VESICO-URETERIC REFLUX

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ALTHOUGH in many systems of the body the introduction of efficient anti-bacterial agents has reduced or eliminated, the need for surgery in diseases due to bacterial infection, the reverse has occurred in the urinary tract. The ordinary infecting organisms are susceptible to many drugs and acute episodes of infection can almost always be controlled by medical means, but recurrent infection and chronic pyelonephritis are no less common than formerly. It may yet prove that in chronic pyelonephritis there is some unrecognized ætiological factor in addition to the urinary infection but it is certain that the recurrent pyuria is a factor and that it is commonly associated with disorders of function of the urinary passages: the hope is that operative correction of these disorders will enable drug treatment to be as successful in preventing the chronic disease as it is in controlling the acute phase. The role of surgery in relieving the major obstructions predisposing to infection has long been recognized but in recent years attention has also been devoted to the surgical prevention of vesico-ureteric reflux as it has become increasingly apparent that chronic pyelonephritis without major obstructive disease is often found together with this abnormality. This association between reflux and the pyelonephritic contracted kidney is therefore the main topic of this paper, but for clarity the incidence of reflux in other urological disorders must be briefly discussed.

Normal Function

In normal circumstances flow in the ureter is in one direction only: downwards towards the bladder. The peristaltic activity of the ureter usually prevents any reversal of this flow, and the valvular mechanism of the uretero-vesical junction precludes escape of urine from the bladder in this direction. The valve is formed by the oblique passage of the intramural ureter through the bladder wall: it is not dependent upon any sphincteric activity. At post-mortem the normal bladder can be distended until the muscle coat begins to rupture before any fluid enters the ureters; indeed the greater the distension of the bladder the longer and more oblique the intra-

mural ureter becomes, and therefore the more efficient the valvular action. Clearly the time at which reflux is most likely to occur is towards the end of micturition, when the bladder is nearly empty and the intramural ureter relatively short, while the intra-vesical pressure is high. Clinically this expectation is borne out by the fact that reflux is found most commonly on the micturating rather than on the simple filling cystogram.

Cystography for Detection of Reflux

The radiological detection of reflux requires the passage of a catheter and the injection of opaque medium into the bladder. This is something of a disadvantage in view of the well known danger of catheterization, but micturition films at the end of the intravenous pyelograms are useless since the filling of the ureter may still be due to the excretion of the medium. It need scarcely be emphasized that the instrumentation must be performed under conditions of strict asepsis and should be avoided altogether in cases of lower urinary obstruction unless all preparations have been made to secure adequate urinary drainage afterwards.

The bladder should be filled to capacity with the opaque medium, and films exposed before, during and after micturition. If ciné film can be taken using the image intensifier, a very clear idea of the degree of reflux can be obtained, but this is in no way essential. It is sometimes difficult or impossible to persuade the patient to micturate while in front of the X-ray tube, and occasionally in young children the investigation must be performed under an anæsthetic: the bladder is then emptied by manual expression. It must be recognized, however, that reflux cannot be excluded unless micturating films have been obtained and it is, after all, reflux occurring during normal micturition which interests us in relation to disease, not reflux under conditions of passive over-distension of the bladder.

In most cases of reflux the post-micturition film will show the entire ureter and renal pelvis filled with opaque medium, but in less severe cases only the lower ureter may be filled and this is often emptied rapidly so that there should be no delay in exposing this last picture.

Mechanism of Reflux

Reflux occurs when disease or injury has rendered the intramural ureter short and wide, or when the presence of a saccule adjacent to the orifice leads to its displacement outwards. Tuberculosis provides the best example of the first category: the infected ureter is rigid and shortened, the bladder contracted, reflux then occurs but is reversible if the disease process is controlled by chemotherapy. The passage of a large ureteric stone or a surgical ureteric meatotomy may have the same effect. In some pyelonephritic contracted kidneys the ureter is shortened and rigid, so that it may be suspected that reflux is secondary to the infective process, but as will be seen later this is not the usual finding and it is believed that reflux is usually a primary abnormality in this group.

