RECURRENT URINARY INFECTION IN GIRLS*

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It is a commonplace that recurrent and persistent urinary infection result from stasis in the urinary tract, and it is the elimination of major obstructions which has proved the worth of urological surgery. This paper is concerned with those children, almost always girls, who suffer recurrent infections, yet whose urinary tracts show no obvious sign of stasis, and in whom the intravenous pyelogram shows no significant evidence of obstruction. During the past few years our approach to these cases has altered somewhat: at first we were inclined to treat them largely by continuous chemotherapy and even if this treatment did not prevent recurrences in all cases it was believed that attacks usually ceased spontaneously in the end, often at the age of puberty. The danger in this approach, however, is that with each attack of pyelonephritis, destruction and scarring of the renal parenchyma becomes more extensive, and that, although symptoms of urinary infection may disappear, loss of renal substance may be severe and precipitate renal failure much later in life, particularly if infection is reactivated, as often occurs during pregnancy. In recent years, therefore, we have tried to assess the extent of this pyelonephritic scarring from radiological data, and to determine whether any minor disorders of lower urinary function could be rendering the child liable to recurrent infection. Such disorders are mild bladder neck or urethral obstruction, producing only some trabeculation but no more than a small volume of residual urine, and vesico-ureteric reflux occurring on micturition, uncomplicated by serious dilatation of the ureters. Bladder neck obstruction in girls has in fact been diagnosed much more often during the past three years than in the earlier period, and only in the past 12 months have we undertaken regular surgical treatment in cases of reflux.

Results of Conservative Treatment

Our first approach has been a retrospective survey of all cases of recurrent urinary infection

seen in The Hospital for Sick Children, Great Ormond Street, during the six-year period 1951-56. Only those who had had urological investigations and who had been considered at the time to have no urinary tract disorder were selected for follow-up. Of a large number of cases reviewed, therefore, only 102 were selected for further consideration and all these patients were asked specifically whether they had suffered from further attacks of urinary infection, and, if so, whether they would be prepared to submit themselves to further urological investigations. The results of the survey are set out in a table (Fig. 1). It will be seen that 24 patients were finally reinvestigated and assessed and that 15 of them had normal urinary tracts.

FIG. 1.—Table showing the result of a survey of 102 girls with recurrent urinary infection.

Clearly these figures have no statistical significance in estimating the incidence of serious complications after urinary infection; the survey was not wide enough and the material too highly selected, but they do give us some idea of what is happening to our patients. None of these girls has proved to have a progressive type of bladder

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neck obstruction and none of those cystoscoped, because of recurrence of symptoms, had trabeculation. It does appear therefore that in our original series we had not overlooked any serious obstruction. By contrast, progressive pyelonephritic scarring has been observed in several, and on re-examining the original films we now consider that at least some signs of scarring were present at the first investigations.

Chronic Pyelonephritis

The radiological signs of chronic pyelonephritis have been admirably described by Hodson (1959), and his findings have been amply confirmed in this series. This author has also drawn attention to the association of pyelonephritic atrophy with vesico-ureteric reflux, to which we will allude later. In the diagnosis of chronic pyelonephritic lesions it is essential to see not only the pyelogram, but also the renal outline: where ordinary films do not reveal this the stomach can be distended with a fizzy drink; alternatively, tomography may be used. A nephrogram can also be obtained by giving an intravenous injection of hypaque while the ureter is blocked by a tight ureteric catheter, or even by aortography. The characteristic sign of pyelonephritic atrophy (Figs. 5 and 7) is an irregular loss of renal substance; the renal outline is indented and approaches close to the calyx, which is usually blunted. Often this narrowing is confined to one pole of the kidney, though such a finding may well underestimate the pathological extent of the lesion. In the differential diagnosis of pyelonephritis with contraction, two other conditions must be borne in mind: first, foetal lobulation, which is usually evident in the early months of postnatal life, but may persist for longer; indentation of the renal outline is then observed, but it is not associated with any narrowing of the renal substance and the indentations bear no relation to the normal calyx. Second, contraction of the whole kidney relative to its fellow, but with a smooth and regular outline, may be seen in renal artery stenosis causing hypertension, and may then be entirely unassociated with pyelonephritis. In advanced atrophy due to any condition, the pelvi-calyceal system is also deformed, so that a diagnosis may be made on simple pyelography; calyces are clubbed and closely packed together and the pelvis is relatively dilated, although without the cut-off seen on the obstructive hydro-nephrosis. Often the whole kidney seems compressed alongside the vertebral column, the pelvis and the ureter lying in the same straight line.

