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# Six year follow up of infants with bacteriuria on screening

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## Abstract

***Objective*—To determine the value of screening for bacteriuria in infants with special emphasis on the natural course of untreated asymptomatic bacteriuria, renal growth, and renal damage.**

***Design*—Prospective six year follow up of infants with bacteriuria on screening in an unselected infant population.**

***Setting*—Paediatric outpatient clinic.**

***Patients*—50 Infants (14 girls, 36 boys) with bacteriuria on screening verified by suprapubic aspiration from an unselected population of 3581 infants in a defined area of Gothenburg.**

***Interventions*—Children with asymptomatic bacteriuria and normal findings on initial urography were untreated, although other infections were treated.**

***Main outcome measures*—Culture of urine and determination of C reactive protein concentration every six weeks for the first six months after diagnosis, every three months from six months to two years, and every six months between two and three years; thereafter yearly urine culture. Evaluation of renal concentrating capacity with a desmopressin test; radiological examination, including first and follow up urography and micturition cystourethrography without antibiotic cover; and measurement of renal parenchymal thickness and renal surface area.**

***Results*—Of the original 50 infants, 37 (12 girls, 25 boys) were followed up for at least six years. Two infants developed pyelonephritis within two weeks after bacteriuria was diagnosed; the others remained free of symptoms. 45 Infants were untreated; the bacteriuria cleared spontaneously in 36 and in response to antibiotics given for infections in the respiratory tract in eight. Recurrences of bacteriuria were observed in 10 of the 50 children, of whom one had pyelonephritis. No child had more than one recurrence. At follow up urography in 36 of the 50 children (9 girls, 27 boys) after a median of 32 months no child had developed renal damage. First samples tested for renal concentrating capacity showed significantly higher values than those from a reference population (mean SD score 0·50, 95% confidence interval 0·21 to 0·79; $p<0·001$), but the last samples showed no significant difference (mean SD score 0·08, −0·24 to 0·40; $p>0·05$).**

***Conclusions*—Mass screening for bacteriuria in infancy results primarily in detection of innocent bacteriuric episodes and is not recommended.**

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## Introduction

Several investigations have indicated that pyelonephritic renal scarring commonly occurs early in life.[1-4] When studying bacteriuria in neonates and infants suprapubic aspiration or urethral catheterisation is required to verify bacteriuria.[5,6] Very few screening studies of neonates and infants have been reported in which such verification has been performed,[6-8] and no long term follow up study exists. A prospective study of infants was therefore conducted to clarify whether screening for bacteriuria might identify individual children at risk of developing renal damage. This paper describes the results of long term follow up of 50 infants with bacteriuria on screening verified by suprapubic aspiration.

## Subjects and methods

### STUDY POPULATION, SCREENING TECHNIQUES, AND YIELD OF SCREENING

Bacteriuria was studied in an unselected population of 3581 infants (1899 girls, 1682 boys) in a defined area of Gothenburg. Screening was performed three times during the infants' first year of life at the ages of 0·25 - 1·9 months, 2·0-7·9 months, and 8·0-11·9 months. The primary screening was performed by bag sampling. In infants with ≥50 000 bacteria/ml in two successive bag samples suprapubic aspiration was performed.

Ninety four per cent of the total population participated in the screening. Altogether, 14 girls and 36 boys had bacteriuria on screening confirmed by suprapubic aspiration, the incidence being 0·9% for girls and 2·5% for boys. The incidence at the three screening occasions was 0·2%, 0·2%, and 0·5% respectively for girls and 1·6%, 0·8%, and 0·2% for boys.[9]

The percentage of infants in the study population contracting symptomatic urinary tract infection before 1 year of age was 1·1% for girls and 1·2% for boys. These infants had their infection diagnosed and treated outside the screening programme.[9]

### INITIAL RADIOLOGICAL INVESTIGATION

Radiological examination was performed after a median time lapse of 23 days from diagnosis (range four to 47 days). Urography was performed in 49 of the 50 infants and voiding cystourethrography without antibacterial prophylaxis in 46. Renal abnormalities were found in two girls and one boy. One of the girls had obstruction of the pelviureteral junction with hydronephrosis and general parenchymal thinning and the other had a duplicated collecting system. The boy had an ectopic kidney with contralateral renal malrotation. Vesicoureteral reflux of grade one or two on a scale of 0-5[10] was seen in one girl and four boys. In addition, one boy had a urethral valve with minimal urethral obstruction that did not require surgical intervention.

