was associated reflux, so that 26 children (25%) had radiological evidence of infection involving the kidney substance. Reflux was present in a third of children and in over 80% of those with renal involvement. There were a total of 45 refluxing ureters, 4 Grade I (reflux to ureter), 32 Grade II (reflux to kidney), and 9 Grade III (reflux up dilated renal tract to kidney).

There was a high incidence of sacculation or trabeculation of the bladder. In some cases the saccules were paraureteric (Fig. 1) but in others trabeculation and sacculation were generalized (Fig. 2). Urethral configurations described as 'spinning top', 'carrot', 'turnip', were frequently seen. None was particularly associated with any

TABLE V

Radiological studies in children with covert bacteriuria

	No.	%
<i>Intravenous pyelogram (106 children)</i>		
Abnormal	39	37
Pyelonephritis*	24	23
Small kidney	4	4
Dilated ureter and/or pelvis and calices	8	8
Duplication of upper urinary tract	10	9
Malrotation	1	1
Stag horn calculus	1	1
Megaureter	1	1
<i>Micturating cystogram (104 children)</i>		
Abnormal	45	43
Vesicoureteric reflux†	36	35
Trabeculation and/or sacculation of bladder	22	21
Large bladder	2	2
<i>Normal IVP and cystogram</i>	55	53

*Pyelonephritis bilateral in 4; †reflux bilateral in 9.

FIG. 1.—Micturating cystourethrogram, shows vesicoureteric reflux in association with a paraureteric sacculum (arrow).

FIG. 2.—Cystogram: generalized trabeculation.

abnormality of the cystogram or intravenous pyelogram.

In the annual re-examination of the 1968 cohort during 1969 and 1970, 24 new cases of covert bacteriuria were diagnosed and these results are included in Table V. In only 12 (50%) was the IVP and micturating cystogram normal, for in 8 (33%) there was radiological evidence of pyelonephritis and in 8 (33%) vesicoureteric reflux.

The chest film was normal in all the children, but the bone age was, on average, a year behind the chronological age in most of the children whose height and weight was less than the 3rd centile.

Prediction of radiological findings from case histories. Correlation of the radiological findings and factors in the child's history are shown in Table VI. The commoner symptoms were not related to the radiological changes, but there was a significant correlation between pyuria and a radiological abnormality. Half the children with a

past history of urinary infection had pyelonephritis or reflux and nearly two-thirds of them radiological abnormality; there was no such relation with a family history of infection. When the combination of a past history of urinary infection, pyuria, and symptoms of lower urinary tract infection was present the radiological findings were usually abnormal and pyelonephritis was commonly found. Children in social classes IV and V had a higher incidence of pyelonephritis, but this just failed to reach a significant level.

Distal meatal stenosis. In 38 of 45 (85%) children examined by cystoscopy, urethral calibration with *bougies à boule* showed a narrowed distal urethra—14 to 22 F (normal around 24 F for this age group—Mr. J. Grieve).

Spontaneous or antibiotic cure. In a number of children only the initial two specimens of urine showed significant bacteriuria. In some cases there had been symptoms of lower urinary tract infection at this time and in others antibiotics had been given concurrently. Prolonged follow-up has shown that most specimens of urine from these children remain sterile, but in 2 cases urinary

TABLE VI

Correlation of radiological findings and case histories

Radiology		A. Symptoms		B. Pyuria		C. Past history urinary infection		A + B + C		Family history urinary infection		Social class	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	I-III	IV-V
<i>Pyelonephritis</i>													
Yes	24	18	6	19	5	11	13	6	18	7	17	9	15
No	82	57	25	40	42	11	71	3	77	26	56	55	27
		NS		P < 0.05		P < 0.005		P < 0.005		NS		NS*	
<i>Reflux</i>													
Yes	36	17	19	25	11	12	24	5	32	13	23	18	18
No	68	33	35	32	36	10	58	4	61	19	49	40	28
		NS		P < 0.05		P < 0.05		NS		NS		NS	
<i>Abnormal x-rays</i>													
Yes	49	26	23	37	12	14	35	8	45	17	32	25	24
No	55	24	31	20	35	8	47	1	53	15	40	34	19
		NS		P < 0.005		P < 0.05		P < 0.05		NS		NS	

* $\chi^2 = 3.81$, $\chi^2 = 3.84$ for 5% level; NS, not significant; P, probability.

infection developed 6 and 18 months later. It is possible that in a number of these children covert bacteriuria was present at the initial examination.