Pyelonephritic scarring may be static or progressive: progress may be accompanied by evident

clinical infection or be entirely silent, with an insidious loss of renal substance. The following cases illustrate these points.

Case 1. J.B., aged 6 years, was first investigated in 1952 for persistent urinary infection of six months duration. The intravenous pyelogram at this time (Fig. 2) was thought to be normal, but on closer inspection it is evident that the left kidney is small with a regular outline and there is some irregularity of the calyces to the upper pole. Pyelography was repeated during this survey in 1959 (Fig. 3) and this showed a small, grossly contracted and pyelonephritic left kidney. Vesico-ureteric reflux was demonstrated on the left side.

FIG. 2.—Intravenous pyelogram (1952). Small left kidney with irregular upper calyx.

FIG. 3.—Intravenous pyelogram (1959) on the same patient as in Fig. 2. Grossly pyelonephritic changes of the whole of the left kidney.

She had remained perfectly well for seven years apart from one attack of urinary infection with pain in the left loin in 1954. This is a good example of a relatively symptomless progression of the pyelonephritic lesion.

FIG. 4.—Intravenous pyelogram (1954). Note clubbed calyx and thinning of the renal cortex of the upper pole right kidney.

FIG. 5.—Intravenous pyelogram (1959) on the same patient as in Fig. 4. Pyelonephritic scarring of the upper one-half of the right kidney.

Case 2. S.L.G. had an intravenous pyelogram performed in 1954 (Fig. 4) and this shows clubbing of the upper calyx of the right kidney with thinning of the renal cortex in this region. At the time these changes were not thought to be significant. Further pyelography in 1959 (Fig. 5) showed that the lesion had progressed to a considerable degree. The patient also demonstrated vesico-ureteric reflux on the right side. During the 12 months before the second investigation she suffered nine attacks of severe urinary infection. Earlier this year (1960) a Hutch procedure was performed to eliminate reflux on the affected side and she has been well since the operation.

Case 3. S.N. had three complete urological surveys

FIG. 6.—Aortogram of a pyelonephritic right kidney, confirmed at nephrectomy. (Reproduced by kind permission of Dr. C. J. Hodson.)

between 1952 and 1959, but on each occasion the intravenous pyelogram did not satisfactorily demonstrate the right kidney, although it was suspected that this kidney might be the source of her repeated urinary infections. In 1959 an aortogram was performed (Fig. 6) and this demonstrated a nephrogram of a small contracted right kidney. Right nephrectomy was performed and the patient has remained well since her operation.

Case 4. J.R., aged 19 years, recently married, developed a urinary tract infection which was thought to be a 'honeymoon pyelitis'. She had had a full urological investigation in 1951 with negative result. An intravenous pyelogram (Fig. 7) made last year (1959) showed extensive pyelonephritic scarring of the upper one-half of the right kidney. A micturating cystogram demonstrated no vesico-ureteric reflux. This progression of the pyelonephritis had been entirely symptomless. Earlier this year (1960) a partial nephrectomy of the upper one-half of the right kidney was performed. At operation there appeared to be well-localized disease of the upper pole of the right kidney.

Pyelonephritic scarring is the result of infection and what we are really seeking is the cause. It is true that the renal lesion itself sometimes seems responsible for the perpetuation of the infective process, so that excision of the damaged element is the only useful treatment, but we hope to find,

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in an increasing proportion of affected children, a curable lesion in the urinary tract, so that renal tissue may be preserved wherever possible.