The incidence of renal abnormalities was 14% (95% confidence interval 2 to 43%) in girls and 3% (0 to 15%)

in boys. The incidence of vesicoureteral reflux was 7% (0 to 34%) in girls and 13% (4 to 29%) in boys.

The only child who was not radiologically investigated was killed in a road traffic accident at the age of 10 years. His kidneys were normal at necropsy.

FOLLOW UP

Regular check ups, including culture of urine and determination of C reactive protein concentration, were performed every six weeks for the first half year after diagnosis, every three months from six months to two years afterwards, and every six months between two and three years. Thereafter a urine specimen was cultured yearly.

Recurrences of bacteriuria were verified by culture of urine obtained by suprapubic aspiration in children less than 2 years of age. From 2 years of age, two voided samples containing $\geq$100 000 bacteria/ml were required for a diagnosis of asymptomatic bacteriuria. In children with acute symptoms associated with the urinary tract only one urine sample containing $\geq$100 000 bacteria/ml was required. Acute pyelonephritis was defined as fever of at least 38·5°C and bacteriuria, together with a C reactive protein concentration >20 mg/l. Requirements for a diagnosis of cystitis were acute dysuria, bacteriuria, a temperature of <38·5°C, a C reactive protein concentration $\leq$20 mg/l, and normal renal concentrating capacity.[11]

Renal tubular function was evaluated by determining the renal concentrating capacity—that is, the maximal osmolality of two separate urine specimens collected 1-5 hours after intranasal administration of 20 μg desmopressin (Minirin, Ferring AB, Malmö, Sweden).[12] The results were compared with those from an age related reference population.[13]

Follow up urography according to a standardised protocol[14] was performed two to three years after the first radiological investigation. In addition to detailed conventional evaluation for renal damage at urography, standardised measurements were made of the parenchyma. The parenchymal thickness was measured from the tip of the papilla to the renal outline at three different sites (upper and lower poles and lateral aspect) according to the method of Claesson *et al.*[15] Renal surface area was measured planimetrically according to Jorulf *et al.*[16] The renal measurements were related to the L1-L3 distance—that is, the distance between the upper border of the first lumbar vertebra to the lower border of the third. The results were compared with the reference material of Claesson *et al*[15] and expressed as standard deviation score units.

If additional urography was performed the last available investigation was used for evaluation.

Fisher's test of difference-score population symmetry about zero was used for statistical calculations.[17]

The study protocol was approved by the ethics committee of Gothenburg University.

## Results

Of the 50 infants with bacteriuria, 37 (12 girls, 25 boys) were followed up until school entry at 7 years—that is, for at least six years (table I). Three infants, all with normal findings at urography, were followed up for less than two years. The parents of two of these infants refused further examinations when the bacteriuria resolved. No symptomatic recurrences were reported for these children when they were contacted at age 7. The third child was lost to follow up while still having bacteriuria, although culture of a urine specimen obtained two years subsequently gave normal results. Of the remaining 10 infants who could not be followed up for the intended six years, four moved abroad; the remaining six reported no symptomatic recurrences when contacted at the age of 7 years.

TABLE I—*Follow up of 50 infants with bacteriuria on screening verified by suprapubic aspiration. Figures are numbers of infants*

| | Years of follow up | | | | | | |
|---|---|---|---|---|---|---|---|
| Sex | 6 | 5 | 4 | 3 | 2 | 1 | <1 |
| Girls | 12 | | 1 | | | 1 | |
| Boys | 25 | 2 | 2 | 2 | 3 | 1 | 1 |

OUTCOME OF BACTERIURIA

Figure 1 shows flow charts of the outcome for girls and boys. One girl developed pyelonephritis 13 days after the verification of bacteriuria, before the radiological investigations. She was given antibiotics and had no recurrence. Two girls with asymptomatic bacteriuria were treated because of renal abnormalities found at urography. One had bilateral stenosis of the pelvoureteral junction with general parenchymal thinning. She had one recurrence of asymptomatic bacteriuria at the age of 3·5 years. The hydronephrosis decreased gradually without surgery. The other girl had a duplex system with reflux grade 2 in the upper part; parenchymal reduction was initially suspected but not verified subsequently. After treatment with antibiotics she had one recurrence, with pyelonephritis, at the age of 2·3 years. In the remaining 11 girls, the bacteriuria cleared spontaneously in 10 and in one after antibiotic treatment for otitis media.[18] Two of them had recurrences of asymptomatic bacteriuria at the ages of 10 and 17 months respectively, which again cleared spontaneously within three months. An

