Posterior Urethral Valves
An Essay in Honour and Memory of Herbert Eckstein

Philip G. RANSLEY

The understanding, recognition and relief of obstructive uropathy has been a central theme of urology for centuries. Although it is more than 75 years since Young produced his classical (although inaccurate) description of posterior urethral valves, it is the last ten years which have witnessed intense discussion to refine the treatment and fetal ultrasound has provided a whole new perspective for this important condition.

Herbert Eckstein would have revelled in this most recent revolution. I had the opportunity to work with him over the last ten years of his surgical contribution and feel that he would not have been surprised by the revelations of antenatal diagnosis. Through his experiences in Turkey and subsequently in England, he had a great understanding of the natural history of disease and the limitations of surgical intervention. He did not suffer, nor practice, unrealistic ambition and his intelligent fatalism based on experience was often misunderstood by colleagues, including the writer. He was always open and receptive to new ideas and all this trainees benefitted by being allowed to flourish through his unprejudiced discussion.

He would not have been surprised to learn what we know now that the populaton of posterior urethral valves, which has traditionally formed part of paediatric urological practice, is perhaps only the tip of the iceberg in terms of severity and, although a major one, only a fraction of the true valve population. It is impossible to know at the present time the absolute numbers of posterior urethral valves created by conception. There are several patterns of lower urinary tract obstruction in utero which may or may not be due to the abnormality we call "valves". It is truly an inappropriate name but attempts to rename the problem have not been attractive so far. Perhaps a millennium competition should be launched to seek an alternative succinct description.

Once urine production begins at about the tenth week of intrauterine life, it has to go somewhere and by the twelfth week there is clearly a bladder containing urine, although the bladder outflow may not yet be ready for emptying. It would be naive to think in any way of the urinary tract at this stage as a miniature version of the mature system. Who knows the resorptive functions of the primitive epithelium or the muscular activity of the bladder with its simple nervous connection? This is an important time for kidney development and nephrogenesis may be critically influenced by lower tract dysfunction at an early stage - a finding well documented in experimental studies. There is a group of developing fetuses which clearly shows obstructive uropathy from the very beginning. The bladder is enlarged with bilateral hydronephrosis and the dilatation progresses inxorably until the bladder fills the abdomen, probably containing every drop of fetal urine ever produced and the pregnancy ends in spontaneous abortion or elective termination. Many of these will be described as "urethral atresia" (HBE would immediately state "whatever that might be") but some have valve morphology.

The size of the fetus, difficulties of retrieval and examination make it difficult to know the precise anatomical nature of the obstructing lesion and what proportion of the valve population fall into this category. It is a problem which is at present only of importance to essay writers and we are not in a position to seriously contemplate rescuing these very early disasters.

However, the spectrum blends imperceptibly with the next group of relatively early valve presenters with enlarged bladders, hydronephrosis and oli-

gohydramnios at 18-20 weeks of gestation. Some survive end some do not but it is from this scenario that we undoubtedly inherit the poor end of the posterior urethral valve spectrum which creates so many headaches for urological management at birth, makes enormous demands on nephrological services and often proceeds to transplantation in infancy. These various and cumulative factors must be taken into consideration as part of the fetal/maternal risk assessment.

This is clearly not happening in most fetal medicine units around the world who have, by and large, backed way from intrauterine intervention. I know that his experience of the postnatal course of many valve patients would have weighed heavily on HBE's mind and he would have promoted a more aggresive intrauterine approach. I would have agreed with him and it is my stance in 1996 that the question of intrauterine intervention for valves has not been properly addressed.

The problem is more than a decade old since early fetal urine sampling demonstrated a crude relationship between fetal urine composition and (renal) outcome but it has to be said that there are no studies with adequate and accurate renal function assessment on even medium term postnatal follow up. Fetal urine sodium and $\beta 2$ microglobulin levels are accepted as reflecting outcome in general terms but there are so many exceptions and so many unknown variables relating to the sample itself - for example the length of time the fetal urine has been in the bladder - that we are still a long way from producing an accurate prognosis based on these criteria. As both fetal urine sampling and vesico-amniotic shunting carry an obstetric morbidity, there was a natural reluctance to interfere when the signs seemed good. As a consequence, the fetus wth a urine sodium in the normal range and normal or mildly reduced amniotic fluid was left alone while, the picture of oligo- or anhydramnios with a high sodium level was considered for shunting.

The results were poor and it appeared that few benefitted from such intervention in that they were still in chronic renal failure at birth. These results combined with the difficulty in maintaining the shunt in position, fetal urinary ascites and fetal loss, led to a sharp reduction in the number of shunts being performed in the late '80s and early '90s. No clear benefit to fetal lung development could be established either and the march of progress slowed to a crawl.

The point is sharply in focus for the writer, as this essay unfolds, as in hospital at this moment is a child whose valve uropathy was clearly defined at 20 weeks with oligohydramnios and a big bladder. A "normal" urine sodium and the return of some amniotic fluid proved to be misleading signs. The morphology of the bladder was even called in to support the non-interventional approach as it supposedly changed from being "big and tense" to "big and floppy". This stable state was observed to persist through to 38 weeks. At one month of life and with a well drained urinary tract, the baby has stabilized with a plasma creatinine of nearly 400 µmol/l and is undoubtedly heading for transplantation, as soon as it passes 10 kg in weight, with all the attendant risks.