Medical and social background. This information was obtained by a questionnaire form which was completed during personal interviews with the parents. Those interviewed were the parents of children with covert bacteriuria and a control group of 500 children selected by random numbers from a year's intake of primary schoolgirls. The information about the administration of an antibiotic during a 12-month period was obtained from the child's general practitioner.

The results are expressed as a percentage with the figures for cases and controls, in that order, in parentheses.

There was no significant difference between the 2 groups in their neonatal history nor in their general health. The family size was similar in the two groups but children with covert bacteriuria were more commonly the third or later child (47%: 18% $P < 0.005$).

There was a significant difference in the distribution of social classes between the two groups (Table VII), and the children with covert bacteriuria lived in poorer housing ($P < 0.005$) with poorer home circumstances ($P < 0.005$) and home care ($P < 0.01$) than the control children.

There was a toilet in the home of most families (92%: 93%) but in 11% in each group there was no bathroom. Significantly more control children bathed daily or on alternate days (29%: 44%) than children with covert bacteriuria, and nearly half

(45%) of the children with bacteriuria bathed once a week or less ($P < 0.01$).

More children with covert bacteriuria had worn napkins by day after the age of 2 years but this just failed to reach a significant level (15%: 8%). Napkins worn at night after 3 years of age were significantly more common among those with covert bacteriuria (11%: 4% $P < 0.05$), and in these children toilet training had been initiated and completed later ($P < 0.005$). Fewer of the controls, whose average age was 5 to 6 years, were enuretic by night (49%: 7%) or day (42%: 0.3%), and frequency (48%: 7%), urgency (44%: 5%), and dysuria (13%: 3%) were significantly more common in the cases than in the controls ($P < 0.005$).

There was no difference in the percentage of control children (33%) and children with covert bacteriuria (37%) who had had one course of antibiotic during a 12-month period. When the children were divided into two socioeconomic groups (social class I to III and IV and V) no

TABLE VII
Social class distribution

Social class	Children with covert bacteriuria (109)	Controls (500)
I, II	6%	14%
III	41%	49%
IV, V	53%	37%

Note: $\chi^2 = 11.01$ d.f. 2 $P < 0.01$.

significant difference in the level of prescription between the groups was found.

13-year-old girls

A group of 1455 13- to 14-year-old girls was screened for covert bacteriuria, but since one school was not included only 82% of available girls had their urine examined. Though 17 girls had two consecutive specimens with 10^5 viable organisms per ml urine, only 10 were finally regarded as having covert bacteriuria. It is possible that some of the other 7 girls had transient covert bacteriuria and it may be that our prevalence of 0.7% is too low a figure (Table I).

There was a past history of urine infection in one girl and one child had obvious symptoms. Neither had been investigated previously and both were found to have unilaterally a small scarred kidney. Two other children had occasional damp pants or wet beds.

None of these children was hypertensive and all appeared healthy. 3 children, all in social class V, were less than the 3rd centile for height and weight, and 6 of them were in social class IV or V.

In only 2 children was there pyuria initially, but in 9 bacilli were seen on microscopy at their first visit to the outpatient department. The only child with a raised ESR (23 mm/hr) had pyelonephritis, but in 2 others with renal involvement the ESR was less than 10 mm/hr. None had a raised urea or total leucocyte count and the Hb level was normal in every case. 3 girls had unilateral pyelonephritis with associated poor renal growth. Reflux was present in 3, in 1 case bilaterally, but was only Grade I in each instance.

Discussion

This report details a 4-year screening programme for covert bacteriuria in Dundee schoolgirls. With Kunin's extensive survey (Kunin, 1971) it identifies and answers some of the problems which must be solved before a decision can be made on the medical and economic advisability of prescriptive screening for covert bacteriuria during childhood. In this decision the results of treatment are equally important and a randomized controlled trial of therapy will be reported later; however, the data already collected do allow certain conclusions to be reached.

