*Personal practice***Management of urinary tract infection**

R H R WHITE

Department of Nephrology, The Children's Hospital, Birmingham

The urinary tract is a common site for bacterial infection in childhood. Population screening for bacteriuria has revealed a slight male preponderance in the neonatal period, but thereafter it is more prevalent in girls, becoming as much as 50 times more common by the age of 5 years. Follow up of asymptomatic bacteriuria in schoolgirls has failed to show any convincing evidence that its discovery by screening can materially alter the outcome.¹ In preschool children the difficulties encountered in obtaining uncontaminated urine samples, together with the low acceptance rate, militate against cost effectiveness.² Moreover, most renal scars observed are already present at initial investigation,³ and their prevalence in infants is, disappointingly, as high as it is in older children.⁴

The practising paediatrician should therefore be concerned mainly with the management of *symptomatic* urinary tract infection (UTI), and the two basic aims of treatment are the relief of symptoms and the prevention, or at least limitation, of damage to the renal parenchyma. Experimental work in refluxing piglets has shown that the scarring process can be initiated within one week of introducing pathogenic bacteria into the bladder,⁵ and there is good reason to believe that this may apply to children. Treatment with antibiotics of first infections in young children should therefore be regarded as a matter of urgency. The wide range of suitable antibiotics now available has made treatment a comparatively simple matter. Management, however, is more than just eradicating infection; it is also concerned with diagnostic reliability, alleviation of associated symptoms not directly due to bacteriuria, assessment of underlying structural abnormalities and the potential risk of future upper tract damage, and careful follow up of selected at risk patients throughout the growth period.

Clinical diagnosis

Despite the availability of simple and reliable techniques, the diagnosis of UTI in practice remains

haphazard. I am still referred patients who have been given antibiotics without having had a urine culture taken beforehand and often without adequate physical examination. It should be remembered that, at initial investigation, one third of girls are found to have vesicoureteric reflux and one fifth associated renal scarring (reflux nephropathy),³ so that imaging of the urinary tract is mandatory in proven cases. How far unconfirmed cases should be subjected to invasive diagnostic procedures often presents a dilemma.

Careful history taking and physical examination are fundamental. The dysuria caused by genital inflammation, especially common in prepubertal girls, and that caused by UTI are indistinguishable. Urge incontinence is often accompanied by vulvitis and constipation, and the latter may cause quite severe, intermittent abdominal pain, especially in the left flank where it is liable to be misinterpreted as having a renal origin. Abdominal examination should therefore take note not only of whether the kidneys and bladder are palpable but also of whether the descending colon is distended. Rectal examination is rarely called for, but failure to inspect the genitalia is inexcusable as vulvitis is many times more common than UTI and is often responsible for a raised urinary leucocyte count. Examination should also include measurement of the blood pressure and neurological screening for evidence of sacral nerve root defects.

Bacterial diagnosis

Confirmation of the diagnosis of UTI requires demonstration of the presence of pathogenic bacteria in the bladder urine by cultural techniques. Infecting species are mostly enterobacteria—for example, *Escherichia coli*, *Klebsiella* species, and faecal streptococci. *Proteus* infection sometimes complicates obstructive uropathy, but this organism often colonises the male genitalia, when it may cause diagnostic difficulty. Staphylococci rarely cause UTI in children. Unfortunately, there are no

simple 'dipstick' tests that are completely reliable; those based on bacterial consumption of the already minimal urinary glucose concentrations, or on conversion of urinary nitrate to nitrite, can be taken as good evidence of UTI when they yield positive results but unfortunately have unacceptably high false negative rates.⁶ The most widely used cultural method is the viable colony count, which relies on the fact that bacteria incubated in the bladder urine at body temperature will have multiplied many times in two to three hours, whereas contaminant bacteria washed off the genitalia during voiding will not. A significant colony count is $>10^5$ /ml; borderline counts of 10^4 – 10^5 /ml can be regarded as unimportant if there is a mixed growth but may require repetition if associated with a single pathogen. The reliability of this method depends, firstly, on the urine specimen having been obtained by 'clean catch' or midstream technique and, secondly, on the midstream sample being plated out within one hour of voiding. Provided that the genitalia are clean, antiseptic swabbing is unnecessary.⁶