The detrusor coat of the bladder is made up of many interlacing, but distinct, muscle bundles. Such a pattern is apt to leave weak points and one such occurs behind and lateral to the ureteric orifice. Here a saccule of vesical mucosa may be pushed out between the muscle fibres during micturition. Saccules of this type may be seen without any other serious abnormality, but they are, of course, usually associated with obstruction to the outflow from the bladder, or with a nerve lesion, and therefore with a hypertrophied detrusor. Hutch (1955) has shown how a saccule in this situation may, as it enlarges, draw the ureteric orifice out with it, until the terminal ureter is no longer intramural and therefore no longer valvular (Fig. 1). It is because of this saccule formation and not because of any simple increase of intra-vesical pressure that reflux occurs in some, but by no means all, cases of urinary obstruction. The saccule may, of course, enlarge until it assumes the proportions of a diverticulum and the ureter may be permanently displaced so that it opens into the diverticulum itself.

Congenital abnormalities of the ureter may facilitate reflux, because a short, wide intramural ureter is present. In many of the pyelonephritic contracted kidneys this is the only local lesion which can be found.

When reflux occurs into a ureter of normal calibre, the refluxed urine does not pass upwards for more than two or three inches; it is then returned by active ureteric peristalsis. This seems to be a harmless condition in the short run since it can be shown radiologically in cases with normal kidneys, but if it continues a change in the ureteric activity is seen. A great deal depends, however, upon the state of the bladder from which reflux occurs.

FIG. 1.—Saccule formation and reflux. Diagrams to show the formation of a saccule causing the intramural ureter to be pushed outwards and therefore to lose its valvular action.

Reflux as the Sole Abnormality

Cystograms are not usually performed on normal, symptom-free subjects, but from such evidence as there is (see McGovern, Marshall and Paquin, 1960) reflux is not found in these individuals. Cystograms have been performed, however, in large numbers of enuretics, and in children with recurrent urinary infection who have normal intravenous pyelograms. In the enuretic group reflux scarcely ever occurs, if the bladder is normal, without evidence of obstruction or trabeculation: in the infected group, however, reflux is relatively common. Radiological detection of chronic pyelonephritis implies, of course, that the disease has already produced deep scars in the kidney and there seems little doubt that in this infected group pyelonephritis is present in its early stages.

It may be mentioned here that reflux is very seldom a direct cause of symptoms: the classical complaint of renal pain during micturition is very infrequently heard, although obviously a pyelonephritic kidney may be painful during an acute episode of infection.

FIG. 2.—Sketches from pyelograms of contracted kidneys with reflux to show the characteristic appearance.

Reflux in the Contracted Kidney

It has already been emphasized that the pyelonephritic contracted kidney is frequently associated with reflux, and in this group there is no great dilatation of the urinary tract (Hinman and Hutch, 1962). The kidney is smaller than normal, as can be seen by measuring the extent of the renal outline in the pyelographic series. Absolutely normal dimensions are hard to establish, but usually it is possible to compare one kidney with the other, or the same kidney in different X-rays taken over the course of years. Pyelonephritis is a patchy disease and the renal outline is irregular, showing that the loss of parenchyma has occurred in relation to the calyces showing the most distortion (Figs. 2 and 3). The affected calyces themselves are blunted but do not have the smooth outline of hydronephrotic calyces. They are crowded together where a large part of the kidney is diseased and approach close to the surface. The renal pelvis is often a little larger than normal and may at first suggest hydronephrosis, but there is no sharp cut-off at the pelvi-ureteric junction, and emptying is reasonably efficient. The pelvis and ureter of the very small kidney are often disposed in one vertical line, close to the vertebral column.

FIG. 3.—Intravenous pyelogram from a girl of 9 years with recurrent pyuria. The right kidney is severely pyelonephritic and reflux was present on this side only.

The refluxing ureter in this group shows a characteristically 'flabby' dilatation (Fig. 4) and its calibre varies according to the circumstances. In intravenous pyelograms it may look completely normal, though the upper part is often a little wide while the compression is applied. During micturition, however, when reflux is occurring the ureter is considerably dilated. After the act, the refluxed urine returns rapidly to the bladder, which therefore contains 'false' residual urine.

