Ten years' experience in general practice of dip-slide urine culture in children under five years old.

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SUMMARY. Of 567 children under five registered with an industrial general practice over a 10-year period, 559 presented with symptoms of ill health in the first five years of life, and of these, 158 (27·9 per cent of those registered) had urine cultured using the dip-slide method. Thirty-four (12·3 per cent) girls and 23 (7·9 per cent) boys had at least one episode of significant bacteriuria. Two boys and three girls were found to have radiological abnormalities of the genito-urinary tract, of which two were obstructive lesions requiring surgery.

Symptoms usually ascribed to the urinary tract in older children and adults did not discriminate for infection in this age group and were not a reliable indicator of the presence, or of the absence, of significant bacteriuria.

The incidence of significant bacteriuria was considerably above that recorded by surveys on asymptomatic children. *Proteus* infections were four times more common among boys than girls, and under the age of three the proportion of boys with bacteriuria exceeded that of girls.

Dip-slide culture is a valuable tool in the diagnosis, management, and follow-up of urinary tract infection.

Introduction

BY the age of five, as many as 20 per cent of children with significant bacteriuria already have radiological evidence of infective damage to the renal tract (Savage and Wilson, 1973). Early diagnosis of bacteriuria is therefore important for two reasons. It may be an indicator of surgically correctable urinary tract anomalies which might otherwise end in irreversible renal failure (Wing, 1977), and failure to control bacteriuria can lead to reduction of kidney growth and renal scarring (Smellie and Normand, 1975).

Significant bacteriuria can be intermittent and symptoms of urinary tract infection in young children are often non-specific and easily attributable to more readily perceptible causes such as red throats or runny noses (DeLuca *et al.*, 1963; Smellie *et al.*, 1964). Outside hospital, traditional midstream techniques and suprapubic aspiration of urine present problems, both of collection and prompt culture. The dip-slide method of urine culture is a reliable discriminator of significant bacteriuria (Kass, 1956; Arneil *et al.*, 1973). It has been found to be cheap, simple, and well suited to general practice (Manners *et al.*, 1973; Asscher *et al.*, 1977).

The detection rate of bacteriuria is greater in symptomatic than asymptomatic children. The rate was doubled when parents used dip-slides when their children appeared unwell at home, compared with tests at routine outpatient follow-up (Hallett *et al.*, 1974). Screening programmes aimed at asymptomatic children may fail to detect much bacteriuria and are in any case difficult to apply to children of pre-school age.

This paper describes 10 years' experience of the application of dip-slides to children under five years of age at times of ill health, in one industrial practice.

Method

The study was based in Glyncorrwg, a geographically isolated industrial village in the South Wales valleys. Ninety-seven per cent of the population are registered with a single practitioner with a list size of 2,081. Of this population 94·2 per cent are drawn from the Registrar General's Social Classes 3, 4, and 5. The practice was single-handed during most of the study period, with one W.T.E. nurse dispenser and a part-time attached health visitor. For the last three years of the study it included a Medical Research Council research assistant, a general practitioner trainee and attached medical students.

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The study was retrospective, using the practice records of children for whom the principal was responsible. It included all 567 children (291 boys and 276 girls), under the age of five years, registered with the practice in the 10-year period from 1 January 1967 to 31 December 1976. Essential data were retained on all 74 boys and 73 girls who entered or left during the study period. A five-year cohort born between 1 January 1967 and 31 December 1971 (100 girls and 109 boys), was extracted to calculate age-specific incidence to the nearest month at risk.

Practice policy aimed to obtain at least one dip-slide urine culture from all children in the first five years of life, preferentially using times of ill health. Dip-slides were to be obtained from all children with specific urinary tract symptoms, or those with non-specific symptoms not satisfactorily accounted for. Follow-up after treatment of bacteriuria was to be continued until negative cultures were obtained, and repeated at any subsequent episode of ill health.

We defined adequate follow-up after treatment of bacteriuria as at least one negative dip-slide within three months. Radiological investigation of the urinary tract was not directly accessible to the practice and indications for it were not strictly defined.