Bladder Neck Obstruction

Until two or three years ago, we were very reluctant to make this diagnosis in the female child: we encountered a few cases with a grossly sacculated bladder which appeared to be obstructed, but might also have been neuropathic; but by contrast with many urologists in the United States, we did not recognize many examples of mild bladder neck obstruction. It was suspected that the practice of transurethral resection made for sloppy diagnosis in this respect; it is too easy to say that there is just a little obstruction which can be treated by just a little resection, whereas if an open operation is required the criteria are apt to be a little stricter. Moreover, the fact that in adult practice very few young women are seen with any degree of bladder neck obstruction, mild or severe, made it seem unlikely that we were missing many mild cases in childhood. However, adult women are commonly afflicted by so-called idiopathic chronic pyelonephritis, accentuated during pregnancy and causing renal failure. Some of these cases do show vesico-ureteric reflux and slight trabeculation of the bladder, suggesting therefore that a mild obstruction is present or has been present at some stage in their evolution. It seems possible, therefore, that in the female we might be dealing with a disease process whose natural history differs from the better recognized male cases of bladder neck obstruction progressing to severe hydronephrosis.

We have therefore been on the look-out for cases of mild obstruction in girls and during the past two years we have made the diagnosis on 28 occasions, though open operation has been performed on only 24 and it is this smaller group only which will be considered. Twenty of the 24 had suffered recurrent or persistent attacks of urinary infection, usually on a very large number of occasions with severe temperatures, and resisting long periods of chemotherapy. Many of the girls with infection also had enuresis, but two had enuresis with sterile urine, one complained only of frequency and one only of loin pain. The age of presentation varied from 4 to 18, with a very considerable preponderance of the 6 to 10 age group.

Physical examination gave very little information and of course spinal cord lesions were excluded. A residual urine was definitely present in 19, it was sufficiently large to produce a palpable bladder in five, but small volumes varying from 20 ml. to 200 ml. were present in fourteen. Intravenous

FIG. 7.—Intravenous pyelogram (1959) of a 19-year-old woman. Pyelonephritis of the upper pole of the right kidney. Partial nephrectomy performed.

pyelograms were reported in the first instance to show slight ureteric dilatation in eight cases, and pyelonephritis unaccompanied by dilatation in three. Thirteen of the children were studied by cine-radiology during micturition and eight more had good micturating cystograms with still pictures. These cystograms have been analysed for four factors: the presence or absence of sacculation of the bladder, residual urine, reflux and the form of the urethra.

Sacculations in the form of two or three small pouches behind the ureteric orifices had been present in many of the cases with trabeculated, thickened bladders. They have not been seen in the simple enuretics who are as near to normal controls as we have been able to get for cineradiology. We regard the presence of saccules as highly suggestive of an obstruction, but not absolutely diagnostic.

A residue in the bladder at the end of an uninhibited micturition was counted as definite evidence

FIG. 8a.—Retrograde pyelograms showing moderate dilatation of the ureters and pyelonephritic scarring of the kidneys in a child aged 3 years with the bladder neck obstruction syndrome.

FIG. 8b.—Micturating cystogram in the same child, showing very considerable dilatation of the ureters during the act of micturition.

of obstruction, and it could often be recognized in the radiographs, particularly in the cine films. There are obvious pitfalls provided by the frightened child who will not perform properly, and by the return of urine which has refluxed into the ureters during bladder contraction, though this latter is usually distinguishable on the cine film.

Reflux was present in eight and absent in 13; it was therefore present much less often than residual urine and was in fact often unilateral. Only those with good micturating films have been included in this count since reflux is found more often during micturition than on a simple filling cystogram. Although reflux appeared to be more common in the obstructed bladder than in the non-obstructed, and experience with the male cases certainly corroborates this, we do not regard reflux alone as evidence of obstruction, since it can obviously be due to local abnormalities in the ureteric orifice.

Reflux, then, has many causes, but it is a relatively common complication of bladder neck obstruction in girls. It has, however, definite associations in the upper urinary tract; when unilateral it occurs on the site of the worse kidney whether this is hydronephrotic or contracted with pyelonephritis. In intravenous pyelograms the ureters often appear

atonic with slight and inconstant dilatations; during micturition, at the height of the bladder contraction, they are considerably dilated (Fig. 8).

Many of the urethrograms have an unusual appearance which has not been satisfactorily explained. The bladder neck appears as a ring-like constriction; the urethra below it may be a tube of uniform calibre, but may show a dilatation tapering at the lower end rather like a spinning top (Fig. 9). This is marked when the bladder contraction is forceful and is accentuated if an attempt is made to restrain micturition. At first it seemed to suggest an obstruction in the lower urethra, but we have not been able to demonstrate such an obstruction either on endoscopy or exploration. Moreover, the dilatation tapers at the lower end; it does not bulge as does the posterior urethral outline in valvular obstruction in boys, nor does the urethra stay full after micturition as it does behind the other obstructions. It is suggested that once micturition has begun and the hypertrophied bladder is contracting forcefully, the bladder neck is no longer a severe obstruction so that the powerful stream distends the thin walled urethra below the internal sphincter.