The ureteric orifice is cystoscopically normal in most patients in this group, though in long-standing cases it may become rigid and wide. The contrasting appearance of the refluxing mega-ureter is discussed below. The bladder may be normal, but in many girls with this type of pyelonephritic kidney there is definite trabeculation and, therefore, evidence of slight obstruction. The role of 'bladder neck obstruction' in these girls with recurrent pyuria is still much disputed, for it is unusual for them to progress to retention or serious upper tract dilatation, but the presence of a hypertrophied detrusor without urethral obstruction strongly suggests some hold-up at the bladder neck and often the beneficial effects of bladder neck surgery confirm this view (Williams and Sturdy, 1961). On the other hand, these bladders may simply be irritable and the frequency and urgency may themselves lead to trabeculation. The small saccule which interferes with the valvular action of the intramural ureter is a corollary of the trabeculation whatever its origin.

Pyelonephritis is in general bilateral but asymmetrical, and in most cases of this group reflux is

FIG. 4.—Cystogram from a girl of 9 years with recurrent pyuria: reflux into the left kidney.

bilateral, though often more marked on one side than the other. It has also been observed that where reflux has been prevented by operation on one side, it has subsequently appeared contralaterally.

It has been stated that the pyelonephritic contracted kidney is commonly associated with reflux. In children this finding is almost constant, though exceptions do occur. An interesting example of this is found in Fig. 5; the patient was a girl of 11 years suffering from recurrent pyuria who had, during attacks, pain in the left loin. The intravenous pyelogram shows a contracted right kidney, and a large, but slightly distorted, left kidney. On cystography reflux was present only on the left, the side of the symptoms, but not the side of the most advanced disease.

The small kidney may, of course, be the result of renal artery stenosis, not of pyelonephritis, and reflux is not then to be expected. It may also be congenitally hypoplastic, and reflux is not then invariable, but the distinction between congenital hypoplasia and pyelonephritic contraction is difficult or impossible to make except by the histological finding of dysplastic elements in the former group: moreover, infection frequently complicates the anomaly.

In adults reflux is less common, and a proportion

FIG. 5.—Intravenous pyelogram from a girl of 10 years with persistent pyuria, and episodes of high fever with left loin pain. The right kidney is contracted but on cystography reflux was present only on the left, the side of the pain.

of cases, male and female, with severely contracted pyelonephritic kidneys have been investigated by cystography on a number of occasions without finding this particular disorder. In the obstructed cases, too, without infection, reflux is less likely in adults than in children; the saccule is not so apt to form. In some children reflux ceases with the passage of time, probably due to the consolidation of the vesical muscularis associated with growth.

Reflux in Double Ureters

Although the complications of ureteric duplication are uncommon in comparison with chronic pyelonephritis in the anatomically normal kidney, evidence from this group is helpful in assessing the role of reflux in renal disease (Fig. 6). If the ureteric duplication is partial, union of the two ducts may take place at any level between the renal pelvis and the bladder. Function appears to be well co-ordinated as a rule and it is rare to find any hold-up at the point of union, though urine may flow from one branch into the other at times. If the common uretero-vesical junction is incompetent, refluxed urine flows more or less equally into both ureters. A number of cases has been observed in which this is complicated by chronic pyelonephritis, and in all the lesion has affected both halves of the kidney (Fig. 7). If the ureteric duplication is complete and both ureters open upon the trigone of the bladder, the ureter from the upper renal pelvis opens nearer the bladder neck than its fellow and has, therefore, a longer intramural segment. It is perfectly possible for both ureters to have an efficient valvular mechanism, but clearly if one fails it will be the ureter from the lower (and larger) renal pelvis which opens higher up in the bladder and has the shorter intramural

FIG. 6.—Diagrams to show double ureters complicated by reflux.

(a) The bifid ureter with reflux into both branches: pyelonephritis affects both halves of the kidney.

(b) The complete duplication: reflux only into the lower pelvis.

(c) The urethral ectopic ureter: reflux into the upper pelvis.

FIG. 7.—Cystogram in a 8-year-old boy showing reflux on both sides. On the left a bifid ureter with pyelonephritis of both renal elements.

course. This situation has been observed in a few examples, and, in each, the lower half of the kidney only has been pyelonephritic, the upper element being healthy. In some the opposite single ureter has also allowed reflux and has been associated with a pyelonephritic kidney, leaving only the one upper segment, with an anatomically anomalous ureter, protected.

If the ureteric duplication is complete, but the ureter from the upper pelvis is ectopic, opening at the bladder neck or into the posterior urethra, its orifice is usually wide and rigid allowing reflux. In these circumstances, the upper renal pelvis is pyelonephritic, the lower normal as long as its orifice is competent. In this group, however, dysplastic elements in the renal parenchyma are common, and some obstructive element may also be involved. The ectopic ureterocele introduces a further complication in some, as has been discussed elsewhere (Williams, 1962).

