Personal practice

Management of prenatally diagnosed uropathies

D F M THOMAS AND A C GORDON

St James's University Hospital and The General Infirmary, Leeds

It is not unrealistic to anticipate that by the turn of the century virtually every child in the United Kingdom with an appreciable urological abnormality will have been diagnosed by ultrasound before birth. There is a possibility, however, that our ability as clinicians to interpret and utilise information derived from prenatal ultrasound will not keep pace with the increasing sophistication and availability of the imaging techniques. Current management of prenatally diagnosed uropathies is based as much on empiricism as on science. Therapeutic strategies and indications for surgery based on experience with symptomatic conditions in older children are not necessarily relevant to neonates with asymptomatic anomalies diagnosed prenatally.

Prenatal diagnosis: accuracy and reliability

It is important to have realistic expectations of ultrasound. It can provide only anatomical information—which in this context usually means dilatation of the urinary tract. As it cannot reliably distinguish between high grade obstruction, low pressure non-obstructive dilatation or reflux, a final urological diagnosis depends upon the use of cystography and isotopes, which are only available postnatally.

Nevertheless, prenatal ultrasound screening can serve two important roles. The first is in identifying grossly affected fetuses at a time when termination of pregnancy is still an option. The second role lies in its ability to identify fetuses with uropathy that require appropriate investigation in postnatal life.

Within this limited framework prenatal ultrasound is highly effective. With modern real time scanners diagnostic errors are more likely to be due to inexperience in obtaining and interpreting the images rather than any deficiency of the equipment. Some skilled specialist radiologists are now able to provide highly detailed anatomical information—particularly in later pregnancy. While this is desirable (it enables us to give a more accurate prognosis to the parents) it is not essential. At present it is

more realistic to regard prenatal ultrasound as a means of screening fetuses for uropathies that will require investigation in postnatal life.

A recent analysis of about 47 000 pregnancies over a five year period in Leeds yielded an incidence of prenatally diagnosed uropathies of 1/570 pregnancies. This figure includes those pregnancies that were terminated and those that subsequently resulted in neonatal death from pulmonary hypoplasia. If these non-viable fetuses are excluded from the calculation, we arrive at a figure of one live born neonate with a significant urological abnormality in every 800 live births. Thus the 'pick-up' rate for prenatal diagnosis is now within the incidence range previously recorded in large postmortem studies. (For example, one study of 245 000 necropsies reported an incidence of renal anomalies of 1/650.¹) Our figures suggest that prenatal ultrasound diagnosis is highly effective and is already capable of picking up most important urological abnormalities before birth.

Although we can rely increasingly on the ability of ultrasound to detect abnormal kidneys that are dilated, this is not the case with kidneys that are small or absent. We should be very reluctant to advise any action or invasive intervention on the basis of an ultrasound diagnosis of renal agenesis.

Obstetric implications of prenatally diagnosed uropathies

The specialised areas of intrauterine diagnosis and fetal intervention are the joint concern of obstetricians, radiologists, and paediatric specialists. The latter are generally better placed to advise on the likely significance of ultrasound findings and to predict the likely prognosis and course of postnatal management. Perhaps the most effective way of ensuring paediatric involvement in obstetric management is to set up a combined prenatal counselling clinic. In practice, however, it may prove very difficult to reorganise the timetables of the various

consultant specialists whose presence at such a clinic is essential.

The gestational age at which routine ultrasound scanning is undertaken is something of a compromise. Most obstetricians settle for the period between 17 and 20 weeks. Scanning before 17 weeks yields less detailed anatomical information and a lower pick up rate for congenital abnormalities. Routine scanning after 20 weeks is more accurate, but leaves less time to acquire additional information on the fetus upon which to base a decision to terminate the pregnancy. Scans undertaken between 17 to 20 weeks can be expected to pick up most of the lethal urological abnormalities. These scans can also yield a great deal of anatomical information: biparietal diameter and fetal length; they can show longitudinal and transverse views of the spine and four chamber views of the heart; and provide information on the stomach, kidneys, and bladder. At this stage in the pregnancy, however, dilatation due to reflux or to less severe forms of obstruction may not yet be evident.