We have found that, though the co-operation of the community is readily obtained, there are appreciable difficulties in adequately screening school-children for covert bacteriuria. A basic problem is to include the total school population. Owing to

illness a few children will nearly always be absent from school so that return visits become necessary, particularly since those with prolonged or recurrent absence might have a higher incidence of covert bacteriuria. We did not find this to be the case but this group did cause considerable difficulties. Another problem is that small children cannot or will not pass urine to order. It is not satisfactory to load them with fluids since diuresis may invalidate the significance of bacterial growth; return visits therefore become necessary. Apart from the time-consuming nature of these return visits, there is the deleterious effect on the child's schooling and the cumulative effect on the teachers' goodwill. It is essential, therefore, that all those involved are well informed and agreed on the necessity of the screening programme.

The radiological and paediatric departments' work load is appreciably increased since every child with bacteriuria required investigation and frequent outpatient visits. The outpatient care is not made easier by the high rate of reinfection (Savage *et al.*, 1971), but unless good follow-up is provided the value of the screening programme is lost.

It has been suggested that cleaning the genitals in young children is essential if satisfactory urine specimens are to be collected. We have not found this necessary and our contamination rate has remained at a satisfactory low level similar to that recorded by Kunin who used antiseptic perineal swabs before urine collection. It is certainly more economical in time and less disturbing for the child to ignore this preliminary cleansing.

Kass has shown that 10^5 or more bacteria per ml urine are indicative of significant bacteriuria (Kass, 1956). The pour plate method is time consuming and other semiquantitative methods of culture have been tested and adopted. The standard loop method described by McGeachie and Kennedy (1963) and Urquhart and Gould (1965) is probably the most efficient semiquantitative method available. In screening, a large number of specimens is examined, and we found the method described by Bradley *et al.* (1967) convenient since it was both quick and efficient.

More recently a dip-slide method of bacterial culture has been described (Guttmann and Naylor, 1967; Arneil, McAllister, and Kay, 1970), but the commercially produced dip-slide kits were not available when this survey began. Our results suggest that dip-slides are satisfactory; the few false positives are not a problem and can be eliminated by further bacteriological examination. False negatives, in this small series, did not occur

when compared with the swab method of culture. Certainly they are more economical in time than routine methods presently in use and seem ideally suited for screening or routine laboratory services.

An immediate consideration in any screening programme is the prevalence and incidence of the disease. Though the prevalence is sufficient to encourage screening of primary schoolgirl entrants, rescreening at 6 and 7 years provides a similar number of girls to those detected at 5 years of age. The only large survey which has comparable data on covert infection is that reported by Kunin who examined Caucasian and Negro children ranging from 5 to 20 years of age (Kunin *et al.*, 1964). Their clinical and radiological data varied with the age and race of the child and in this report we have compared our figures only with his group of young white girls aged 5 to 9 years (screened 3,120). The prevalence in this age group of 1.2% was similar to our own but the annual incidence of infection was 0.4%. With these data Kunin (1968) estimated that 5% of schoolgirls would, by the time they leave school, have had a urinary infection. Our figures for the annual incidence are twice as high, and suggest that this estimate will be exceeded.

In Kunin's series 40% of the children had a past history of urinary infection and our figure of 20% is appreciably lower. Only a third of these children in our series had previously been investigated. This is surprising since every child with urinary infection should have an intravenous pyelogram and micturating cystogram performed, not only to detect those who may benefit from surgery, but also because the radiological findings influence therapy and management.

Since three-quarters of the bacteriuric children were symptomatic, the screening programme might be thought to be economically more acceptable if concentrated solely upon them. However, a number with reflux and pyelonephritis was symptom free so that this would not be effective in detecting all those with significant radiological abnormalities.

Symptoms of lower urinary tract infection were common and the great majority of these children have, in effect, overt disease. Many of the mothers had informed their general practitioners about their child's symptoms but few children appear to have had their urine examined. This is probably because these symptoms mimic so closely the child's natural pattern with its transition from bedwetting and daytime accidents to full bladder control, and therefore convey a false impression of security. However, our figures for a control group show that

at this stage these symptoms are infrequent and the child's urine should be examined whenever they are present.

