Current Practice

URINARY TRACT DISEASES

Acute Urinary Tract Infection in Children

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British Medical Journal, 1970, 4, 97-100

In the past confusion has arisen over the terminology used to describe infections of the urinary tract. In this article the following terms and definitions will be used:

A urinary tract infection is a condition in which actively multiplying bacteria persist in bladder urine. This state is indicated when a pure growth of 100,000 organisms or more per ml. is obtained on culture of two consecutive clean specimens of urine, or by any growth on culture of a specimen of urine obtained by suprapubic aspiration of the bladder. Symptomatic infections are usually accompanied by more than 10 white cells per cu. mm. of uncentrifuged fresh urine. The presence of pus cells is evidence of an inflammatory process in the genito-urinary tract but is not synonymous with bacterial infection of the urine.

Acute pyelonephritis is a term used to describe attacks of urinary infection in which loin pain, fever, and frequency of micturition occur, and in which infection of renal tissue is suspected. Direct evidence of involvement of the renal parenchyma or pelvis, however, can be obtained only by methods inappropriate for routine use in children—such as by ureteric catheterization or culture of renal biopsy specimens. Indirect evidence may be obtained by measuring the antibody response to the infecting organism or by the presence of a positive blood culture.

Chronic pyelonephritis.—Severe or persistent infection of the renal parenchyma may be followed by the coarse irregular scarring characteristic of chronic atrophic pyelonephritis. This can be recognized on pyelography by reduction in renal size, localized thinning of the renal cortex, and blunting of the corresponding calyx (Fig. 1). When this sequence of

FIG. 1b.

FIG. 1.—Micturating cystogram and tracing of pyelograms from a girl presenting aged 9 with a history of at least five previous urinary tract infections. (a) Renal tracings from the second normal I.V.P. aged 8½. (b) Cystogram showing gross left vesico-ureteric reflux, aged 9. (c) Renal out-lines 1 year after (a) showing the development of left chronic pyelonephritis. This series illustrates the need for both investigations in the management of children with urinary tract infections.

FIG. 1a.

FIG. 1c.

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events is observed in childhood vesico-ureteric reflux (the backflow of urine from bladder to ureter) is almost invariably present.

Acute urinary infection is thought to affect about 1% of children and occurs three to four times more commonly in girls than boys except in the first year. It is a frequent diagnostic problem because it does not cause the symptoms expected in adults and antibacterial treatment is often started in the sick infant before a specimen of urine has been obtained for culture.

The common misconception that urinary tract infection is a benign condition has arisen for several reasons, partly from over-diagnosis and partly from under-investigation. Firstly, the diagnosis is often based on symptoms localized to the lower urinary tract, such as frequency and dysuria, but without bacteriological confirmation. In fact, urine culture in these children often gives negative results since these symptoms are usually the result of vulvitis. Of 36 untreated infants and children referred to our clinic for urine culture with suspected urinary tract infection only one had a positive urine culture. One child with loin pain, dysuria, and frequency was actually suffering from osteitis of the lumbar spine. Secondly, involvement of the kidney with damage of the parenchyma during an acute infection can be discovered only by x-ray studies or other specialized investigations. Hence without early investigation many years may elapse before this damage is discovered—for instance, when an adult is investigated for hypertension, renal failure, or following pre-eclamptic toxæmia or urinary infection in pregnancy.

The need for urgent diagnosis and surgical relief of obstructive lesions of the urinary tract is well known. These lesions are usually found in boys in early life and may be suspected when the bladder or kidneys are palpable and the stream poor. The importance of early diagnosis and investigation of apparently uncomplicated urinary tract infections should also be recognized so that the development of later damage can be prevented by suitable therapy. This is especially the concern of the family doctor and the paediatrician.

Natural History

Evidence is accumulating in favour of an ascending route for urinary infection in children. The common pathogens are *Escherichia coli* (in the great majority), *Proteus mirabilis*, and *Klebsiella aerogenes*. In complicated cases or following instrumentation *Pseudomonas aeruginosa* and *Streptococcus faecalis* are occasionally found. These are all inhabitants of the bowel, and by serotyping strains of *E. coli* it has been shown that the organism infecting the urinary tract is usually the same as the predominant organism in the bowel flora at that time.