The double ureters thus present something like an experiment in the effects of reflux upon the kidney.

Reflux in the Mega-ureters

The term mega-ureter implies chronic dilatation without organic obstruction. One group has a terminal ureteric segment of normal calibre, and a competent uretero-vesical valve: these patients have clearly a functional obstruction of as yet unknown origin, but are not of concern in the present paper. The other group has bilateral

FIG. 8.—Cystogram in girl of 4 years with mega-ureter-megacystis syndrome. (Other films showed also dilated right ureter.)

dilatation with free reflux, gaping ureteric orifices and a large-capacity bladder—the mega-ureter-megacystis syndrome. Mention has already been made of the fact that in cystograms the refluxing ureter is often dilated although it appears normal in the intravenous pyelograms, and there is great difficulty in defining what is a mega-ureter. It is, in fact, possible that reflux alone is responsible for the mega-ureter type of dilatation, but against this we have the extremely large calibre (Fig. 8) even though the bladder is not obstructed, the persistence in the ureters of powerful, although ineffective contractions, and the characteristic appearance of the ureteric orifice at cystoscopy. At rest the orifice gapes widely, so that an endoscope is easily introduced into it, yet it exhibits brief, powerful contractions which bring it momentarily to a normal size. Although, therefore, there is no proof, it is believed that the mega-ureter-megacystis syndrome is distinct from the simple refluxing ureter with pyelonephritis. The effect on the kidney, however, is similar;

FIG. 9.—Cystogram showing reflux from a neurogenic bladder due to myelo-meningocele.

there may be some progressive hydronephrosis, but ultimately failure is more likely to be due to the complicating infection.

Reflux in Severe Obstructions

When reflux occurs from a severely obstructed and hypertrophied bladder, as for instance in the congenital urethral or bladder-neck obstructions, the full force of the detrusor contraction is brought to bear upon the comparatively thin-walled ureter, and a rapidly increasing dilatation of the ureter and renal pelvis follows. This effect is well demonstrated in unilateral cases of reflux, when the affected kidney is always the more hydronephrotic and functionally the poorer. The same effect may be seen in the hypertrophied, neuro-pathic bladder and again increasing hydronephrosis is the usual effect (Fig. 9).

Reflux: Cause or Effect of Renal Disease?

Our therapeutic attitude towards reflux must obviously depend on whether we regard it as an interesting but innocuous side-effect of other disorders, as a dangerous complication, or as a

primary factor in the disease process. The evidence from clinical observation is to some extent confusing, while animal experiments are as yet inconclusive. Nevertheless, some assessment must be made as a practical guide.

In severe urethral and bladder-neck obstructions, reflux is a dangerous complication accelerating the renal damage: this cannot be disputed, but it may be that persistent reflux is innocuous if the obstruction has been completely removed.

In tuberculosis, renal disease leads to ureteric and vesical inflammation: reflux again is a complication but it may not be serious if the original disorder is adequately treated.

In chronic pyelonephritis the ureter may be thickened and rigid, but this is exceptional. In many cases reflux occurs into ureters which are normally supple and muscular. In the double ureter 'experiment', reflux is related to the anatomy of the orifice and this appears to determine the distribution of pyelonephritis. Here, then, is a strong suggestion that reflux is a primary factor in causation. If we allow it to be a cause, how does it produce its effect? If the effect were mechanical one might expect progressive hydronephrosis in all cases, as in the obstructed ones: this does not accord with the clinical observations. As an alternative a mechanical effect upon the renal blood vessels adjacent to the calyces has been suggested, because in some cases chronic pyelonephritis presents in a severe form without pyuria or a history of infection (Hodson and Edwards, 1960). Nevertheless the majority of cases have recurrent infection and the simplest suggestion is that reflux, like obstruction, predisposes to urinary tract infections, while it certainly facilitates the spread of infection from the lower to the upper tract. It is obviously not the only predisposing cause of infection and it must be allowed that chronic pyelonephritis can occur without reflux or progress after reflux has ceased.