The findings of an appreciable urological abnormality on the initial dating scan should be confirmed by a second examination—ideally performed by a radiologist with particular expertise and experience in prenatal diagnosis. Some form of radiological 'second opinion' is highly desirable if termination of pregnancy is one of the options under consideration. Indeed there is a strong case for referring the mother to a regional centre to be scanned by a radiologist working in conjunction with an obstetrician trained in intervention techniques and a paediatric urologist (or surgeon).

Obstetric intervention can take the form of intrauterine drainage (fetal surgery), termination of pregnancy, or induction of premature labour.

(1) INTRAUTERINE DRAINAGE

Fetal surgery—to drain the obstructed urinary tract—is a logical and, at first sight, attractive extension of prenatal diagnosis. Unfortunately there are several flaws in this concept.

The first is that the renal dysplasia and pulmonary hypoplasia may already be irreversible by the time the urinary tract dilatation is first detected at 17 to 20 weeks. This dilemma is illustrated by the first published case of fetal surgery, which was reported by Harrison and his colleagues in San Francisco.² In this case a fetus with severe outflow obstruction was operated upon via a hysterotomy at 21 weeks' gestation. Despite adequate decompression of the urinary tract by cutaneous ureterostomy, the affected neonate died of pulmonary hypoplasia after delivery at 35 weeks. Early fetal lung development appears to depend on an adequate volume of

liquor—of which fetal urine is a major constituent. In its analysis of fetal intervention for obstructive uropathy, the International Fetal Surgery Registry reported neonatal death from pulmonary hypoplasia in 27 (37%) of 73 fetuses treated in utero.³ In a further 11 cases the pregnancy was subsequently terminated. It is highly likely that these fetuses would also have succumbed to pulmonary hypoplasia if the pregnancies had proceeded to term. These figures and those published in a recent review of the literature suggest that intrauterine surgery to drain the urinary tract is unlikely to reduce neonatal mortality from pulmonary hypoplasia.⁴

There is another major concern about intrauterine intervention. Dilatation is not synonymous with obstruction. Ultrasound imaging cannot distinguish between dilatation, which is a consequence of high pressure obstruction (for which it is possible to make a theoretical case of intervention) and non-obstructive dilatation or reflux for which intervention would be inappropriate. Furthermore, fetal intervention has a published procedure related complication rate of 44%⁴ and a procedure related mortality rate of anything up to 10%.^{3,4} The published data do not show a benefit from fetal intervention that justifies these risks.

Fifty nine fetuses with bilateral uropathy have been managed in Leeds during the last five years. In no instance has intrauterine drainage been attempted. In 15 cases the fetus was severely affected (oligohydramnios, etc, see below) and the pregnancy was terminated. A further eight cases resulted in neonatal death from pulmonary hypoplasia. Thus in this series of fetuses managed without intrauterine drainage, a total of 23 (39%) were non-viable as a result of severe urinary tract obstruction. The mortality reported by the International Fetal Surgery Registry was 59% despite intervention.³ It would be unwise, however, to draw any firm conclusions from these figures as there may have been important differences between the two groups of fetuses. Long term follow up is essential. Nevertheless our limited experience does not suggest that intrauterine intervention offers any great benefit. It is our view that the continuing use of these procedures can only be justified in the context of a formal prospective controlled trial.

(2) TERMINATION OF PREGNANCY

The most important indicator of poor prognosis is oligohydramnios, but others include 'bright' (dysplastic) renal parenchyma, a high concentration of urinary sodium (greater than 100 mmol/l) on fetal bladder puncture, and evidence of serious coexistent anomalies. The decision to offer termination should

be taken on the basis of several scans, ideally performed by more than one radiologist.

(3) INDUCTION OF PREMATURE LABOUR

The theoretical benefits from premature delivery and prompt ex utero surgery have to be set against the additional morbidity associated with prematurity. In our view it is not justifiable to induce premature labour in cases of fetal uropathy, but there may be an argument for allowing premature labour to proceed if it occurs spontaneously after 34 weeks.