Information obtained from mothers often reveals that the specimen has been carefully collected at home at 0730h, reaches the doctor's surgery by 0900h, and is later despatched to the local hospital laboratory, so that a delay of some three hours is not uncommon. Contaminant bacteria will continue to proliferate at room temperature to yield borderline or even 'significant' counts and, as they are enterobacteria themselves, distinction from true bacteriuria may be impossible. If a delay between micturition and culture is unavoidable metabolism of contaminants can be inhibited by either refrigeration at 0–4°C or the addition of sodium borate to the specimen. The problem can also be overcome simply by inoculating a dipslide, by either immersion or 'dipstick' technique.⁶ Colony counting has fortunately obviated the need for catheterisation in children old enough to void urine on request, but there remains a problem in very young children. The application of a Hollister U-bag, in which the voided urine seeps through pores into a separate space that isolates it from contact with the perineum, is an acceptable initial procedure in that a negative result reliably excludes UTI. As a result of the high false positive rate, however, bag specimens that yield raised bacterial counts must be repeated and, if doubt remains, a suprapubic aspiration may be required.

The paediatrician with a special interest in renal disorders will find a simple microscope and Fuchs-Rosenthal leucocyte counting chamber of great help in the outpatient clinic. With the minimum of training, bacteria and cells can be identified and the latter counted. Routine Hema-Combistix testing and microscopy has been the practice in my renal

clinic for more than 20 years and has the twofold advantage that the accompanying parent can be warned of a possible UTI or reassured as appropriate and that only those samples that show suspicious abnormalities (about 10% of the total) need be submitted to the microbiology laboratory for the more costly procedure of culture and sensitivity testing. In a prospective survey we failed to identify either bacteria or leucocytes in only 6% of infected specimens, whereas 15% of uninfected samples gave leucocyte counts >10 /mm³,⁷ indicating that pyuria is less reliable evidence of UTI, contrary to popular belief.

Investigation

It is still widely taught that girls do not need to be investigated unless UTI is recurrent. This is an unwise policy, particularly in preschool children, who are vulnerable to upper tract damage if vesicoureteric reflux is present. Imaging of the urinary tract should be carried out after treatment of the first documented infection, preferably after an interval of two weeks, to allow acute inflammation to subside.

The conventional method of visualising the upper urinary tract is intravenous urography (IVU). This entails both venepuncture and radiation, and in older children it is being progressively replaced by ultrasonography as radiologists gain experience with this non-invasive technique. It is prudent to combine this procedure with a plain abdominal radiograph to exclude radio-opaque calculi and facilitate review of the lumbosacral spine. At present we still perform IVU in proven UTI in children less than 3 years old, but in older children, and in younger ones where doubt exists about the diagnosis of UTI, we have found ultrasonography to be a reliable screening procedure. When abnormalities are revealed IVU is performed subsequently. In a comparison of simultaneous ultrasonography and IVU in 100 children with UTI it was recently reported that ultrasonography missed 12 out of 37 abnormalities detected by IVU.⁸ As these consisted mostly of minor urinary tract dilatation and there was only one instance of failure to detect serious scarring, however, these results may be regarded as encouraging.

Conventional, fluoroscopic voiding cystourethrography is the only fully reliable means of diagnosing vesicoureteric reflux. Fluctuations in the excretion curve of ^{99m}technetium labelled diethylene triaminopenta-acetic acid may suggest reflux but the discrimination from intermittent partial obstruction is poor, and the anatomical detail needed to plan treatment cannot be obtained by this method. The instillation of a radionuclide into the bladder may

yield semiquantitative information and minimises the radiation hazard but does not eliminate the need for catheterisation, which, in inexperienced hands, can prove so traumatic to a small child. We have solved this latter difficulty by having the catheterisation performed by our urodynamics nurses, whose success is attributable not only to their technical skill and experience but also to their patience and sympathy in first explaining the procedure to parents and children. We therefore continue to perform cystourethrography routinely in children under 5 years old, even in the light of a normal IVU, which can sometimes be obtained despite the presence of appreciable reflux, and in older children if renal scarring is seen on the IVU. It is not a good practice, however, to perform cystourethrography without first having reviewed the IVU or ultrasound films as an occasional child with UTI will show, for example, pelviureteric obstruction, and cystourethrography would become a needless investigation.