On cystoscopy the cardinal feature has been

trabeculation indicating detrusor hypertrophy, and it is upon the presence of trabeculation that we have relied in the diagnosis of those mild cases without residual urine. It may be difficult to judge the limits of normal in respect of trabeculation and one must be careful to avoid an over-distended bladder or an inadequately anaesthetized and straining child. It is a subjective observation in which experience is of great importance; it has been misjudged on at least one occasion recently, and the bladder at operation was not found to be hypertrophied; this case was therefore excluded from the bladder neck obstruction category. The bladder neck may appear as a prominent ring through the right-angle cystoscope and it usually does so through the urethroscope. It closes down promptly as this instrument is withdrawn down the urethra.

The operation performed has been a Y-V plasty in 23 cases and a simple myotomy in one. The upper part of the bladder has been opened as well in order to assess the detrusor hypertrophy present in all cases included in this series. The bladder neck can be felt as a hypertrophied ring, but it is slack so that it will admit the finger, whereas a normal one often will not. When incised longi-

tudinally the hypertrophied ring is evident, but the urethra below it is thin walled and capacious. Histologically there has been no evidence of the urethral-fibroelastosis which Bodian (1957) found in some boys with Marion's disease. We do not know the exact nature of the pathology therefore; some features do suggest a lower urethral obstruction but we are calling these cases bladder neck obstruction simply because the muscle around the bladder neck is hypertrophied and we have not found a distal obstruction. Moreover, operations on the bladder neck lead to an improvement.

This brings us to an analysis of the results; of 14 cases of recurrent infection with more than six months' follow-up, 12 have remained sterile. The two who recurred have both got severe bilateral reflux. One case with simple frequency has been relieved, also one with loin pain alone. Enuresis alone was present in two; one is relieved, the other is not. In general the continence has been much better after the operation than it was before, though some of the cases with recurrent infection who have sterile urine now are still wet at night.

The conclusions drawn from this series are as follows: among the girls who suffer recurrent infections without gross deformity of the urinary tract are some with a mild degree of obstruction which in the absence of clearly defined pathological evidence we label bladder neck obstruction. It differs from the disease seen in the male in that progression to retention and hydronephrosis is uncommon, but it predisposes to infection and chronic pyelonephritis. In the diagnosis true residual urine is of great significance, as is unquestionable trabeculation of the bladder: a micturating cystogram should always be performed to detect complicating reflux. Y-V plasty is a satisfactory treatment in the majority, but may fail to relieve the condition where reflux is severe.

Reflux

Reflux has already been discussed as a complication of bladder neck obstruction, but has many other causes. It is also seen in association with hypoplastic kidneys, double ureters and other malformations, or it may be due to local abnormalities such as vesical diverticula encroaching upon the ureteric orifice. In this study of recurrent infections in girls where pyelograms do not show any gross abnormality a further condition, the megacystis syndrome, requires mention. Large non-trabeculated, thin-walled bladders associated with lax ureteric orifices and bilateral reflux have been described by Marcel (1952) and more recently by Paquin, Marshall and McGovern (1960). The

FIG. 9.—Micturating cystogram in a child of 7 years with the syndrome of bladder neck obstruction, showing a trabeculated bladder, a sacculum on the right side and the tapering dilatation of the urethra below the bladder neck.

cases of mega-ureter—megacystis syndrome previously described by one of us (Williams, 1954) appear to be severe examples of the same disease, and several cases without mega-ureter have now been investigated. In the past we have been inclined to treat these conservatively, as Marcel has done; more recently we have undertaken operations to prevent reflux as Paquin *et al.* advocate. Comparative results are not yet available, however, and will not be discussed here.

Reflux unassociated with any identifiable bladder abnormality has also been encountered in cases of

recurrent urinary infection: whether it is the cause or the result of an inflammatory process is not yet apparent. Once again surgical treatment is being tried and will be reported later.

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