Urine is an excellent culture medium, and organisms gaining access to the bladder by the urethra will multiply and persist if conditions prove favourable, as when residual urine remains at the end of micturition. This residue may result from mechanical obstruction to outflow, from incomplete emptying due to neurological defects, or from the return to the bladder of urine refluxed up the ureter during voiding.

The acute infection is usually rapidly cleared by antibacterial therapy. A child who has had one infection, however, is likely to develop further infections and two-year and three-year follow-up studies have shown recurrences in up to three-quarters of the children. These are usually reinfections with a different organism or serotype and not relapses of an inadequately treated initial infection. Furthermore, many of them are symptomless and are discovered only by routine urine culture at follow up.

Investigation of the urinary tract shows anatomical or functional abnormalities in half the children with proved urinary tract infection. Vesico-ureteric reflux is found in one-third of the children and is the most common defect, being almost

invariably present in the 12% who are found to have established renal scarring on first investigation. Obstructive lesions such as posterior urethral valves, ureteroceles, lesions such as bladder diverticula causing stasis, and stones will all require surgical care; they represent 5 to 10% of all the children with urinary tract infection.

Vesico-ureteric reflux may be trivial, moderate, or gross—when it may extend up to the kidney, dilating the ureter and renal pelvis. In each case, however, a route of access is available for the ascent of organisms from the bladder to the ureter and kidney, converting a simple infection of the lower urinary tract to acute pyelonephritis. In children with reflux and urinary tract infection approximately 30% have scarred kidneys when they are first investigated. The proportion in whom scarring is present increases with age, and with the duration of exposure to the risk of further infection. Thus the young child with reflux is less likely to have scarred kidneys than the older one (Fig. 2).

FIG. 2.—Age at diagnosis of reflux related to the presence or absence of chronic pyelonephritis in children investigated for urinary infection. (Reproduced by courtesy of the Oxford University Press, from *Urinary Tract Infection*, ed. O'Grady and Brumfitt, 1968).

Probably reflux has a natural tendency to stop spontaneously in all but the most severe cases, and this has also been observed in children with scarred kidneys. The adult found to have chronic pyelonephritis, the end result of childhood urinary infection, may have no demonstrable reflux.

Symptoms

The older child with acute urinary tract infection may develop the classical picture of fever, loin pain, dysuria, and frequency—perhaps even haematuria. Often, however, the diagnosis is only made incidentally—for instance, when urine is cultured for the first time after years of bed wetting, or when febrile episodes persist after tonsillectomy for recurrent upper respiratory infections. The younger child and the young infant may have few symptoms or only non-specific malaise, anorexia, gastrointestinal upsets, or periods of crying and misery or fever. Symptoms localized to the urinary tract are unusual. Clearly the diagnosis will be made only if the possibility is kept in mind during the examination of any sick child (Fig. 3). Moreover, a specimen of urine *must* be obtained before starting any antibacterial therapy.

Diagnosis

Satisfactory clean specimens of urine can be obtained with patience but little difficulty in most children. In the young child and infant a plastic bag can be applied to the cleaned

FIG. 3.—Micturating cystogram showing bilateral reflux in a boy aged 5 months with congenital laryngeal stridor and vomiting due to hiatus hernia (A urinary tract infection was an incidental finding).

and dried perineum. Supporting the infant on the mother's knee in an upright position or allowing the toddler to run around until a specimen is passed minimizes the risk of contamination. Transfer into a sterile container without delay and immediate cooling of all specimens to 4°C. in a refrigerator prevents the growth of any contaminant organisms, which might confuse the result. Ideally the specimen should be transferred, still cold, to the laboratory for culture and microscopy as soon as possible.

In domiciliary practice one of the most difficult problems in managing children with urinary tract infection is the availability of adequate bacteriological facilities. Only by close co-operation with public health authorities or local hospital pathology services can a satisfactory service be achieved. Screening techniques such as the filter paper method can greatly reduce the load on the laboratory. Surface viable counts and sensitivity tests can then be carried out on the positive specimens (Brumfitt, 1967). Where bacteriological facilities are not readily available slide culture techniques such as Uricult offer a promising alternative (Arneil *et al.*, 1970). While enumeration of both cells and organisms is the most reliable method of making the diagnosis, the result is of no value if the counts are made on unsatisfactory specimens of urine.

In young infants, or if repeated mixed growths of organisms are obtained, the diagnosis can be clarified or confirmed by suprapubic aspiration of urine for culture. This technique should also be used in addition to blood culture and lumbar puncture in the urgent investigation of the severely ill infant admitted to hospital for diagnosis.