Kunin defined pyuria as 4 leucocytes per high power field, and found it in 46% of the children. Our figures are not directly comparable since we used a count per mm³, but we do agree that pyuria is less commonly seen than in acute urinary infection; interestingly, a similar situation arises in bacteriuria of pregnancy (Little, 1966). Since pyuria is not consistently present, an awareness of the value of microscopy for bacteriuria is important. Microscopical examination of urine for bacteriuria is simple and its use in the diagnosis of urinary infections has been stressed by many authors (Kass, 1956; Pryles and Steg, 1959; Lam *et al.*, 1967). We would endorse the value of this examination of unspun, unstained fresh urine specimens for bacteriuria which in no way replaces, but should always complement, bacteriological examination. It should be remembered that microscopically clear or bacteriologically sterile urine may intermittently be present in a child with chronic urinary infection, and persistent urinary symptoms should lead to repeated urine examinations.

The haematological and biochemical data were usually normal though a few children with renal disease did have low Hb levels. This may be a reflection of the higher incidence of pyelonephritis in children of social classes IV and V, rather than an effect of the pyelonephritis *per se*. The ESR was raised in a number of children, but was normal in many with radiological abnormalities. These children's defect in renal concentrating ability has been reported (Savage, Wilson, and Fee, 1972).

We have previously remarked on the unexpected small stature of many of these children (Savage *et al.*, 1969) and this has now been confirmed. The effect, if it is an effect, on the child's stature does not seem to be due to renal involvement for there is no radiological evidence, in this larger series, of renal damage causing a significant difference in height and weight. Furthermore, those children with radiologically normal renal tracts are also significantly smaller in stature than the controls. This difference in stature may be related either to their bacteriuria, to their poorer environment, or to a combination of these factors.

The incidence of radiological pyelonephritis is high when compared with the 13% found in girls under 12 years of age with overt infection (Smellie and Normand, 1968). Our own figure of 23% contrasts with Kunin's 16%, though this rises to 20% if those children in his survey with unilateral

small kidneys are included. As in most series the incidence of reflux in children with pyelonephritis was high. The prevalence of reflux in our survey is similar to the 36% in girls with overt infection (Smellie and Normand, 1968) and the 35% of 5- to 9-year-old white girls with reflux in Kunin's series. The higher incidence of pyelonephritis in our group may reflect the covert and recurrent nature of the infection, or may be explained by the inclusion of a number of children with a history of urinary infection. There are 22 of these children in our series and 11 have radiological evidence of pyelonephritis. Since in overt disease children with radiological abnormalities relapse more frequently than those with normal renal tracts, their inclusion will increase the proportion of children with radiological abnormalities. If this group is excluded from our series then 13 out of 84 children (15%) have radiological evidence of pyelonephritis and 24 of 82 children (29%) vesicoureteric reflux.

Trabeculation and sacculation are not commonly reported, but Altman *et al.* (1971) recorded it as the most frequent abnormality seen on cystography in children with urinary infection, and Shopfner (1970a) showed it in 15% of children who required radiological evaluation of the urinary tract. Kunin noted it in 14% and we have found it in nearly 25%. It has been argued that these patterns might be normal variations which occur during the dynamics of micturition, but we regard them as pathological and have not included the minor crenations of the posterior bladder wall which are so frequently seen. Furthermore, on cystoscopy trabeculation of the bladder was a frequent finding and always seen when present radiologically. It is perhaps not surprising that chronic inflammation of the bladder wall may give rise to this picture and that it is therefore commoner in covert infection. Paraureteric sacculi (Fig. 1) were frequently associated with a refluxing ureter and it may be that a sacculi in this area interferes with the mechanics of the vesicoureteric valve and initiates reflux. This thickened trabeculated bladder with refluxing ureters is ideally suited for continuing infection and reinfection; not only does the reflux maintain a reservoir of infected urine in the urogenital tract, but the chronically inflamed and thickened bladder wall, unable to appose its mucosa, loses its bacteriocidal and bacteriostatic mechanism (Hinman and Cox, 1966).

The micturating cystourethrograms gave a widely differing range of urethral shapes, all of which were regarded as normal, and were not related to differences in calibre of the distal urethra. Most of the children examined by cystoscopy were

reported as having a narrowing of the distal urethra (Mr. J. Grieve); in Kunin's series only one case was thus diagnosed. Though Lyon and Tanagho (1965) found distal urethral stenosis in 90% of little girls with urinary tract infection, many authors would regard this narrowing as normal (Govan and Palmer, 1969; Shopfner, 1970b) and we are in agreement.

