Current Practice

CHILD CARE IN GENERAL PRACTICE

Urinary Infection

D. INNES WILLIAMS,* M.D., F.R.C.S.

A refresher course article on this subject appeared in the *B.M.J.* some 12 years ago (Neale, 1953). It was entitled "Pyelitis in Children," and the opening paragraph pointed out that the term pyelitis was purely conventional, since inflammation was apt to affect the whole of the mucosa of the urinary tract rather than part of it; readers were also reminded that involvement of the renal parenchyma, pyelonephritis, was a complication to be feared when the symptoms were severe.

Such explanations are probably not required to-day. We have all become accustomed to think of infection of the urinary tract as a whole, though in any one instance the signs may be predominantly in the upper or lower tract. Emphasis must now be upon the long-term danger of chronic pyelonephritis, insidious in its onset, rather than on the immediate problem of acute pyelonephritis, which can be controlled by antibiotics. It is true that sometimes the chronic pyelonephritic contracted kidney may cause renal failure without a history of acute urinary infection, but the more common history is that of recurrent acute episodes leading to steadily deteriorating renal function. It is by the adequate treatment of such patients that we can hope to avert the irreversible renal failure which threatens them in early adult life.

Many cases of urinary infection in young children are missed or diagnosed late because the symptoms are so non-specific that the possibility is not considered; many more are treated inadequately, and have persistent pyuria for many years with progressive renal scarring. All these cases could be diagnosed with the help of simple routine tests, and recognizing and treating them is an essential task of the family doctor. However, it is now known that dysfunction of the urinary passages is frequently the cause of susceptibility to infection and of its persistence. This demands specialist investigation of an increasing number of patients. Apart from the major urinary obstructions, the routine use of the micturating cystograms has now shown the importance of vesico-ureteric reflux, which is a much more common problem. It is in the reflux group that we find the cases of progressive pyelonephritic contraction of the kidney.

Bacteria

The common invaders of the urinary tract of the child are *Escherichia coli* and *Streptococcus faecalis*, both normal inhabitants of the bowel. The former in particular may be responsible for the mild and recurrent attacks, as well as for the severe and persistent ones. In a proportion of the recurrent cases it has been demonstrated that the type of *E. coli* varies from one attack to another, indicating a fresh invasion rather than a persistent nidus of infection. Other Gram-negative bacilli are also involved: *Klebsiella pneumoniae* and *Aerobacter* usually represent infections more difficult to eradicate; *Proteus* is frequently associated with stone-formation; *Pseudomonas*

pyocyanea is an organism introduced by instruments and is resistant to most antibiotics. The staphylococci are relatively seldom found.

It is as well to remember that the normal urinary tract will rid itself of bacteria, though it may be powerfully aided by drugs, and the persistence of infection after a reasonable course of treatment indicates the need not so much for further cultures and determination of sensitivities as for a more thorough investigation of the urinary tract.

Tuberculosis of the kidneys, though it may appear in adolescence, is now exceptionally rare in children in Britain, and should be diagnosed only on positive culture or the result of guinea-pig inoculation.

Mode of Infection

Arguments as to whether the bacteria ascend the lumen of the urethra, are carried up in the lymphatics, or reach the kidney via the blood stream still continue, and new evidence does not settle the problem. The fact that girls, with a short urethra, are affected three or four times as often as boys, and that chronic renal infections are found particularly in cases of vesico-ureteric reflux, prejudices me in favour of the theory of ascending infection. Residual urine, if present, forms a culture medium in which bacteria can multiply to an extent which enables them to overcome the normal resistance: it may be in the pelvis or the ureter, though the relative rarity of infection in obstructions of the upper urinary tract casts some doubt on the theory that the bacteria always enter the tract through the kidney. It may be in the bladder because of failure of complete emptying, or it may be present as a result of reflux—a proportion of the bladder contents is pushed back up to distend the ureters during micturition, returning as soon as the bladder relaxes. Some sort of urinary abnormality, either anatomical or functional, will be found in at least half of the children with urinary infection, reflux being the most common.