While radiological investigation of the urinary tract may seem straightforward, in practice a number of difficulties are encountered and attention to detail is essential. For some 15 years it has been the practice at this hospital to hold weekly meetings of nephrologists, surgeons, and radiologists, at which current radiographs, ultrasound scans, and radionuclide scans are reviewed. This is an important occasion that improves communication, to the benefit of the patients, and facilitates discussion of techniques. It is widely used by district hospital paediatricians as a means of obtaining expert radiological opinion, and from our observations it is clear that techniques vary considerably. A common fault is inadequate bowel preparation before IVU, leaving the renal outlines concealed by gas and faecal shadows. As most children with UTI have unrecognised constipation pretreatment with laxatives is essential. Deficient cystourethrographic technique is also common; failure to take post-micturition films and to include the renal areas make it impossible to assess the severity of reflux.

Treatment with antibiotics

While there is now a bewildering array of urinary antimicrobials available, most are needed only for dealing with the problem of bacterial resistance, which is fortunately rare in childhood, and the list of antibiotics for regular use is best confined to a few, well tried drugs. Most initial infections are caused by bacteria that are sensitive to trimethoprim, and in young children, in whom it is generally advisable to begin treatment without awaiting the result of laboratory sensitivity tests, this is the drug of choice.

It need be given only twice daily. Even first infections are often at least partially resistant to sulphonamides, nowadays, and co-trimoxazole has no advantage over plain trimethoprim.

Nitrofurantoin is equally effective but may cause nausea and vomiting, especially in young children who can only take the liquid preparation. Although four doses a day are recommended, in practice two are adequate. Nalidixic acid can also be used, but parents should be warned of the possible occurrence of severe headaches and vomiting due to a hypersensitivity reaction causing benign intracranial hypertension.⁹ Amoxycillin and cephalixin are also suitable for short term use, but bacterial resistance readily develops, and these drugs are unsuitable for prophylaxis.

The recommended duration of treatment has varied from six months to a single dose. Controlled comparisons of treatment for six months versus two weeks¹⁰ and one week versus a single dose¹¹ have shown the shorter courses to be equally effective. Longer treatments merely postpone the next relapse and are unnecessary except where prophylaxis is indicated. The pharmacokinetics of trimethoprim indicate that this drug is suitable for single dose treatment,¹² which has obvious advantages in terms of both cost and compliance and is therefore an appropriate way to treat infrequent, recurrent UTI in children with radiologically normal tracts. In children aged less than 5 years, in whom the risk of reflux nephropathy is higher, it is wise to follow the treatment of first infections with a single nightly half dose of the same antibiotic until investigation has been undertaken.

Low dosage chemoprophylaxis is indicated in children with appreciable reflux, in children awaiting surgical relief of urinary obstruction, and in selected patients with neuropathic bladder who experience repeated symptomatic UTI or in whom there is considered to be a risk of upper tract damage. Asymptomatic bacteriuria in the child with a radiologically normal urinary tract requires no treatment as there is a high spontaneous remission rate, and treatment may be followed by symptomatic relapse.¹ Prophylaxis plays a useful role, however, in those puzzling prepubertal girls who experience repeated, symptomatic infections despite a normal urinary tract and lose much school time. It may have to be continued until the menarche, and parents require sympathetic explanation and reassurance that such prolonged treatment is not harmful. The two most used drugs are trimethoprim and nitrofurantoin, both given in a single nightly dose of 1–2 mg/kg/day. Older children can take the slow release, encapsulated nitrofurantoin preparation, 'Macro-dantin', which eliminates nausea.

Symptomatic management

A liberal fluid intake should be encouraged because the ensuing polyuria exerts a bladder washout effect, which helps to reduce bacterial colonisation. Children with symptomatic UTI generally experience involuntary frequency, but those without this symptom should be discouraged from 'holding on' (as they often do when voiding causes dysuria) as this will lessen the washout effect.

The treatment with antibiotics of bacteriuria typically gives prompt relief from dysuria, but urge incontinence, with or without nocturnal enuresis, often persists. In a urodynamic study of 37 girls with reflux we found that these symptoms correlated strongly with the finding of detrusor instability, which was present in as many as 28 patients.¹³ Urge syndrome seems to be an associated condition rather than the cause of UTI. Some important relations between urge syndrome, constipation, and UTI have emerged from years of clinical observation¹⁴ and have recently been confirmed by means of combined urodynamic studies and rectal manometry.¹⁵ The Figure attempts to explain these relations, from which it is evident that successful management of urge incontinence might favourably influence the treatment of UTI.