In Kunin's series pyelonephritis was more frequent in children with pyuria though not significantly so; we have found a significant correlation not only between pyuria and pyelonephritis but also with reflux. However, not all children with these abnormalities had pyuria, and a number might be missed if it was used as a screening technique. Kunin did not find a past history of infection helpful in predicting lesions on the intravenous pyelogram, but we have found a correlation between this and radiological evidence of pyelonephritis or reflux.

A family history of urinary infection was not helpful in predicting radiological abnormalities, but there was a fairly high incidence of sibs with urinary infection, a point previously expressed by other authors (Kunin *et al.*, 1964; MacGregor and Freeman, 1968). That vesicoureteric reflux and pyelonephritis may be familial is recognized (Mulcahy *et al.*, 1970) and is further shown by our data and emphasized by pyelonephritis in identical twins.

There is little information about the medico-social background of children with urinary tract infection and we have only been able to compare our data with those of Stansfeld (1966) and Kunin (1971).

Our data suggest that significantly more children with covert bacteriuria are found in social classes IV and V and that pyelonephritis is more common in these lower socioeconomic groups. Neither Stansfeld (1966) nor Kunin (1971) found this association, though Kunin noted a higher incidence of pyelonephritis in children of lower socioeconomic status. That the standard of housing, home circumstances, and home care were also significantly poorer in children with covert bacteriuria, even when allowance was made for differences of social class, suggests that many of these children come from homes in which there is poverty and a poor environment. In adults, patients of lower socioeconomic groups may be more frequently bacteriuric than are those from more privileged levels (Norden and Kass, 1968).

There was a significant difference between the children with covert bacteriuria and the controls in the period of wearing napkins and completion

of toilet learning. Possibly this reflects the early onset of infection, and many authors suggest that the majority of urinary infections arise in the first 3 years of life (Stansfeld, 1966; Smellie *et al.*, 1964). Another interpretation might be that this particular group of children has a longer period in which the perineum is in contact with soiled napkins and therefore is at greater risk from urethral contamination. Personal hygiene was poorer in these children and since the vulval flora may enter the bladder via the urethra, producing urinary infection some weeks after they become established on the introitus (O'Grady *et al.*, 1970; Stamey *et al.*, 1971), it is possible that infrequent bathing may be of some importance in the aetiology of bacteriuria in these children. That significantly more of these children were the third or later child in the family might be a reflection of the less intense toilet learning which later children often receive.

It has been suggested (Norden and Kass, 1968) that a wider prescription of antibiotics among the higher socioeconomic group might be the reason for the lower incidence of bacteriuria. Our study suggests that this is not the case for there was no difference in the prescription of antibiotics over a 12-month period, either between controls and patients, or among those of different social classes.

The group of 13-year-old girls had a lower prevalence of bacteriuria, but there was a similar proportion with radiological abnormality when compared with the younger girls. It is not possible to be certain how long they had had their bacteriuria, but, untreated, the majority one year later still had infected urine so that the bacteriuria was probably chronic.

This survey attempts to assess the need for prescriptive screening of covert bacteriuria in childhood. It has shown that during the school health examinations a satisfactory urine specimen can be obtained from the child without undue inconvenience to her, and that the semiquantitative estimation of bacteria in this urine is effective as a screening method. Both the programme and manner of investigation are acceptable to the community. The yield from screening is important in evaluating the programme, and our results suggest that there are a considerable number of schoolgirls with bacteriuria. In 1970 there were approximately half a million 5-year-old primary schoolgirls in England and Wales, and our results suggest that in this age group there may be 8000 schoolgirls with covert bacteriuria, of whom approximately 3000 would have vesicoureteric reflux and 2000 radiological evidence of pyelonephritis. However, a considerable number of

children will be missed if screening is limited to school entry, for it would seem to detect less than 20% of the children at risk during their school years.

Justification of prescriptive screening for covert bacteriuria of childhood will depend upon showing that there is a relation between it and acute symptomatic disease, or that it may progress to chronic pyelonephritis, and that the resulting chronic pyelonephritis is an important cause of illness and renal failure (Brumfitt and Reeves, 1968).