Counselling during pregnancy

When fetal uropathies were first diagnosed with relative frequency, there was some debate about the wisdom of informing parents of the abnormal ultrasound findings. It was argued, by some, that this information would provoke unnecessary anxiety during pregnancy. There is no question, however, of the need to inform parents of the presence of a severe uropathy for which termination (or possibly intervention) might be appropriate. The argument centres on whether parents should be told about the less severe anomalies for which no treatment is envisaged until delivery. We believe that parents should be informed as soon as the presence of a fetal uropathy has been confirmed. This information should be followed by appropriate counselling and the opportunity for the parents to meet the specialist who will be supervising their child's management after delivery. Apart from any virtue that an open approach might have, it is difficult, in practice, to conceal from parents the fact that an abnormality has been detected on ultrasound scanning. Most mothers seem to sense that 'something is wrong' and are aware of the unusual level of interest being shown in their scans.

Postnatal management

For practical purposes the value of prenatal diagnosis lies in its ability to identify clinically undetectable urological abnormalities that would otherwise only have come to light in later life as a result of infection or impaired renal function. It is important, however, not to overstate the contribution of prenatal diagnosis to survival or well being. In a review of 145 live born neonates with prenatally diagnosed uropathy, we found that there were 24 (17%) who had relevant physical signs or stigmata of urological disease that rendered the prenatal diagnosis largely irrelevant. In 121 neonates (83%), however, there were no physical signs and the infant's urological abnormality was picked up solely on the basis of information from the prenatal ultrasound scans. In 25 neonates (17%) we felt that the prenatal diagnosis had been

of definite value in identifying appreciable treatable pathology affecting both kidneys or a solitary kidney. It is likely that prenatal diagnosis did make a useful contribution to the prognosis for renal function in this group of neonates. In 65 neonates (45%) an appreciable uropathy was present, but was confined to one kidney—the contralateral kidney being healthy. In this group we categorised the prenatal diagnosis as being of 'probable' value. Finally there was a sizeable group—31 (21%)—with mildly dilated systems of uncertain significance. In most of these cases the dilatation has resolved spontaneously in the first year of life. It is possible that some had reflux in utero. Alternatively, some of these infants may have incipient pelviureteric obstruction, which may yet cause problems in later life. Time will tell.

INVESTIGATIONS

There is little doubt that the initial investigation should be an ultrasound scan of the urinary tract performed within the first 24 or 48 hours of life. Further investigation then flows from the initial ultrasound findings (figure).

(a) Initial postnatal scan normal

There is no evidence of dilatation. The parents are reassured, the infant is discharged from hospital at the normal time, and is brought back to be scanned again at 1 month. If this second scan is also normal we would discharge the child from further follow up.

(b) Initial scan shows mild or equivocal dilatation of the pelvicalyceal system

Although some radiologists regard 1 cm as the upper limit of normal for the diameter of the renal pelvis, this is a somewhat arbitrary figure. Most of these mildly dilated systems are probably normal, but

Figure Simplified scheme for postnatal evaluation. MCU=micturating cystography.

within this group there will be some cases of vesicoureteric reflux and some potential pelviureteric junction obstructions. Until recently we have not had a uniform policy for the investigation of these mildly dilated systems. Micturating cystography has been undertaken in some children, but not in others. We are, however, in the process of setting up a prospective study to try to determine whether the frequency of vesicoureteric reflux in this group is sufficient to justify screening of all infants with mildly dilated systems by cystography.

(c) *Unequivocal dilatation*

The initial scan will not only confirm the presence of dilatation, but should also provide additional information on the likely aetiology—that is, thick walled bladder, urethral valves, ureterocele, etc. We have come round to the view that virtually every neonate with unequivocal dilatation of the urinary tract should undergo a micturating cystogram to show possible bladder outflow obstruction or vesicoureteric reflux.

Functional imaging—for example, intravenous urography, isotope renography—is generally unhelpful and may even be misleading in the period of 'transitional nephrology' in the first month of life. Furthermore these investigations are unlikely to contribute to practical management at this early stage. Unilateral uropathies (which constituted two thirds of our cases) do not constitute a threat in the neonatal period, and functional imaging can reasonably be deferred. Bilateral uropathies are usually the consequence of bladder outflow obstruction, reflux or bilateral pelviureteric junction obstruction. Initial treatment of urethral valves can be undertaken on the basis of the findings on the micturating cystography. Similarly the treatment of reflux (antibiotic prophylaxis) can be instituted without functional imaging of the upper urinary tract. Bilateral pelviureteric junction obstruction may, however, call for an early ^{99m}Tc diethylene triamine penta-acetic (DTPA) scan to plan management and to determine the possible need for percutaneous nephrostomy.