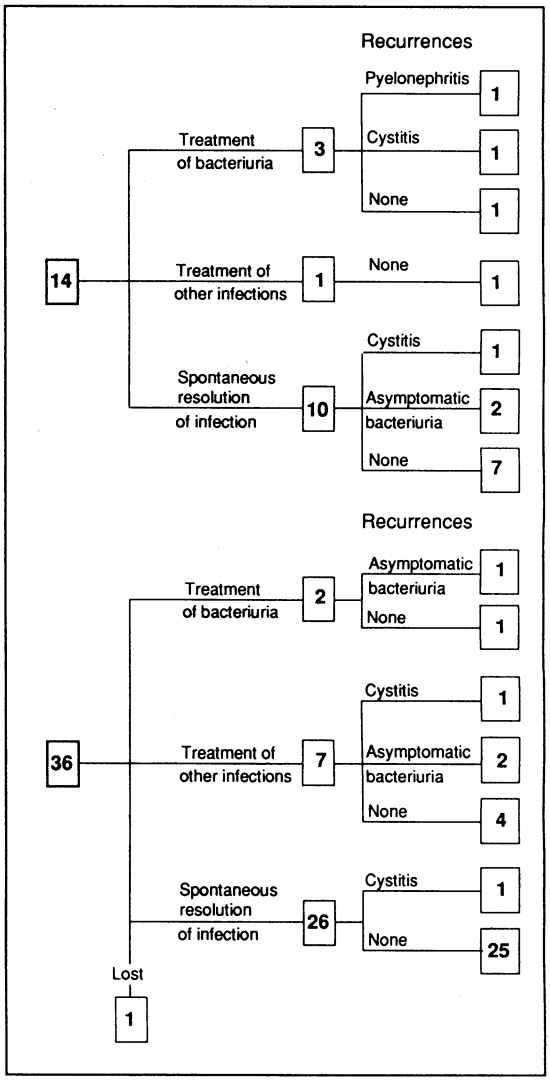


FIG 1—*Six years' follow up of infants with bacteriuria on screening. Top: girls (n=14), bottom: boys (n=36)*

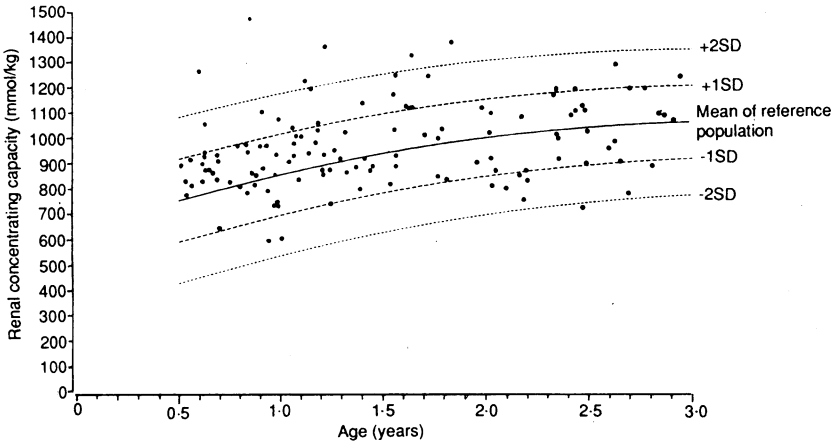


FIG 2—*Renal concentrating capacity (mmol/kg) determined by desmopressin test on 125 occasions in 43 children.* ●———● *Indicates mean of the reference population.* ●·····●, ●------● *Indicate one standard deviation intervals*

additional girl had a recurrence of cystitis at the age of 4·5 years. No other recurrence was observed among the girls. The overall rate of recurrence was 36% (95% confidence interval 13 to 65%).