It thus appears that in controlling recurrences of infection whose entry we cannot prevent, we have two possible lines of attack: either to render the urine bacteriostatic by long-term drug treatment or to correct the abnormality of the emptying system.

Natural History of Urinary Infections

The essential elements of a urinary infection are the multiplication of bacteria in the urine and inflammation of the urinary passages, with changes of varying degree in the renal parenchyma. On chemotherapy the urine clears very rapidly, and though the urinary mucosa takes a little longer to return to normal it is unlikely to be affected by any permanent change. Healing in the renal parenchyma is apt to leave a scar, however, and the repetition of acute infections may lead to a contracted kidney.

* Genito-urinary Surgeon, The Hospital for Sick Children, Great Ormond Street, London W.C.1.

When the urinary tract is obstructed and dilated it may prove impossible to rid the urine of pus; a deterioration of the kidney is then inevitable, even though it may be slow. Persistent or recurrent pyuria may occur because there is some nidus of infection, perhaps in the kidney, perhaps in the urethral glands. However, in many other cases where the urinary tract is apparently normal repeated infections occur even though the immediate response to drugs is satisfactory. It is well known that girls afflicted in this way often cease to have attacks somewhere about the age of puberty, and this has been the basis for the reassuring advice that "she will grow out of it." The danger lies in the possibility that chronic pyelonephritis is already well established by the time overt attacks cease, and will cause renal failure or hypertension years later, perhaps during pregnancy.

Symptoms and Signs of Infection

Urinary infections come in all grades of severity; they may be acute in onset and obvious in their manifestations, or insidious and obscure, but none the less dangerous. The younger the child the less likely are there to be local signs related to the urinary tract. A great many infants present simply because they have ceased to thrive: they are no longer gaining weight, and tend to bring back their feeds. In others the signs are a little more acute, with fever, persistent vomiting, abdominal distension, constipation, or sometimes loose stools. The frequency of micturition, if present, is concealed by their napkins, and there does not appear to be any pain on micturition. In the infant stage boys are more commonly affected than girls, because of the greater incidence in the male of severe obstruction of the lower urinary tract. Where such obstruction exists signs are much more acute, so that at times infection can be rapidly fatal. During the neonatal period acute infections are often accompanied by septicaemia, with collapse and jaundice tending to divert attention from the urinary tract.

The older child is more apt to complain of discomfort during micturition and of frequency, but the urinary symptoms are never as prominent as in the adult, and frequency and enuresis are as often due to emotional factors as they are to infection. The boys quite often complain of burning pain on micturition, but in the girls an onset of incontinence or a little urgency may be the only signs. Haematuria is uncommon but can occur in severe attacks, especially when a stone is present. Pain in the loin during the attacks occurs in some but almost always indicates some complicating abnormality. Again, the general symptoms may dominate the picture in many of the more serious cases, fever with headaches and malaise but without localizing pain being characteristic. Children with chronic pyelonephritis and a recent finding of pyuria often have a history of feverish attacks which were never fully explained, or were attributed to tonsillitis.

It is obvious enough that the urine should be examined in children with frequency, dysuria, or onset type of enuresis, but the non-specific signs of urinary infection have been emphasized in order to draw attention to the need for routine urine tests in all children with unexplained fever and vague signs of general ill-health. Physical examination of the child is of little value in diagnosing the infection, though it may reveal other causes for frequency and dysuria, such as vulvitis in a girl, and it is of vital importance in the diagnosis of a urinary obstruction which has predisposed to infection. The male infant particularly must be examined from this point of view—palpable distension of the bladder or enlargement of the kidneys indicates the need for urgent surgical treatment.

Examination of the Urine

The diagnosis of urinary infection may be suspected from the symptoms but can only be made conclusively by examination of the urine. In the laboratory the bacterial colony-count method is probably the most reliable, but it is not always avail-

able, and the general practitioner must be in a position to screen a large number of urines quickly. Microscopical examination of the urine for pus cells is the only method applicable for immediate use in the surgery, and deserves to be very widely employed.