Urine specimens were cultured on a variety of commercially available dip-slide media, using both cystine lactose electrolyte-deficient (CLED) and MacConkey gels. Parents were instructed in the technique of midstream specimen collection, and no special cleansing was advised unless there was gross soiling. Dip-slide specimens were usually obtained at home and then incubated for at least 24 hours at 37°C in the practice premises. Collecting bags were never used. Dip-slides were read by a nurse or doctor and equivocal or positive slides were sent to the Public Health Laboratory Service or hospital for organism identification and antibiotic sensitivities. Dip-slides showing evidence of drying were discarded (Meers and Sandys, 1977).

The criterion for a positive dip-slide and significant bacteriuria was a single count of $\geqslant 10^5$ bacteria per ml. All cases of balanitis were excluded and no dip-slides were attempted in the first month of life. In the event of recurrent bacteriuria, a new episode was defined either by an intermediate negative culture or a change of organism.

Results

A total of 567 children under five registered with the practice in a 10-year period, of whom 559 presented with symptoms of ill health during the first five years of life. Dip-slide urine culture was obtained from 158 (27·9 per cent) of those registered. Thirty-four (12·3 per cent) girls and 23 (7·9 per cent) boys had at least one episode of bacteriuria. Of these, 10 (29·4 per cent) girls and six (26·1 per cent) boys had more than one episode.

Out of a total of 123 positive dip-slides, 91 (73·7 per cent) yielded a significant pure growth, five (4·7 per cent) a significant mixed growth and 27 (21·9 per cent) yielded an unidentified bacterial count of $\geqslant 10^5$ per ml. Pure *Escherichia coli* was grown in 59·7 per cent of episodes of bacteriuria in girls and 53·1 per cent of episodes in boys. Pure growths of *Proteus* were recorded in 6·4 per cent of episodes of bacteriuria in girls and 28·1 per cent of episodes in boys ($p < 0·05$).

Forty-nine (85·9 per cent) children with bacteriuria had their first detected episode under the age of three. Of the 57 children with bacteriuria at some time, 10 girls and four boys were followed up by radiological investigation. Abnormalities were detected in two boys (one megaureter with stones; one abnormal calyceal system) and three girls (one urethral stenosis, one vesicoureteral reflux, and one duplex kidney). The two obstructive lesions were amenable to surgery.

Symptoms usually ascribed to the urinary tract in older children and adults were not found to be discriminating for bacteriuria in this age group, and the symptoms associated with the request for a dip-slide (at patient-initiated consultation rather than doctor-initiated follow-up), could not be used to predict the presence or absence of bacteriuria. Of those children with symptoms 'specific' to the urinary tract (frequency, dysuria, enuresis, smelly or cloudy urine, loin or abdominal pain, haematuria) 26·9 per cent had bacteriuria. In those with 'non-specific' symptoms (sore throat, cough, misery, nappy rash, anorexia, or vomiting) 29·2 per cent had bacteriuria.

Out of a total of 440 dip-slides requested, 27·9 per cent yielded significant bacteriuria. This high yield suggested that a greater degree of suspicion among those with non-specific symptoms was necessary. Of the dip-slides requested, 9·6 per cent were not subsequently recorded, owing to parent or staff error. In the three months succeeding treatment of bacteriuria, 40·5 per cent of the cultures remained positive. However, only 54·7 per cent of episodes of bacteriuria were followed up. Thus follow-up was a useful test of continuing or recurrent infection, but poorly applied.

In the cohort followed for the first five years of life, 36 per cent of children were tested with dip-slides at some time. Twelve (12·0 per cent) girls and 14 (12·8 per cent) boys had at least one episode of bacteriuria, and of these a quarter had recurrent episodes.

The incidence of bacteriuria in the cohort was an average of 33·8 episodes per year at risk per 1,000 population in girls, and 47·2 episodes per year at risk per 1,000 population in boys under five. The sex ratio of girls to boys crossed over from an average girl:boy ratio of 0·5 under three years of age to 2·5 at age 3 to 5 years (Table 1).

Discussion

The age range in which medical intervention is considered most likely to be effective in alleviating or preventing chronic renal disease has narrowed over the years. Screening of neonates (Abbott, 1972), school-

Table 1. Number of episodes of bacteriuria per year at risk per 1,000 population under five by sex and age group.