Disappointingly, treatment with anticholinergic drugs has, in our experience, been associated with a

high incidence of both therapeutic failure and side effects.¹⁴ The key to the problem is defective perineal muscular relaxation, the result of 'holding on' in an attempt to prevent wetting. Simultaneous contraction of the urethral and anal sphincters is unavoidable because of their common nerve supply. The increased sphincter activity promotes faecal retention, and treatment of constipation is an essential component of management. I do not favour the aggressive regimen of daily enemas that has been advocated¹⁵ but recommend the adoption of a high fibre diet and, if necessary, prescribe Senokot initially. Unfortunately, the suggestion of wholewheat foods often meets with resistance, and success ultimately depends on patiently persuading the whole family to participate in dietary changes for their own benefit.

As uninhibited detrusor systole prompts voluntary closure of the external urethral sphincter the intravesical pressure generated is often higher than that associated with voiding.¹³ Cystometry shows that, as the bladder fills, these isometric pressures increase until, sooner or later, they exceed the maximum urethral pressure, at which point mechanical leakage occurs. The child must therefore be trained to void urine sufficiently often to prevent this happening, usually at intervals of not more than two hours. Defective perineal muscular relaxation often defeats this aim, and it is the passage of soft, bulky motions without straining or discomfort, afforded by the high fibre diet, that facilitates such relaxation.

Successful treatment of urge incontinence is desirable as this condition serves to encourage both vulvitis and ammoniacal dermatitis of the labia, and these in turn may aggravate sphincter spasm through increased sensory input and promote bacterial colonisation. Severe, symptomatic vulvitis usually responds to two to three weeks' application of 0.01% dionoestrol cream, which stratifies the epithelium and may yield a lasting effect. Asymptomatic vulvitis is almost normal in prepubertal girls, however, and requires no treatment; in the absence of diabetes mellitus or immune deficiency it is never caused by vaginal candidiasis, and antifungal creams, so commonly prescribed, are useless. A small but none the less important detail is that many schools, state or private, supply toilet paper that is abrasive, and girls with perineal soreness will not use it; the remedy is to take soft tissue from home. Naturally, girls should be taught to wipe the anus backwards and bathe daily, but there is no evidence that more rigorous perineal hygiene helps, except where there is the problem of faecal incontinence resulting from severe constipation or more rarely from sacral neuropathy.

Figure Hypothetical interrelations between urge syndrome, constipation, and urinary tract infection.

Underlying defects

Where imaging reveals an obstruction or the presence of calculi in the urinary tract surgical relief should be sought without delay to minimise permanent renal parenchymal damage, and chemoprophylaxis should be maintained until this has been achieved. The management of neuropathic bladder has been transformed by the introduction of intermittent self catheterisation as an alternative to urinary diversion. Our comparatively recent experience suggests that, provided the patient is initially instructed in correct catheter technique and regularly monitored by skilled and sympathetic nursing staff and that faecal incontinence can be minimised by dietary management with or without laxatives, bacteriuria can be satisfactorily controlled by means of chemoprophylaxis. Indeed, in the absence of reflux or upper tract dilatation it is worth a trial without regular antibiotics, and it is questionable whether asymptomatic bacteriuria in such patients needs treatment.

Vesicoureteric reflux

The relation between vesicoureteric reflux and renal parenchymal scarring is firmly established and the term reflux nephropathy is preferred to chronic pyelonephritis.^{16 17} We previously reported that 98% of scarred kidneys were drained by refluxing ureters and that the incidence of scarring increased with the severity of reflux.¹⁶ The scarring produced experimentally in pigs with reflux and sterile urine is not comparable with human reflux nephropathy in that it entailed obstruction, through progressive occlusion of the urethra.¹⁸ There is little evidence, if any, that childhood reflux nephropathy occurs in the absence of UTI at some time. In our series 47% of kidneys drained by refluxing ureters were not scarred,¹⁶ and it now seems clear that intrarenal reflux must also be present if scarring is to develop. This is caused by the fusion of neighbouring papillae during embryogenesis to form compound structures in which some of the collecting ducts emerge in a concavity rather than tangentially to the surface.²⁰ The development of typical, coarse renal scarring in the absence of reflux is, in our experience, quite rare.¹⁶ Whether P fimbriated *E. coli*, which adhere to uroepithelium through recognition of receptors related to the human P blood group, are capable of inducing pyelonephritic scarring by ascending the non-refluxing ureter, is still controversial.²¹ An equally reasonable assumption is that the scarring had been caused by past reflux that had resolved spontaneously.