In children old enough to co-operate the urine should be collected by a clean-catch technique in a sterile receptacle after cleansing the genitalia. In the infant a stick-on plastic bag can be applied after similar cleansing, and the urine taken from it. It is desirable that the specimen should be examined as soon as possible after voiding. A urine of perfect clarity is very unlikely to contain pus cells, but any haziness persisting after the addition of acetic acid should give rise to suspicion. The presence or absence of albumin is of no direct relevance to the possibility of infection, and chemical tests for pus are inaccurate.

After shaking a specimen, a little is drawn up in a pipette and one drop placed on a microscope slide, where it is covered with a coverslip. Under the high-power lens, the presence or absence of motile bacilli may be noted, and the number of white cells in each of 20 high-power fields is then counted. Clumping of the cells may lead to a little difficulty in counting, but is of significance in the diagnosis of infection. In the acute infections pus cells will be very numerous—more than 50 cells per field—and there is then little doubt as to the diagnosis. If, however, an average of more than five or six cells per high-power field is found, infection may be suspected and further urines examined.

False positives may be due to pus cells derived from under the inflamed prepuce or from the vagina. A catheter specimen is obviously less likely to be contaminated but it is only justifiable to take such a specimen where doubt remains after other methods have been tried, or in the course of a complete urological examination, and then only under circumstances allowing for the greatest care in asepsis.

Where a diagnosis of infection is made or suspected the urine specimen should be sent for culture. Such specimens must be collected with the greatest care and must reach the laboratory within two hours. If there is any likelihood of delay they should be refrigerated. Where the colony-count technique is used a report of more than 100,000 bacteria per ml. indicates a definite infection; if there are under 10,000 bacteria per ml. it may safely be concluded that the organisms are contaminants. Between these two limits there is room for doubt and need for further examinations. Where reports are made on ordinary culture methods, bacterial growth is usually classified as scanty, moderate, or profuse. A scanty growth is obviously more likely to be due to contamination, particularly if diphtheroids, micrococci, or mixed organisms are reported. In the absence of pus cells scanty growths can usually be ignored, but if doubt remains further cultures should be made.

Immediate Treatment

If a diagnosis of acute infection is made from the observation of heavy pyuria, treatment should be started without waiting for the result of urine culture. First of all a decision must be made on the need for hospital treatment. Infants in their first year are dangerously prone to sudden changes in their condition which make domiciliary care difficult, and except in the mildest cases they are better admitted to hospital. Children with urinary obstruction require drainage as well as drugs, and a careful examination for bladder distension or renal enlargement is essential. The majority of children, however, can be as well treated at home as in hospital, though they must be watched and repeated urine examinations must be made.

Chemotherapy

The best drugs for immediate use before the culture report is available are the sulphonamides and nitrofurantoin. Of the former group sulphadimidine is reliable and cheap, while

sulphafurazole (Gantrisin) has a reputation for being particularly suited to infections of the urinary tract. It may be useful to alkalinize the urine, particularly when sulphadimidine is being given, but a very high intake of fluid is not essential. The long-acting sulphonamides have not gained great favour in this type of disease: they maintain their blood levels because they are excreted slowly in the urine, and in these cases it is a high urinary concentration that we require. It must be remembered, incidentally, that the sulphonamides, and particularly Gantrisin, are potentially dangerous in the neonatal period. Nitrofurantoin has a high urine but a low tissue concentration, and the latter feature has been held to be a disadvantage in the treatment of pyelonephritis, but clinically the drug is remarkably and rapidly effective, except where repeated vomiting makes its use impossible. In most cases on this routine treatment pus cells will clear from the urine in 48 hours, but the treatment should be continued for at least two weeks. The urine must be checked for pus cells again a week after the cessation of treatment, as in many instances there is an early recurrence, showing that the infection has not been eradicated.

It will be noted that penicillin is not advised for immediate treatment. It is true that some of the Gram-negative bacilli are sensitive to this drug when used in very large doses over a long period, and there will be occasions for its administration after bacteriological study, but there can be no doubt about the superiority of sulphonamides and nitrofurantoin for immediate use. Streptomycin, though a drug that must be used with caution, is in fact very effective for many urinary infections and has a definite place in the treatment of infants. The tetracyclines are also valuable, but are best reserved for use where the simpler drugs have failed. Chloramphenicol is a drug to which many organisms are susceptible but one which must be used only for short courses. Cycloserine is effective and in reduced doses can be used over a long period. The newer drugs, nalidixic acid and colistin, are invaluable where the organisms resist the simpler methods, though the former requires to be used with caution on account of side-effects, and the latter has to be given by injection. Hexamine mandelate is often useful for *Str. faecalis*. The dosage appropriate to children is shown in the Table.