	0 to 1 yr	1 to 2 yrs	2 to 3 yrs	3 to 4 yrs	4 to 5 yrs
Female	23.1	35.5	36.4	49.6	24.6
Male	40.7	63.0	99.1	22.2	11.0

children (Asscher *et al.*, 1973), and cross-sectional study of pre-school infants (Davies *et al.*, 1974) has proved disappointing and treatment of schoolgirls with covert bacteriuria may not prevent progression of pre-existing scarring (Cardiff-Oxford Bacteriuria Study Group, 1978). The post-neonatal, pre-school age group may prove to be the most rewarding to study and treat.

This age group poses problems of data collection and follow-up (Asscher, 1974) particularly if symptomatic populations are under consideration. These problems are not insurmountable when viewed from primary care. In the RCGP Second National Morbidity Study (RCGP *et al.*, 1974), 79·6 per cent of boys and 77·9 per cent of girls under the age of five were seen in general practice in any one year, with an average of four consultations per patient per year. In the study practice only eight children out of the 567 at risk were not seen during the first five years of life, and these were all either outmigrants or late entrants to the study. Urine testing improved over the 10 years of study with increasing awareness of the non-specificity of symptoms. The introduction of A4 files and modified problem-orientated note recording assisted follow-up. Involvement of the whole practice team and the mothers was a prerequisite for even our limited success.

However, only 36 per cent of children in the full five-year cohort were tested. More alarming was the failure to follow up adequately episodes of bacteriuria. Fifty per cent follow-up of those most at risk is obviously unsatisfactory, and effective tagging of notes, the use of flow charts, and routine laboratory requests for repeat samples in those with positive cultures have yet to be fully developed. The outstanding conclusion is that the elaboration of a policy is only a first step. It is a constant battle to get the whole staff, including doctors with a vigorous commitment, to adhere to agreed protocols. We are convinced that this cannot be done without periodic practice audit.

Four factors may have contributed to our relatively high prevalence: less rigorous criteria (a single count of $\geqslant 10^5$ bacteria/ml), response to a wide range of symptomatic consultations (only two per cent of dip-slides were requested on asymptomatic children), the social class composition of the population (Fairley *et al.*, 1971), and of course a selected population due to a low response rate.

Incidence derived from the five-year cohort was also high, and of a similar order and distribution to that found by Brooks and Houston (1977) in their study of symptomatic children in general practice. Most striking, however, was the reversal of the sex ratio in children under three and the assumption of a female preponderance only after this age. This was due to a fall in the incidence of episodes in boys, rather than a rise in girls.

Conclusion

A 36 per cent response rate and relatively small numbers demand that results be treated with some caution. However, if confirmed by more rigorous studies, our high incidence of bacteriuria, the failure of traditional symptoms to discriminate between the presence or the absence of bacteriuria, multiple episodes in a quarter of those with bacteriuria under five years, and a preponderance in boys under three years has considerable implications for diagnostic policy and follow-up. The former has become more conservative in recent years, and the latter more rigorous. We would find radiological investigation for first episodes of bacteriuria for eight to 12 per cent of the population under five difficult to justify on present evidence. Indeed, this may not be desirable for hospital populations of boys (Hallett *et al.*, 1976). This is not true for those with recurrent bacteriuria, where up to 50 per cent may have underlying radiological abnormalities.

The routine use of dip-slides is still widely ignored and is not effectively taught in many medical schools. If such methods are not applied at times of ill health to whole populations of young children, an opportunity to anticipate, prevent, and cure renal disease with an infective component may be missed.

We believe that this is feasible from primary care, if we can organize sufficiently to reach beyond conscience. Mond and colleagues (1970), in a study of asymptomatic bacteriuria in an urban general practice, have shown the response rates of over 90 per cent that can be achieved with children.

References

Abbott, G. D. (1972). Neonatal bacteriuria: a prospective study in 1,460 infants. *British Medical Journal*, **1**, 267-269.

Arneil, G. C., McAllister, T. A. & Kay, P. (1973). Measurement of bacteriuria by plane dip-slide culture. *Lancet*, **1**, 94-95.