The essential aim of treatment of reflux is to protect the renal parenchyma from infection and the

subsequent development of scarring. As it is not possible to diagnose intrarenal reflux reliably during life those children at risk of reflux nephropathy cannot be accurately predicted, and it must be assumed that all children with vesicoureteric reflux have the potential for scarring. The few reports of radiologically diagnosed intrarenal reflux, however, have all been in children aged under 5 years;¹⁹ moreover, the incidence of new scar formation declines steeply after the age of 7.^{16 22 23} Therapeutic endeavours are therefore more likely to be effective when concentrated on younger children.

There are two treatment options: the surgical correction of reflux and the maintenance of uninfected urine. Although improved renal growth after ureteric reimplantation has been claimed, prolonged follow up of patients treated medically indicates a continuing trend towards resolution of reflux.¹⁷ The Birmingham reflux study group recently reported the results of a prospective, controlled trial of operative versus non-operative treatment of severe vesicoureteric reflux, which showed no significant differences in renal function, renal growth, the development of new scars and progression of existing ones, and the incidence of breakthrough UTI, after an observation period of two years.⁴ This is a short duration of follow up for a chronic condition; the results after five years' observation,²² however, confirm the earlier findings, and it is concluded that neither form of management has any particular advantage. Further studies are continuing, but in the meantime the choice of treatment remains an individual one; the inconvenience of admission to hospital and a permanent abdominal scar, the relative risks of a surgical procedure compared with prolonged chemotherapy, and the likelihood of compliance with the latter all need to be considered in reaching a decision.

If chemoprophylaxis is the option chosen, how long should it continue? An interesting finding of our study was that the development of new scars and the progression of existing ones occurred only during the first two years' observation and not between two and five years. Moreover, these developments bore no relation to the occurrence or absence of breakthrough UTI during the first two years,^{4 22} so that an over-obsessional attitude to chemoprophylaxis can no longer be justified. My current practice is to continue chemoprophylaxis for not more than two years in older children, and in younger children until they are 7 years old, when the risk of further renal damage becomes minimal.

Ongoing care

Most children with UTI in whom the urinary tract is

structurally and functionally normal can return to general practitioner care, but a minority will suffer from repeated infections and may benefit from continued paediatric supervision. These are mostly prepubertal girls; resolution usually occurs around the time of the menarche, although some girls later experience recurrence with the advent of sexual activity and may need guidance. A small number of patients will reach adulthood with persistent reflux but normal kidneys. Preliminary information suggests that they are not at greater future health risk than those without reflux; the degree of reduction of renal function is related to the presence of renal scarring rather than the reflux itself.²⁴ These patients may therefore be discharged with reassurance during adolescence.

Children with reflux nephropathy should, ideally, be followed up in a paediatric clinic until physical and renal growth have ceased, when a final radiological and functional assessment should be performed. When scarring is unilateral a healthy contralateral kidney will undergo structural and functional hypertrophy so that there is no measurable reduction of total glomerular filtration rate.¹⁴ The development of persistent proteinuria in the presence of scarring, however, is usually indicative of secondary glomerular sclerosis, possibly owing to hyperfusion of surviving, undamaged nephrons, and should be carefully monitored. A potential risk is hypertension and, on discharge from paediatric care, the patient without proteinuria should be advised to obtain an annual blood pressure check from the general practitioner. Patients with either proteinuria or extensive bilateral reflux nephropathy are under threat of impaired renal function, and possibly end stage renal failure, and should be referred to an adult nephrologist for ongoing care.

Compliance is a potential impediment to successful long term care, and it is essential to develop rapport with the patients and their families. Confidence is more likely to develop if consultations are unhurried and sympathetic. As children grow older they should be addressed directly rather than through their parents, and older teenagers should be encouraged to attend the clinic unaccompanied, so that personal health matters can be discussed privately. Most girls will appreciate a few words of counsel regarding the pill and pregnancy. Oral contraceptives are associated with an increased risk of hypertension, and young women with reflux nephropathy should be advised to undergo regular blood pressure checks; they would very likely ignore advice to avoid the pill. There is an increased risk of bacteriuria during pregnancy, and patients should be cautioned to mention their previous health problems at the antenatal clinic to ensure vigilance.

Conclusion

Experience during the past 20 years, and the careful collection of data by research workers, has led to considerable rationalisation of the management of UTI. It must be acknowledged that our inability to diagnose reflux, and particularly intrarenal reflux, and in many cases to begin treatment before renal scarring develops is a major handicap. Nevertheless, correct management may at least diminish some of the misery associated with symptomatic UTI and limit the progression of renal damage.

The importance of accurate diagnosis and prompt treatment in children less than 5 years old cannot be overemphasised.