Need for Investigation

In ideal circumstances it would be desirable to perform at least an intravenous pyelography on every child who had

Chemotherapy of Urinary Infections

Drug	Adminis- tration	Dose	Notes
Sulphadimidine (Sulphamezathine)	Oral	50 mg./lb. (110 mg./ kg.)/day in four doses	Course of 14 days. For longer main- tenance 250–500 mg. twice daily, depending on size of child
Sulphafurazole (Gantrisin)			
Nitrofurantoin (Furadantin)	,	2.5 mg./lb. (5.5 mg./ kg.)/day in four doses	Course of 14 days Maintenance dose 25–50 mg. twice daily
Nalidixic acid (Negram)	,,	25 mg./lb. (55 mg./ kg.)/day in four doses	Short course
Hexamine mandelate	,,	Under 1 year: 250 mg. twice daily Over 1 year: 250 mg. three times daily	Urine must be acidi- fied and checked with litmus paper. Long courses appropriate
Streptomycin	Intra- muscular	20 mg./lb. (44 mg./ kg.)/day in two doses	Four–five day course only
Cycloserine	Oral	5 mg./lb. (11 mg./ kg.)/day in two doses	Maintenance on half doses
Chloramphenicol	,,	37.5–50 mg./lb. (82.5– 110 mg./kg.)/day in four doses	Short courses only
Colistin methane sulphonate (Colomycin)	Intra- muscular	Under 1 month: 25 mg./lb. (55 mg./ kg.)/day 25,000 units/lb. (55,000 units/kg.)/ day in three doses	Short courses only
Tetracycline (Achromycin)	Oral	10–20 mg./lb. (22– 44 mg./kg.)/day in four doses	Oxytetracycline less likely to stain teeth under 4 years of age.
Oxytetracycline (Terramycin)			Usually in short cour- ses but can be pro- longed
Chlortetracycline (Aureomycin)			Usually for short courses only.
Benzyl penicillin	Intra- muscular	250,000 to 1 mega unit per day in two–four doses	Suitable for long courses where there is pyelonephritis due to organism sensitive to peni- cillin
Phenoxymethylpeni- cillin Ampicillin (Penbritin)	Oral	0–2 years: 62.5–125 mg. six-hourly 3–10 years: 125–250 mg. six-hourly	

FIG. 1.—I.V.P. in a boy with recurrent urinary infection.

FIG. 2.—Cystogram in the same boy, showing the dilatation of the renal pelvis during reflux.

suffered a proved urinary infection, and a micturating cystogram as well in very many of them. Probably this is a task beyond the capacity of our present radiological facilities, and for this and other obvious reasons some discretion must be exercised in the selection of cases for investigation. Every boy should undoubtedly be referred for I.V.P., while girls should be investigated when the first infection is severe, when it causes pain in the loin, palpable kidney, or haematuria, or when it fails to respond to chemotherapy. A girl with more than two proved attacks, even where the symptoms have been slight, is also better investigated.

Intravenous pyelography will show most of the major abnormalities, but it will not necessarily reveal reflux even where this is quite severe (Figs. 1 and 2); hence the need for a micturating cystogram in addition. Cysto-urethroscopy is also required to detect minor degrees of obstruction in the bladder neck and changes in the urethral mucosa.