One boy developed pyelonephritis 11 days after the verification of bacteriuria, before the radiological investigations. He was treated and had no recurrence. One boy was inadvertently treated for bacteriuria; he had a recurrence of asymptomatic bacteriuria at the age of 3 months, which cleared spontaneously. A further seven boys became free of bacteriuria when given antibiotics for upper respiratory infections. Two of the seven had a recurrence of asymptomatic bacteriuria at the ages of 2·5 and 15 months respectively. In one the bacteriuria cleared spontaneously and in the other during treatment for otitis. One boy with glandular hypospadias had recurrent acute cystitis at the age of 6 years. Of the remaining 27 boys, one was lost during follow up; in 26 the bacteriuria cleared spontaneously.[18] In this group one boy with diabetes mellitus had acute cystitis at the age of 4·5 years. No other recurrence was observed, and the overall rate of recurrence was 14% (5 to 30%).

### RENAL CONCENTRATING CAPACITY

The desmopressin test was performed in 47 of the 50 children, a median of three (range one to six) times in each child. Figure 2 shows the results of 125 tests performed at ages ranging from 6 months to 3 years, excluding the three children who had had attacks of acute pyelonephritis and the girl with stenosis of the pelviureteral junction. To avoid duplicate readings in the statistical analyses the first and the last samples of each individual child were analysed separately. When the first samples were analysed the infants in the group with bacteriuria on screening showed significantly higher values than the reference population (mean SD score 0·50, 95% confidence interval 0·21 to 0·79; $p<0·001$). When the last samples were analysed no significant difference was observed (mean SD score 0·08, −0·24 to 0·40; $p>0·05$).

### FOLLOW UP UROGRAPHY

Follow up urography was performed in 36 children (9 girls and 27 boys) after a median time of 32 (range six to 82) months from the first urography. Apart from the girl with stenosis of the pelviureteral junction and generalised renal parenchymal thinning, no case of caliceal deformity was observed at conventional evaluation.

A total of nine children were not included in the statistical analysis of the measurements of renal parenchyma and surface area. The purpose of the analysis was to investigate the effects of bacteriuria on the kidneys in the absence of known risk factors. Therefore the girl with stenosis of the pelviureteral junction and the two children who developed acute pyelonephritis shortly after the initial diagnosis of bacteriuria were excluded. To allow sufficient time for renal damage to develop four children who had a short interval (<two years) between their first and follow up urographic examinations were excluded. Two additional children, with a malrotated kidney and a duplicated collecting system respectively, were also excluded as the measuring technique and reference values were not applicable in these cases. A separate analysis of the renal measurements obtained in these nine infants showed normal results in all except the girl with stenosis of the pelviureteral junction, who had bilateral generalised reduction of the parenchyma.

Figure 3 shows the results of the measurements of renal parenchymal thickness in the remaining 27 children as standard deviation scores. In children with duplicate readings (left and right sides) the mean of the two values was used for statistical comparison. No significant differences compared with the reference population were observed for parenchymal thickness at the upper pole, lateral aspect, and for renal surface area (table II). The parenchyma at the lower pole was significantly thicker in the group with bacteriuria on screening.

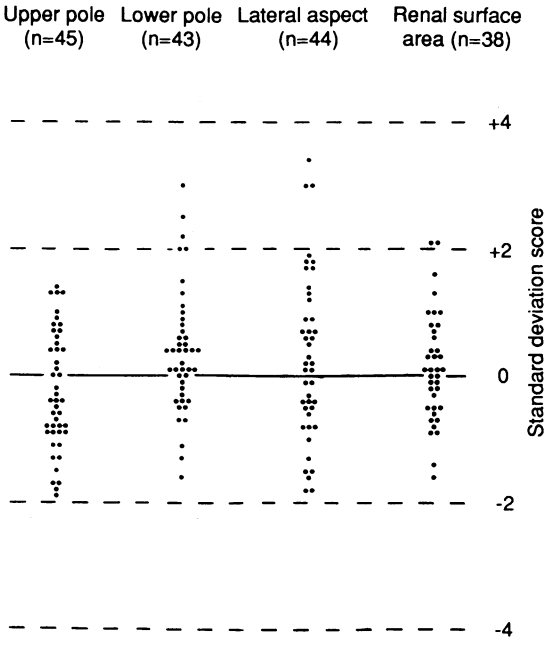


FIG 3—*Renal parenchymal thickness (at upper pole, lower pole, and lateral aspect) and renal surface area at follow up urography in 27 children. Measurements are expressed as standard deviation score units; each dot represents one kidney*