References

- Cardiff-Oxford Bacteriuria Study Group. Sequelae of covert bacteriuria in schoolgirls: a four-year follow-up study. *Lancet* 1978;ii:889-93.
- Taylor CM, White RHR. The feasibility of screening preschool children for urinary tract infection using dipslides. *Int J Paediatr Nephrol* 1983;4:113-4.
- McLachlan MSF, Meller ST, Verrier Jones ER, et al. Urinary tract in schoolgirls with covert bacteriuria. *Arch Dis Child* 1975;50:253-7.
- Birmingham Reflux Study Group. Prospective trial of operative versus non-operative treatment of severe vesicoureteric reflux: two years' observation in 96 children. *Br Med J* 1983;287:171-4.
- Ransley PG, Risdon RA. Reflux nephropathy: effects of antimicrobial therapy on the evolution of the early pycelonphritic scar. *Kidney Int* 1981;20:733-42.
- Edwards B, White RHR, Maxted H, Deverill I, White PA. Screening methods for covert bacteriuria in schoolgirls. *Br Med J* 1975;ii:463-7.
- Robins DG, White RHR, Rogers KB, Osman MS. Urine microscopy as an aid to detection of bacteriuria. *Lancet* 1975;i:476-8.
- Lindsell D, Moncrieff M. Comparison of ultrasound examination and intravenous urography after a urinary tract infection. *Arch Dis Child* 1986;61:81-2.
- White RHR. Urinary tract infection in children. *Br Med J* 1977;i:1650-2.
- Stansfeld JM. Duration of treatment for urinary tract infections in children. *Br Med J* 1975;iii:65-6.
- Pitt WR, Dyer SA, McNee JL, Burke JR. Single dose trimethoprim - sulphamethoxazole treatment of symptomatic urinary infection. *Arch Dis Child* 1982;57:229-39.
- Rylance GW, George RH, Healing DE, Roberts DGV. Single dose pharmacokinetics of trimethoprim. *Arch Dis Child* 1985;60:29-33.
- Taylor CM, Corkery JJ, White RHR. Micturition symptoms and unstable bladder activity in girls with primary vesicoureteric reflux. *Br J Urol* 1982;54:494-8.
- White RHR, Taylor CM. The nonoperative management of primary vesicoureteric reflux. In: Johnston JH, ed. *Management of vesicoureteric reflux*. Baltimore: Williams and Wilkins, 1984:117-36.
- O'Regan S, Yazbeck S, Schick E. Constipation, bladder instability, urinary tract infection syndrome. *Clin Nephrol* 1985;23:152-4.
- Shah KJ, Robins DG, White RHR. Renal scarring and vesicoureteric reflux. *Arch Dis Child* 1978;53:210-7.
- Smellie J, Edwards D, Hunter N, Normand IC, Prescod N.

- Vesico-ureteric reflux and renal scarring. *Kidney Int* 1975;**8** (suppl 4):65–72.
- ¹⁸ Hodson CJ, Maling TMJ, McManamon PJ, Lewis MG. The pathogenesis of reflux nephropathy (chronic atrophic pyelonephritis). *Br J Radiol* 1975;suppl 13.
 - ¹⁹ Rolleston GL, Maling TMJ, Hodson CJ. Intrarenal reflux and the scarred kidney. *Arch Dis Child* 1974;**49**:531–9.
 - ²⁰ Ransley PG, Risdon RA. Renal papillary morphology and intrarenal reflux in the young pig. *Urol Res* 1975;**3**:105–9.
 - ²¹ Harber MJ, Asscher AW. Virulence of urinary pathogens. *Kidney Int* 1985;**28**:717–21.
 - ²² Birmingham Reflux Study Group. A prospective trial of operative versus non-operative treatment of severe vesico-ureteric reflux: 5 years' observation. Nineteenth annual meeting of the European Society for Paediatric Nephrology. *Helv Paediatr Acta* 1986;**41**:130–1.
 - ²³ Smellie JM, Ransley PG, Normand ICS, Prescod N, Edwards D. Development of new scars: a collaborative study. *Br Med J* 1985;**290**:1957–60.
 - ²⁴ Verrier Jones K, Asscher AW, Verrier Jones ER, Mattholie K, Leach K, Thompson GM. Glomerular filtration rate in school-girls with covert bacteriuria. *Br Med J* 1982;**285**:1307–10.

Correspondence to Professor R H R White, Department of Nephrology, The Children's Hospital, Ladywood Middleway, Ladywood, Birmingham B16 8ET, England.