PRACTICAL CONSIDERATIONS

The first practical difficulty may be in identifying affected but asymptomatic neonates on the post-natal wards. We have certainly had experience of infants with significant uropathy who have been examined and discharged by an unsuspecting paediatric senior house officer. It is important that the presence of a prenatally diagnosed uropathy is indicated clearly on the maternal case notes—for example, by use of a sticker on the folder.

The management of prenatally diagnosed uro-

pathies can be effectively undertaken on a shared basis between a consultant paediatrician in a district hospital and a paediatric urologist or paediatric surgeon based in the relevant regional centre. It is likely that the specialist surgeon will already be working in conjunction with a regional paediatric nephrologist and a paediatric radiologist with a particular interest in these problems. Communication is important to avoid unnecessary duplication of investigations.

The aims of postnatal management can be summarised as the preservation of renal function and the prevention of infection. It is becoming clear that obstruction in the absence of infection gives rise to gradual rather than rapid deterioration of renal function in this age group. The tendency of some surgeons to proceed to pyeloplasty in the first few days of life has very little justification. The use of antibiotic prophylaxis in infants with prenatally diagnosed uropathies has not been subjected to a controlled trial. Nevertheless the use of antibiotic prophylaxis in reflux seems a logical extension of experimental and clinical work on reflux nephropathy in older children. The importance of prophylaxis in cases of obstructive uropathy is less clear. Before the advent of prenatal diagnosis urinary infection was the most common form of presentation of pelviureteric junction obstruction in infants under 1 year of age.⁵ For this reason we routinely prescribe trimethoprim prophylaxis in this group, at least for the first year of life.

Aspects of surgical management

Indications for surgical intervention that have been derived from experience with symptomatic abnormalities may not be relevant to the management of asymptomatic conditions such as multicystic kidney, mild pelviureteric junction obstruction or reflux diagnosed on prenatal ultrasound scanning. It is important that the management of prenatally diagnosed uropathies evolves on the basis of analysis of results and appropriately controlled studies.

POSTERIOR URETHRAL VALVES

Male infants with urethral valves represent about 10% of the total live born infants with significant prenatally diagnosed uropathies. Posterior urethral valves, however, account for one third of the cases of bilateral uropathy in surviving infants. At present, posterior urethral valves appear to be about the only condition for which fetal surgery (vesicoamniotic shunting) might be of benefit. It is possible, however, that the renal dysplasia seen in this condition may be irreversible by the time it is first detected on ultrasound, and thus not amenable to

decompression in utero. A further problem lies in the difficulty in distinguishing urethral valves from other causes of bilateral fetal uropathy such as the prune belly syndrome and primary vesicoureteric reflux. It is possible that the main benefit of prenatal diagnosis in this condition may be in preventing severe urinary infection (often accompanied by septicaemia), which used to be a common presentation in the past.

It seems likely that prenatal diagnosis of posterior urethral valves will improve the prognosis for these boys. Some form of controlled trial of fetal surgery (or early delivery) compared with conventional delivery and prompt ex utero surgery is desirable. Follow up into the teens will be essential if any reliable conclusions are to be drawn from such studies.

At present we do not favour fetal surgery nor premature delivery. Management consists of prompt investigation after delivery and early endoscopic surgery to ablate the valve tissue.

PELVIURETERIC JUNCTION OBSTRUCTION

Obstruction of the pelviureteric junction is the single most frequently diagnosed form of fetal uropathy. The initial surgical response (particularly in the United States) was to proceed to pyeloplasty in the neonatal period. It is becoming clear, however, that some of these pelviureteric obstructions resolve spontaneously in infancy. (Whether they will recur in later life is, of course, unresolved.) Furthermore this form of obstruction appears to be relatively benign and only gradually progressive. Even in the days before prenatal diagnosis, it was unusual to have to remove one of these kidneys because of non-function. It is possible that neonatal pyeloplasty may result in the preservation of a small percentage of the glomerular filtration rate that would otherwise be lost. This theoretical benefit must be offset against the likelihood that some kidneys will be lost or badly damaged by anastomotic obstruction and other complications of this technically difficult surgery.