Asscher, A. W. (1974). Urinary tract infection. *Lancet*, **2**, 1365-1367.

Asscher, A. W., Harvard Davis, R. & MacKenzie, R. (1977). Dip-slide diagnosis of urinary tract infection. *Lancet*, **2**, 202.

Asscher, A. W., Verrier Jones, R., Sussman, M., McLachlan, M. S. F. & Meller, S. *et al.* (1973). Screening for asymptomatic urinary-tract infection in schoolgirls. *Lancet*, **2**, 1-4.

Brooks, D. & Houston, I. B. (1977). Symptomatic urinary infection in childhood: presentation during a four-year study in general practice and significance and outcome at seven years. *Journal of the Royal College of General Practitioners*, **27**, 678-683.

Cardiff-Oxford Bacteriuria Study Group (1978). Sequelae of covert bacteriuria in schoolgirls. *Lancet*, **1**, 891-893.

Davies, J. M., Littlewood, J. M., Gibson, G. L. & Meadow, S. R. (1974). Prevalence of bacteriuria in infants and pre-school children. *Lancet*, **2**, 7-10.

DeLuca, F. G., Fisher, J. H. & Swenson, O. (1963). Review of recurrent urinary-tract infections in infancy and early childhood. *New England Journal of Medicine,* **268**, 75-77.
Fairley, K. F., Carson, N. E., Gutch, R. C., Leighton, P., Grounds, A. D., Laird, E. C., McCallum, P. H. G. & Sleeman, R. L. (1971). Site of infection in acute urinary tract infection in general practice. *Lancet,* **2**, 615-618.
Hallett, R. J., Pead, L. & Maskell, R. (1974). Follow-up of urinary-tract infection in children. *Lancet,* **2**, 104.
Hallett, R. J., Pead, L. & Maskell, R. (1976). Urinary infection in boys. A three-year prospective study. *Lancet,* **2**, 1107-1110.
Kass, E. H. (1956). Asymptomatic infections of the urinary tract. *Transactions of the Association of American Physicians,* **69**, 56-63.
Manners, B. T. B., Grob, P. R. & Beynon, G. P. J. (1973). Diagnosis of urinary infection in general practice. *Lancet,* **1**, 575-578.
Meers, P. D. & Sandys, G. H. (1977). Dehydration of dip-inoculum outfits. *Lancet,* **1**, 600.
Mond, N. C., Grunberg, R. N. & Smellie, J. M. (1970). Study of childhood urinary tract infection in general practice. *British Medical Journal,* **1**, 602-605.
Royal College of General Practitioners, Office of Population Censuses and Surveys, and Department of Health and Social Security (1974). *Morbidity Statistics from General Practice 1970-1971.* London: HMSO.
Savage, D. C. L. & Wilson, M. I. (1973). Covert bacteriuria in childhood. In *Urinary Tract Infection.* Ed. Brumfitt, W. & Asscher, A. W. London: Oxford University Press.
Smellie, J. M., Hodson, C. J., Edwards, D. & Normand, I. C. S. (1964). Clinical and radiological features of urinary infections in childhood. *British Medical Journal,* **2**, 1222-1226.
Smellie, J. M. & Normand, I. C. S. (1975). Bacteriuria, reflux, and renal scarring. *Archives of Disease in Childhood,* **50**, 581-585.
Wing, A. J. (1977). Diseases of the urinary system. Prospects for the treatment of renal diseases. *British Medical Journal,* **2**, 881-884.

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A new design for randomized clinical trials

A new method has been proposed for planning randomized clinical trials. The method is especially suited to comparison of a best standard or control treatment with an experimental treatment. Patients are allocated into two groups by a random or chance mechanism. Patients in the first group receive standard treatment; those in the second group are asked if they will accept the experimental therapy; if they decline, they receive the best standard treatment. In the analysis of results, all those in the second group, regardless of treatment, are compared with those in the first group. Any loss of statistical efficiency can be overcome by increased numbers. This experimental plan is indeed a randomized clinical trial and has the advantage that, before providing consent, a patient will know whether an experimental treatment can be used.

Reference

Zelen, M. (1979). A new design for randomized clinical trials. *New England Journal of Medicine,* **300**, 1242-1245.