Fetal urology has failed to help this baby. Could we have done better? Who knows? The urethra was obstructed with a thick spiral ("valve") membrane with a pinhole opening. Whatever changes occurred in utero from 20-22 weeks as the bladder altered its appearance cannot be ascribed to a lesser obstruction given the postnatal findings. The urine suggested some salvageable renal function and it is probable that this baby would have been better off shunted.

The argument that the outcome would not have been different because nephrogenesis is largely over by 20 weeks is theoretical. We do not know how nephrogenesis proceeds in the face of an obstructive lesion or how established nephrons are eroded by continued impairment to urine flow. Surely the next step must be to apply vesico-amniotic shunt diversion to the "good" valve fetus as well as the bad and assess the outcome at one, five and 10 years of life. There are covert calls for a trial of vesico-amniotic shunting but very often - in the same breath - there is the recognition that this would be unworkable.

A trial would be very difficult not only logistically but also to ensure that like was compared with like. The precise timing, severity and duration of obstruction might have a huge dampening affect on any variation created by intervention. If the scientific purity of a trial is beyond us at the moment then a more liberal application of shunting to "good" obstructed fetal urinary tracts (dare I say all) must provide more information and better guidelines for the next generation. Such a policy would undoubtedly shunt some bladders unnecessarily as not

all big systems have valve pathology but, with a few precautions, those inappropriately shunted should be few. Vesicoureteric reflux and the probably genetically abnormal megacystis/megaureter system may mimic valve pictures at about the 20 week mark, or later, and valve rupture undoubtedly occurs spontaneously in some cases to produce a transient period of obstruction only. If the big bladder were subject to intense observation, perhaps on a daily basis over a two week period before shunting, then these different pathologies might be recognised for what they were and unnecessary shunting avoided.

So far we have argued over the small proportion of the valve population that would never have troubled Herbert Eckstein at the time of his professional career. It is the most interesting area of valve debate at the present time, if not the most important (the pathology and management of the valve bladder must still rank as No. 1 but who knows whether this would be altered for the better or the worse by fetal urinary diversion?). The great majority of the valve patients have lesser problems in utero and indeed more than half of them are not detected by ultrasound before 24 weeks of gestation. Why this should be remains a mystery.

The simple prejudice that this was due to undiscerning ultrasonographers at the earlier scan has been proven not to be case so many times that it cannot be the fundamental explanation. Why, therefore, does the urinary tract not distend until relatively late in gestation in the presence of an obstructed bladder outflow? Our old friend the urachus would provide an elegant solution were it correct but, as the twentieth century draws to a close, we actually know little about the urachus in human development. There seems to me little evidence that the urachus ever functions for, if it does, there must be a very efficient active closure mechanism to allow valve pathology to progress in the last trimester.

The writer's personal experience of the few patent urachuses observed in the prune belly syndrome suggests that some of these may actually be infraumbilical bladder ruptures rather than the persistence of the embryological urachus. Whatever the explanation, the consequence is self evident that most valves will present to paediatric urological units without a prenatal warning flag until a late gestation ultrasound becomes routine obstetric practice.

It is difficult for a practitioner in central London in 1996 to imagine the sort of valve pathology that HBE would have seen in Turkey 35 years ago. The moribund septicaemic baby with valves was a classical presentation through the '60s until paediatricians became more familiar with the diagnosis and the mortality was high. Indeed the truism of the time was that the earlier the presentation the worse the prognosis and later presenting valves did well -undoubtedly reflecting the severity of the obstruction and the consequent renal pathology. Drainage was of paramount importance and ureterostomies were an essential part of the armamentarium when endoscopic instruments were less well developed and antibiotics less sophisticated. Undoubtedly effective, they did create some major problems for reconstruction, probably not inherently but because there was a determination to reimplant the ureters as well. The combinaton of ureterostomy formation and closure together with reimplantation into the defunctioned valve bladder makes the modern urologist squirm with discomfort but it was the perceived wisdom of the day.

The persistence or return of upper tract dilatation after ureterostomy closure was seen as an obstructive dysfunction of the ureterovesical junction not the bladder as a whole. Our understanding of the non-compliant nature of the valve bladder wall and the recognition that upper tract dilatation is an inevitable long term consequence has reduced the amount of iatrogenic morbidity in the valve urinay tract but the proposition requires re-emphasis for each new generation.

The security which allows conservative management of such systems requires an intimate understanding of urinary tract function and a finely balanced judgement of clinical progress and laboratory urodynamics. Pressure measurements have shown the enormous values present in the obstructed newborn system with voiding detrusor pressures often in excess of 300 cm of water. Two points are of particular interest - one being that the detrusor muscle was still active in all cases examined (admittedly a small number) and the other that pressures did not fall dramatically following valve resection. It could be that the lack of forceful urine passage down the urethra during development led to relative urethral hypoplasia which takes some time to catch up. (Indeed the normal neonatal urethra may be relatively small and normal neonatal voiding pressures surpris-

ingly high.) If the detrusor is still good at birth then we need to learn how best to preserve it in order to prevent the late onset of detrusor failure which remains part of the late valve bladder dysfunction spectrum.