In general our management of 37 infants (47 obstructed kidneys) has been based on the criteria suggested by Ransley and Manzoni.⁶ On the basis of their experience these authors suggested that kidneys that show good preservation of function (greater than 40% of the differential function on an isotope scan) can be managed conservatively even if there is evidence of active obstruction. Conservative management takes the form of antibiotic prophylaxis, serial ultrasound imaging, and further dynamic isotope imaging at 6 to 12 months of age. Evidence of impaired function (less than 40% of differential function) is an indication for early pyeloplasty. In

those cases where the kidney is functioning very poorly (less than 20% function) it may be helpful to insert a percutaneous nephrostomy and to reassess function with an isotope scan before deciding between pyeloplasty or nephrectomy.

This conservative approach to the management of prenatally diagnosed pelviureteric obstruction may prove to be misguided. At worst, however, it will lead to the deferment of surgery, in the knowledge that function is most unlikely to deteriorate rapidly. At best it will save some children from undergoing an unnecessary major operation.

MULTICYSTIC KIDNEY

Multicystic dysplastic kidney is a more common anomaly than was previously recognised. In the days before prenatal diagnosis most of these abnormal kidneys almost certainly went unrecognised. A recent analysis of about 47 000 live births yielded an incidence of this condition of around 1/4500 live births.⁷ It was common practice to remove those multicystic kidneys that presented clinically because of the possible risks of hypertension and malignant change. In fact these risks appear to be very slight—particularly in relation to the true incidence of the condition. We recently undertook a literature search covering a 20 year period. This identified only three documented cases of hypertension and six cases of malignancy. The risk of complications, therefore, seems to be extremely small and for this reason we have abandoned 'prophylactic' nephrectomy. Follow up imaging with ultrasound shows that the multicystic kidneys regress, in fact we have had two that have disappeared completely. It is likely that regression of a multicystic kidney accounts for a substantial proportion of those cases of apparent unilateral renal agenesis.

The main importance of multicystic kidney is as an indicator of coexistent urological abnormalities. These should be sought by appropriate investigations.

VESICoureTERIC REFLUX

Prenatal diagnosis offers an exciting opportunity to study the natural history of vesicoureteric reflux and of reflux nephropathy. Several interesting features are already emerging. Reflux is generally viewed as a disorder of females. In our series of 22 cases of prenatally diagnosed reflux, however, only three were girls. This suggests that asymptomatic reflux is more common in boys than is generally recognised. It is widely believed that reflux nephropathy results from the combination of reflux (particularly intrarenal reflux) and urinary infection occurring in infancy. If this view is correct, then the prenatal diagnosis of reflux should result in a reduction of

scarring and its associated morbidity by ensuring that affected children are started on antibiotic prophylaxis from the first day of life. Our limited results so far suggest that this may indeed be the case. The interpretation of these results, however, is complicated by the high proportion of boys—many of whom might have escaped infection and scarring even if they had not been managed by antibiotic prophylaxis.

Reimplantation surgery is best avoided in the infant. Not only is it technically difficult and less successful, but in the context of prenatally diagnosed reflux, it is usually unnecessary.

Prenatal urological diagnosis will inevitably lead to increasing surgical specialisation. There can be very little justification for anyone other than a suitably trained paediatric urologist or surgeon operating upon the urinary tract of a small infant. This contrasts with the 'medical' aspects of management (checking for urinary infection, blood pressure measurements, biochemical investigations, and general follow up) that are best undertaken in paediatric departments in district hospitals.

Communication and cooperation will prove essential if we are to utilise prenatal diagnosis for the maximum benefit of the children under our care.

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Correspondence to Mr DFM Thomas, Department of Paediatric Surgery, St James's University Hospital, Beckett Street, Leeds LS9 7TF.