The relation between covert bacteriuria of childhood and acute symptomatic urinary tract disease is not clear. Kunin (1971) believes that prescriptive screening should be provided since he found that many of the children developed symptoms including clinical evidence of pyelonephritis. In our experience it is rare for these children to develop symptoms of an acute urinary tract infection or clinical pyelonephritis even when—unlike Kunin—we have not treated their infection (Savage *et al.*, 1971). Many of the children, however, do continue to have annoying symptoms of lower urinary tract disease. Kunin's data show that some women with pyelonephritis of pregnancy had covert bacteriuria during childhood and, though there is good evidence to favour antenatal screening for covert bacteriuria of pregnancy (Beard and Roberts, 1968), this is not to say that the screening should be done in childhood.

There is a clear relation between covert bacteriuria and radiological pyelonephritis but this is not sufficient to justify screening; it is necessary to show that the pyelonephritis causes ill health. In our series of 110 schoolgirls only 1 has serious bilateral renal disease. If this child's bilateral small scarred kidneys are due to pyelonephritis, then screening at primary school entrance is too late to detect those seriously at risk and confirms the observations of others that most of the severe renal damage seen in children with chronic pyelonephritis occurs in the first 2 to 3 years of life. Furthermore, it appears that the incidence of children with severe renal disease, the very children for whom this screening programme has been designed, is very low; in the total school population of 5-year-old girls in the United Kingdom our figures suggest less than 100 children with a similar pathology. The remaining children in our series in general have shown no radiological evidence of progressive disease during our relatively short follow-up and are in good health whether or not they have received treatment (Savage *et al.*, 1971).

If the purpose of the programme had been to detect children with surgically correctable uro-

genital lesions then it would have been equally unfruitful, for only one child—with a staghorn calculus—required surgical intervention. Surgery in the treatment of reflux is controversial, but we did not think any of the children required reimplantation of their ureters.

The relation of hypertension to pyelonephritis is uncertain. Some studies (Freedman *et al.*, 1965) have shown an increase in hypertensive disorders among bacteriuric patients, but others disagree (Savage, Hajj, and Kass, 1967). It seems probable that hypertension is more dependent on azotaemia than on a specific type of renal disease (Stamey, 1965). None of our patients was hypertensive.

In the majority of children with overt urinary infection the outlook is not as unfavourable as is sometimes suggested. We agree with MacGregor (1970) that for most of them recurrent episodes of urinary infection become less frequent as they grow older, that there is no permanent ill effect on their health at any age, and that at the most, unilateral loss of renal substance may be found after death from some other cause. Since controlled trials have not been done it is not even certain that these children's prognosis is affected by therapy. However, some children run a less favourable course and a number of women, though few when compared with the total number with infection, will succumb in late middle life to a disease initiated by their childhood urinary tract infection. In addition, there are a few children who will rapidly progress to renal failure in later childhood or early adult life. These two groups of children can be identified by their bilateral disease with vesicoureteric reflux up markedly dilated renal tracts; they require early identification in the first 2 years of life and intensive therapy if their prognosis is to be improved.

Our continuing experience in treating children with covert bacteriuria confirms our previous observations (Savage *et al.*, 1971) and those of Kunin (1971) that recurrent infection in them is more frequent than in those with overt disease. We believe, however, that their outlook is similar to those with overt infection, but long-term data will be required to determine this and to see whether treatment has any effect on prognosis. It may well be that therapy has little effect on what is for most of these children a relatively benign disease.

McKeown (1968) has stressed the importance of considering these biological factors in validating any screening programme. As far as covert bacteriuria in childhood is concerned the biological criteria have not as yet been met, for the natural history of the disease is still uncertain and know-

ledge of the effectiveness or even necessity of therapy is incomplete. Accurate attempts to evaluate the economic aspects are impossible until these questions have been answered.

This screening programme of primary school entrants has, however, shown that the very small group of children at risk of developing severe pyelonephritis already has a considerable degree of renal damage at the age of 5 years. It also suggests that the great majority of these children are not greatly at risk from their bacteriuria. This, in association with the unknown factors mentioned above, is the basis for our belief that prescriptive screening at this or at a later age during childhood, should not at present be recommended.

We have previously expressed our thanks to the many colleagues for their help and co-operation during this survey (Savage *et al.*, 1969). We would like to thank again Mr. J. Grieve for the cystoscopic findings and Mr. J. Pearson for statistical analysis of the figures. To the parents and children without whose co-operation the survey would never have been completed we are most grateful. The work has been supported by a grant from the Secretary of State for Scotland.

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