The issue of the direct mechanical effect versus predisposition to infection is important in relation to surgical treatment. If the former factor is paramount, reflux-preventing operations are always advisable; if the latter, operation is only required when infections are not controlled medically. Pending further evidence, the present writer favours the theory of predisposition and, therefore, of limited surgery.

Surgical Treatment

Patients and their diseases are so infinitely various that it is rare for any controlled observation to establish once and for all the indications for any operation: after wild swings of favour and disfavour a middle course is usually reached as a

result of the imperfectly analysed experience of many surgeons. Reflux-preventing operations are still in the early stages of development; there is no consensus of opinion and very little published evidence of results capable of analysis.

The place for operative prevention of reflux is suggested by the clinical observations recorded above. Most pressing is the need to prevent recurrent or persistent pyuria in children from progressing to chronic pyelonephritis with renal failure, and it is in this group that reflux seems likely to be a primary factor and here, therefore, is an opportunity for prophylactic surgery. If drug therapy is failing to control or prevent pyuria, we may hope by operation to halt the progress of the disease and to preserve what healthy tissue remains. Clearly there will come a point at which the damage is so advanced that in unilateral cases, nephrectomy will be better than conservation, and in bilateral cases the risk of surgery will be greater than any possible improvement could justify. In hypertensive cases, no effect on the blood pressure levels can be expected, though occasionally operation may prevent further deterioration of renal function.

In the severe lower urinary tract obstruction the primary need is to establish free urinary flow; reflux may then cease spontaneously. Some cases may have persistent symptoms justifying reflux preventing procedures at a later stage but these are uncommon.

In the neurogenic bladder, where the problem of reflux has been studied for many years, Hutch presented the case for operative prevention, but it is not universally accepted. In the 'spina bifida' bladder, where upper urinary tract changes seem severe enough to justify surgery, it has been found that the place of such conservative measures is very limited; most cases do better with the skin diversion of the urine by cutaneous ureterostomy.

In the mega-ureter-megacystis group it has long been observed that, in the absence of pyuria, good health may be preserved for very many years without pyelographic deterioration. Recurrent pyuria here, as in the simple atrophic pyelonephritis cases, is a good indication for reflux-preventing surgery, but technical difficulties may limit its usefulness. When dilatation is very far advanced any operation is hazardous: moreover reflux prevention is more difficult to achieve, the ureter must be narrowed and shortened as well, a process which may endanger the blood supply. In these advanced cases, therefore, surgery is better avoided and a 'triple micturition' regime should be adopted to reduce the false residual urine in the bladder.

Operative Technique

It is not intended to discuss the details of technique in this article and reference should be made to the original papers. All operations to prevent reflux aim essentially at producing a long and stable intramural ureter: in some the continuity of the ureter is preserved, in others it is cut across and re-implanted. In the first category, the Hutch procedure (1955) is perhaps most widely practised. After preliminary extravescical mobilization, the terminal ureter is exposed through the open bladder by an incision made upwards and outwards from the ureteric orifice. The ureter is drawn up into the bladder lumen and the incision closed behind it. The ureter lying within the bladder is quickly covered by ingrowth of mucosa and a long intravesical segment is thus produced. In the Bischoff (1957) procedure the ureter is prolonged downwards towards the bladder neck by burying a strip of mucosa in an operation analogous to the Denis Browne hypospadias operation.

In the author's hands, however, neither of these procedures is so reliable or free of complications as the tunnel re-implant, using a method adapted from Politano and Leadbetter (1958) and Paquin, Marshall and McGovern (1960). The ureter is divided at its entrance into the bladder and re-

introduced through a long intramural tunnel: it is re-anastomosed with a small everted nipple to prevent stenosis.

Re-implantation is usually accompanied by a bladder neck Y-V plasty or myotomy to reduce voiding pressure.

Results

In this type of prophylactic surgery many years must pass before an assessment can be made. Several different techniques have been employed, with and without bladder-neck surgery, which at present makes comparisons difficult or impossible.

Pyelographic changes are naturally slow to appear and for the time being the cessation of recurrent attacks of pyuria seems the best evidence of success. Although figures are not yet available, current impressions are that in this respect reflux prevention is well worthwhile; there have been failures, but it is noticeable that these now have pyuria without the pyrexia which was previously a feature, suggesting that the kidney is now less severely involved.

At this stage it would not be justifiable to advise operation in all cases of reflux with pyelonephritis, but where chemotherapy fails surgery has something to offer.

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