Though these recommendations may appear to be a counsel of perfection, it is essential to establish and confirm a bacteriological diagnosis of urinary tract infection in view of the necessary investigation, the prolonged treatment and follow-up which may be entailed, and the serious prognosis in some children.

Treatment

Most acute urinary tract infections in childhood not acquired in hospital are due to sulphonamide-sensitive *E. coli*. For these sulphadimidine or sulphafurazole is still the treatment of first choice. They are effective, inexpensive, and

well tolerated. When there is no clinical response, or the result of culture remains positive, the bacterial sensitivity of the original pathogen will indicate the appropriate change of treatment. Other useful drugs are ampicillin, nitrofurantoin, nalidixic acid, and the recently introduced trimethoprim-sulphamethoxazole combinations.

Though symptoms are rapidly relieved, 7 to 10 days' full-dosage treatment is usually recommended. Intermediate specimens of urine should be examined to ensure that the organism has been eradicated.

Period of Prophylactic Treatment

Many paediatricians have found that further urinary infections develop soon after completing a short course of treatment, usually within six months; and the practice has developed of continuing with a prophylactic dose (about one-third of the therapeutic dose) for some months after the presenting infection. Though no controlled trials of this long-term treatment have been made, low-dosage sulphonamide or nitrofurantoin appears to be effective in reducing further infections (Smallpeice, 1968; Stansfeld and Webb, 1954; Normand and Smellie, 1965). Given in two doses (when the teeth are brushed morning and evening), and with regular reminders when the bacteriological urine check is carried out at three-monthly intervals, children and parents co-operate surprisingly well. The duration of treatment will depend upon the state of the urinary tract.

Investigation

The nature of the symptoms is of no value in predicting which children have anatomical or functional abnormalities in the urinary tract. Since the risk of renal damage from infection depends largely on this—in particular the presence of reflux or obstructive lesions in the ureter or urethra—an attempt should be made to discover these abnormalities at the earliest opportunity. Every child in whom a bacteriologically proved diagnosis of urinary tract infection has been made should be investigated. Both an intravenous pyelogram and a micturating cystourethrogram should be carried out to delineate the upper and lower urinary tract and detect the presence of vesico-ureteric reflux. The omission of one of these investigations can give an incomplete picture, as illustrated in Fig. 1. As can be seen from Fig. 2, it is desirable to discover reflux before renal scarring has occurred, so that the corresponding kidney can be protected from further infection for as long as reflux is present. Cystoscopy and retrograde pyelography, involving hospital admission and general anaesthesia, are usually unnecessary and are warranted in only a very few children.

To obtain the maximum information with the minimum irradiation requires careful instruction of the parent and preparation of the child and should be carried out where possible on an outpatient or a mobile child. A large-dose technique is useful for obtaining clear renal outlines. Four films of the renal areas, taken before and at intervals of 3, 12, and 20 minutes after injection (the last film including the bladder and lower ends of ureters), provide all the information necessary in the great majority. A micturating cystogram should be carried out with a screen image intensifier to reduce irradiation.

Further Management

From what is known of the natural history of urinary infection in childhood one attack cannot be managed as an event in isolation. The parent should be warned that follow-up and perhaps even treatment may need to be continued for years.

There is no standard method of treatment. Nevertheless,

we have found that it is possible to group children for purposes of further care on the basis of their initial radiological assessment.

The first group, about half the children with urinary infection, show no abnormality. These children receive continuous prophylaxis with one-third of the therapeutic dose for 6 to 12 months, and are then followed for two years. In the few who develop further infections it may be necessary to consider reinvestigation to ensure that nothing had been missed. In most the kidneys grow normally and the prognosis is good.

The second group (about 15%) includes the children with an abnormality of the kidney or lower tract, but no reflux. Those with stones, bladder diverticula, ureteroceles, or obstructive lesions require surgical correction. They require careful follow-up and may need long-term prophylaxis if they continue to develop infections. The remainder with anomalies such as duplex or horseshoe kidneys receive 1 to 2 years' prophylaxis and follow-up at lengthening intervals for several years. The prognosis in the latter is good.