Long-term Treatment

A child whose first attack responds promptly to treatment needs to be checked soon after the infection and again after a

year. Other cases will normally be investigated, and various forms of surgical treatment may be required: these are beyond the scope of this article. A few will have chronic renal infection, which cannot be cleared immediately and requires a long course of drugs—the penicillins being useful in this respect. However, there will remain many cases of recurrent infection associated with normal urinary tracts or with minor abnormalities which require long-term prophylactic drug therapy. After the urine has been sterilized by whichever drug is appropriate, a sulphonamide or nitrofurantoin is given in small doses for perhaps a year, perhaps longer. Often when this treatment is stopped too early infection recurs within a few days, and such cases obviously require fresh assessment. Ultimately, however, the liability to infection ceases and treatment is no longer necessary. This long-term prophylaxis is a most valuable method, but it is, of course, vital that it is only employed after full investigation, that the dose is in fact kept to the minimum, and that the child is watched for any signs of drug toxicity. Clearly leucopenia is a possibility with the sulphonamides, and peripheral neuritis with nitrofurantoin.

REFERENCE

Neale, A. V. (1953). *Brit. med. J.*, 2, 34.

TO-DAY'S DRUGS

Principles of Prescribing (1)

Prescribing is the simple procedure of ordering for the patient the drugs which he may require as part of his treatment, and ensuring that medication is conveniently and properly regulated.

Prescription writing is not an occult science, and it should not be enshrouded in mystery. There are a few general principles inherent in the practice of prescribing. It is perhaps worth while to recall Sir Robert Hutchison's dictum that the first step in treatment is diagnosis. It must then be decided whether drug therapy is necessary for the treatment of the disability. In many instances it is more important to explain the cause of the illness to the patient and to make it clear why drug therapy has no place in the therapeutic plan. However, when the decision is taken to prescribe a particular drug, other steps follow logically—such as choice of preparation, method of administration, and dosage. Confidence in ordering a drug stems from understanding its mode of action in man, stated in simple physiological terms. We can then forecast the effect in a particular patient and assess the efficacy of the pharmaceutical preparation selected. For example, a knowledge of the toxic effects of the digitalis glycosides ensures that the practitioner will carefully note the cardiac rate and rhythm and inquire closely about the patient's appetite during the phase of intensive therapy. No practitioner can be expected to be familiar with the pharmacology of all available drugs, but it is the responsibility of each practitioner to familiarize himself with the mode of action and possible side-effects of those drugs which are in common use.

It is imperative that a doctor should acquire the habit of reviewing the range of pharmaceutical preparations available for a specified purpose—for example, suppression of cough, relief of pain, etc. Facility in selecting a preparation presents no difficulty for the doctor who has taken the trouble to devise a simple classification of pharmaceutical products, and his choice can conveniently be based upon the *British National Formulary (Alternative Edition)*. It is rarely necessary for the doctor to prescribe drugs which are not listed in either the *British Pharmaceutical Codex (B.P.C.)* or the *British National*

Formulary (B.N.F.). These books are invaluable to the medical practitioner. The *British Pharmacopoeia (B.P.)*, on the other hand, is a book of reference principally for pharmacists.

The prescription itself is a written instruction to the pharmacist to supply drugs in a specified form for a particular patient. Simplicity is the keynote, and the prescription should be written in legible English. The significance of the different parts of the prescription is self-evident:

Mr. A— B—

R (addressed to pharmacist, is an abbreviation for *Recipe* (take))

Sodium bicarbonate	1 g.)	ingredients.
Potassium citrate	1 g.)	
Peppermint water to	16 ml.)	

Make a mixture	}	Instructions to the pharmacist
Send 16 doses		
Label: a tablespoonful in water as directed		

X— Y— (Doctor's signature)

Address.

—/—/65 (date).

There are several rules which should be followed in the writing of all prescriptions:

(i) *Quantities should be expressed in metric measure.*

(ii) *The "single dose" method should be adopted.*—This allows the pharmacist to see at a glance precisely how much of each drug the patient is to receive every time he takes the medicine. There are, of course, occasions when drugs can be prescribed in bulk and the patient may be instructed to take the preparation in approximate quantities (domestic measure). For example, some of the antacids may be prescribed in bulk and ordered to be taken by the teaspoonful.

(iii) *Whenever possible, the preparation should be selected from those listed in the B.P.C. and the B.N.F.*—In this way the practitioner can give appropriate treatment and avoid the unnecessary use of medicines which are relatively expensive; he will prescribe few drugs which are not of proved therapeutic value; and by referring to the selected pharmaceutical prepara-