TABLE II—*Renal measurements at follow up urography in 27 children. Values are standard deviation score units obtained by comparison with a reference population*

| Measurement | No of children | Mean score (95% confidence interval) | p Value |
|---|---|---|---|
| Upper pole | 25 | −0·25 (−0·59 to 0·09) | 0·135 |
| Lower pole | 24 | 0·36 ( 0·00 to 0·72) | 0·049 |
| Lateral aspect | 26 | 0·15 (−0·29 to 0·59) | 0·478 |
| Area | 23 | 0·15 (−0·22 to 0·52) | 0·407 |

## Discussion

A prerequisite for this study was the Swedish child health care system, which has a participation rate of close to 100% for regular check ups. Over two thirds of the infants with verified bacteriuria on screening could be followed up for six years; only a few parents refused further examinations after the bacteriuria had cleared.

To our knowledge, no other long term follow up study exists of infants with bacteriuria on screening, and comparisons can thus be made only with studies of symptomatic urinary tract infection. The rates of recurrence of bacteriuria seemed to be lower than in infants with symptomatic urinary tract infection[19] and the rate of radiological abnormalities was also low.[20-22] The small number of infants with bacteriuria in our study, however, makes such comparisons uncertain.

The purpose of this study was to clarify whether screening for bacteriuria in the infant period might identify individual children at risk of developing renal damage. Among the 14 girls and the 36 boys found to have bacteriuria only two girls and one boy experienced attacks of pyelonephritis, with risk of subsequent renal scarring.[13 23 24] These children might have been detected outside the screening programme because of their symptoms. A urethral valve was found on radiological examination in the boy with pyelonephritis. Although the urethral obstruction was minimal, the finding may itself be regarded as a risk factor. In addition, one girl had obstructive nephropathy (stenosis of the pelviureteral junction) at initial urography without progression at follow up. She was free of symptoms and would probably have been undetected outside the screening programme. The remaining 11 girls and 35 boys had episodes of asymptomatic bacteriuria, which cleared either spontaneously or when antibiotics were given for reasons other than the bacteriuria; they did not show recurrences of a serious nature. Neither measurements of the renal concentrating capacity nor detailed analyses of the radiological follow up indicated a risk of renal damage in infants with bacteriuria on screening.

Previously, screening at school entry disclosed bacteriuria in about 1% of girls.[1 25-27] In our group of girls with bacteriuria on screening in infancy no recurrence of infection was observed after the age of 5 years. Therefore, they probably consititute a different population from those detected with bacteriuria at school entry.

Mass screening for bacteriuria in infancy seems to result primarily in the detection of infants with innocent bacteriuric episodes and is not therefore recommended.

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# Where and when to detoxify single homeless drinkers

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Oxford has a large population of homeless people, many of whom are alcohol dependent. Acute detoxification is offered by two facilities, a regional alcohol unit based at this hospital under the supervision of a consultant psychiatrist and Simon House, a hostel run by a charitable foundation. We compared the service offered by the two facilities.

The regional alcohol unit offers medical detoxification to inpatients, who are treated by doctors, trained nurses, and others; subsequent treatment may be offered after the patients have been discharged. Treatment as an inpatient cost over £100 a day at the time of the study. The hostel detoxifies new residents, giving drug treatment under the supervision of a general practitioner; there are no trained staff, and the emphasis is on the community and on peer support. Once a patient has been detoxified moving on is seen as a medium term goal, although abstinence and reasonable behaviour are the only conditions of indefinite residence. The cost was roughly £25 a day at the time of the study.

## Patients, methods, and results

Over 20 weeks all homeless people requesting alcohol detoxification at any of the agencies to which they would normally present—a night shelter, a general practitioner's surgery for the homeless, the probation service, and the two units being compared—were assessed for the study. They were then randomly allocated to either the regional alcohol unit or the hostel provided that (*a*) immediate admission to a psychiatric or general hospital was not needed, (*b*) they had not been abstinent for more than 24 hours, (*c*) they had not previously been in the study, and (*d*) their consent was obtained. After allocation the normal arrangements for admission to the facilities operated. In addition to the subjects' routine care the daily withdrawal symptom score was recorded[1] and the total dose of chlordiaze-