The third group, of about 35%, includes all the children found, after control of their infection, to have reflux. With a few exceptions these are all treated on a conservative regimen of uninterrupted prophylactic chemotherapy so long as reflux persists, and until there have been two consecutive negative cystograms. Double micturition is also practised daily at bedtime. Surgical reimplantation of the ureters is, however, indicated if it is not possible to prevent further infections by conservative treatment, or if there is evidence of fresh scarring in a further pyelogram. In a young infant with grossly dilated ureters and renal pelvis early surgery is advisable because these ureters may eventually become atonic.

Whenever prolonged antibacterial therapy is undertaken the child should be seen at regular intervals and his urine

examined by microscopy and culture. Regular visits also remind the family about medicine taking. The rationale of treatment is to prevent reinvasion of the urinary tract from below and not to suppress a persisting renal infection.

Prognosis

Clearly not every child with a urinary tract infection will develop chronic pyelonephritis with hypertension and renal failure. The difficulty, however, of deciding on clinical grounds which children require special care and follow-up makes investigation essential. Not only does it reveal those in whom prophylactic therapy or surgery may be useful, but it enables the doctor to reassure the others, in whom the prognosis is likely to be good. Since normal renal growth without scarring can take place in children with reflux if infection is prevented, it is of paramount importance to make the diagnosis as early in life as possible, so that the susceptible growing kidney can be protected.

FURTHER READING

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Risks of Long-term Tetracyclines

Q.—Are there any serious risks in long-term treatment with tetracyclines—for example, for otherwise intractable acne?

A.—Tetracyclines have been given in moderate doses for long periods to large numbers of patients, notably for chronic bronchitis, without even noticeable effects in most of them. The only usual complaint is of diarrhoea, consequent on disturbance of the intestinal flora. Deposition of the antibiotic in bone is without known harmful effect, and if dentition is complete the cosmetic objection to deposition in teeth does not apply. Unless given in large doses parenterally—which may affect the liver—or in patients with nitrogen retention due to renal disease—which may be aggravated—tetracyclines have no toxic effect, such as that of chloramphenicol on the bone marrow or of aminoglycosides on the eighth nerve.

Carrying Weights and Cervical Spondylosis?

Q.—Is it known whether constantly carrying heavy weights on the head has any bearing on the incidence or severity of cervical spondylosis?

A.—The carrying of weights on the head has the effect of improving the posture of the servocodorsal spine, as is well known in

the remedial gymnastics and physical education world, where posture is often improved by making people walk with books on their heads. The effect of this is to make the centre of gravity of the head and shoulders go through the centre of the cervical and upper dorsal vertebrae and it takes the weight and strain off the posterior intervertebral joints. Hence carrying relatively light weights on the head is likely to decrease the incidence and severity of cervical spondylosis, and could indeed be used as a treatment.

Habitually carrying heavy weights on the head, on the other hand, is likely to result in disc degeneration at an earlier stage than it would normally be expected to occur. This would produce x-ray changes, but not necessarily signs or symptoms. In cervical spondylosis signs and symptoms are nearly always due to radiculitis or posterior joint arthritis associated with traumatic or other inflammatory changes.

Noise Levels in Schools

Q.—Are there any official standards for maximum permissible noise levels in schools, and if so, what are they?

A.—There are no official standards as such laid down for the maximum permissible noise levels in schools. This problem is mentioned in paragraphs 147 and 148 of the Report of the Committee on the Problem of Noise,¹ which deal with insulation and

grouping of classrooms, etc. The report suggests that research is necessary into this problem.

REFERENCE

- ¹ Committee on the Problems of Noise, Final Report. Cmnd. 2056. London, H.M.S.O., 1963.

Survival of Intestinal Pathogens

Q.—What is the duration of life outside the body of intestinal pathogens in dry and in slightly moist conditions?

A.—The factors affecting the recovery of bacteria in natural conditions are so complex¹ that general statements about the duration of their survival have very little meaning. Plainly enterobacteria can survive for prolonged periods in the dry state since they can be successfully preserved for laboratory purposes by drying, even at raised temperatures.² *Salmonella* have been recovered from soil and faeces for periods up to a year¹ but in such situations the organism may be maintained by cycles of multiplication when the supply of nutrients and moisture is favourable. Enterobacteria are undemanding in their nutritional requirements and in many materials—for example, moist animal feed-stuffs—extensive multiplication of salmonella can occur.³

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² Anear, D. I., *Nature*, 1966, 211, 761.
³ Taylor, J., in *Proceedings of the National Conference on Salmonellosis*. Atlanta, Georgia, U.S. Communicable Disease Center, 1965.