Undoubtedly the exciting contemporary studies of fetal and postnatal valve bladder composition and development will lead to better understanding of the mechanics involved, if not the way to control them. If it is confirmed that the overwhelming problem of non-compliance is due to an excess of collagen type III instead of collagen type I in the fetal bladder then the ability to control development at the molecular level may ultimately reduce the surgery required. For the moment we have to struggle with the awful bladder. Vesicostomy has become the popular method of decompressing the disastrous urinary tract at birth, patricularly when renal function is severely compromised and it works well in the short term but it is not a long term solution.

Like prenatal vesico-amniotic shunting, it defunctions the bladder and it is therefore not an exceptional scenario to see children at the age of three years in chronic renal failure whose bladders have not stored urine since 20 weeks of gestation. How this affects the development, innervation and function of the bladder wall will become clearer in the years ahead but let it be known that such bladders can work when called upon to do so at the geriatric age of 3-5 years. The transition from conduit to storage tank is not easy and a Mitrofanoff channel may be essential to establish complete emptying and to provide night time drainage.

Night time is bad news for the valve urinary tract. First of all, the dilated upper tracts do not drain well in the horizontal position. Lacking effective peristalsis, they are dependent upon gravity and vis-à-tergo (glomerular filtration) to transport urine to the bladder. At night the all important gravity element is removed leaving glomerular filtration to do the work - perhaps the most subtle of all obstructive uropathies. Add to this a bladder filled to the limit of safe compliance by midnight and the rest of the night is potentially detrimental.

Long ago it was shown that, from a given referral base, approximately 50 % of children with valves went into chronic renal failure and that the most reliable clinical predictor of this was being wet by day at the age of five years. At first this seemed a somewhat anachronistic finding since if some form of sphincter damage were a cause of the incontinence then the wetting would at least be protective of the urinary tract, if inconvenient. However what it really reflected was the combination of bladder compliance/capacity and urine output. There is a clear inverse relationship between GFR and 24 hour urine volumes in the valve population representing a fine illustration of high output renal failure. Those wet patients had not had accurate GFRs and plasma creatinines alone had not proved to be a sensitive enough index of their true renal failure.

The urine volumes swamped the system and highlighted the problems by creating day time wetting. Even so, it was probably the night times that were more destructive. Three litres of urine a day in a five year old would equate to a very low GFR and herald end stage status in a few years. Asking the urinary tract to handle 1,500 ml over night in the horizontal position with dilated ureters and a poorly compliant bladder is a tough demand and may accelerate the decline in renal function. Mitrofanoff drainage over night may lessen this problem but should be seen as part of a wider debate on lower urinary tract reconstruction for the long term. Here is the central issue of debate. Prenatal management should probably be more aggressive; postnatal management more conservative but long term supervision and intervention is still an art form and not a science.

For many years bladder augmentation was synonymous with the need for intermittent catheterization since experience was largely gained in the management of neuropathic and exstrophy bladders. There was a reluctance to approach the valve bladder in the same way in the presence of a urethra with normal sensation. The Mitrofanoff principal neatly circumvented this argument but the truth is that the great majority of valve boys can void after a simple clam cystoplasty, at least sufficiently well to live through the day and Mitrofanoff catheterization can be used morning and evening to ensure complete emptying at least twice a day.

This being the case it is relatively easy to address the problem of the wet valve five year old but the real question is whether this short term solution by augmentation is justified in the longer view. Firstly, this high output state is self limiting and will hopefully disappear with (subsequent) transplantation. If the urinary tract is good enough to cope with a nor-

mal urine output then perhaps it should not be interfered with for the short time problem associated with the big urine volumes of chronic renal failure. It is also proposed, although with little documented support, that the bladder improves with age in the teenage period or after transplantation which are so often coincident. Does the quality of urine stored affect the function of the urinary tract or does the bladder finally recover from its prenatal insult? We know little of the importance of good quality urine for normal urinary tract development and maybe there is a growth factor there which can effect the molecular switch for which we are searching.

At the moment we must juggle these arguments in each individual case but the modern urologist must think dynamically in the fourth dimension of time - time in terms of urinary tract function in the 24 hours and time in terms of years and the events which lie ahead. If we can identify the major sources of embarrassment to the urinary tract then measures such as augmentation or nocturnal urine drainage may have an important role in improving quality of life and postponing the ultimate decline in kidney function.

Herbert Eckstein would have loved to have been part of these arguments and to have explored the way forward. We miss his intellectual input. The irony is that after all the surgical adventures in valve management over the last half century the outcome may not be so very different from his experiences in Turkey all those years ago. As we become more conservative by experience and choice he must have been forced to be conservative by circumstance. We have yet to prove that we have achieved more and we salute his contributions over many years.

Philip G. Ransley, FRCS
President,
European Society of Paediatric Urology