An important question that has not yet been addressed is whether the presence of organ damage caused by sickle cell disease will prejudice the outcome of the transplant procedure itself. This may be particularly important for the neurological manifestations. Another issue unresolved by the present BMT studies and the literature relating to regular blood transfusion regimens and suppression of HbS production is whether progression of end organ damage will be halted or, even, whether there can be improvement or resolution of organ damage with time.

One of the most catastrophic events for children with sickle cell disease is stroke, which occurs in approximately 7% of children.¹³ All physicians in developed countries treat these children with hypertransfusion regimens with the associated low risk recurrence. Unfortunately, even after five to 12 years of transfusion treatment, there is a high risk of recurrence of stroke if the blood transfusions are stopped.¹⁴ These children are, therefore, faced with a life very similar to that of a child with β thalassaemia major – that is, possible lifelong transfusions with all the associated problems of iron overload. Life is even more complicated for children with sickle cell disease on hypertransfusion regimens as they have to be subjected to intermittent partial exchange transfusions in order to maintain a low percentage of haemoglobin S. If BMT is ethically acceptable for β thalassaemia major then it must be considered for these children and others on hypertransfusion regimens.

The Paediatric Haematology Forum, a subcommittee of the British Society for Haematology which has British Paediatric Association representation, has now defined the recommended criteria for selection and exclusion for BMT in sickle cell disease as shown in the table. These criteria are to be used for a national controlled study with BMT performed in Birmingham and Manchester Children's

Hospitals and the Hammersmith Hospital. We intend to address the questions posed above by following up not only the children who have been transplanted but also those who qualify by the inclusion criteria for BMT but have no histocompatible sibling or refuse BMT.

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The value of urodynamic studies

The International Continence Society has defined urodynamics as the assessment of the function and dysfunction of the urinary tract by any appropriate method.¹ Such investigations may focus on the upper or lower urinary tract. Upper urinary tract urodynamic studies, which include measurement of the pressure and flow of urine from the renal pelvis to the ureter, may be of benefit in assessing difficult cases of possible pelviureteric junction obstruction. Confusion arises when the terms 'urodynamics' and 'urodynamic studies' are used to denote the specific measurement of the pressure/volume and flow relationships of the lower urinary tract. Such investigations are more correctly termed cystometric studies or cystometry and will be the main focus of this paper.

Non-invasive urodynamic studies

The initial assessment of any child with suspected lower urinary tract dysfunction must include a detailed history, emphasising voiding pattern, bowel habit, and neurological status. A diary (frequency volume chart), completed at home over a period of one week, recording the number of voids during the day and night and episodes of incontinence, is particularly useful. Examination of the

abdomen, genitalia, lumbosacral spine, and lower limbs is essential. The child is observed voiding and a urine flow rate obtained (uroflowmetry). The value of this study is dependent on the child voiding an adequate volume, usually greater than 100 ml, into the flow meter. An ultrasound scan before and after micturition to measure bladder capacity (voided volume plus residual volume) and assess the presence of diverticula, bladder wall thickness, and upper tract dilatation provides further additional information. The urine is examined for organisms and protein. This simple protocol can exclude major lower tract dysfunction without recourse to more invasive procedures.

Cystometry

Cystometry refers to the measurement of the intravesical pressure/volume relationships and requires both bladder and rectal catheterisation. The main aim of cystometry must be to reproduce as accurately as possible the child's pattern of micturition when he or she is awake, non-sedated, and cooperative.² In children the type of bladder access is of particular importance as the level of cooperation decreases in direct proportion to the discomfort of the study. For this reason the suprapubic route of bladder

catheterisation is favoured by many, particularly in boys with normal urethral sensation, although this invariably necessitates a general anaesthetic for catheter insertion. In children with decreased urethral sensation (for example the myelomeningocele) and in older girls, urethral catheterisation is performed. During cystometry the bladder is filled with fluid and the pressure is measured via specially designed double or triple lumen catheters. Intravesical pressure is also measured during micturition. The rectal catheter records abdominal pressure, which is subtracted from the measured bladder pressure to give the true detrusor (intravesical) pressure. Contrast material rather than saline may be instilled into the bladder, allowing radiological screening during filling and voiding, this investigation is termed videocystometrography (VCU).³ The VCU provides information on the behaviour of the bladder neck mechanism, the presence of vesicoureteric reflux, and the appearance of the bladder wall. Every precaution must be taken to maintain low levels of radiation during the VCU.

Commonly used cystometric terms include detrusor instability, which implies any involuntary rise in bladder pressure during filling, which may or may not be symptomatic. In practice a contraction of greater than 15 cm H₂O is regarded as significant.⁴ Compliance indicates the change in pressure for a change in volume within the bladder ($C = \Delta V / \Delta p$), and is expressed as ml/cm H₂O.¹ A compliant bladder is one that permits storage of adequate volumes of urine at low or safe pressures. Detrusor sphincter dyssynergia is the incoordinated contraction of the detrusor muscle and the external urinary sphincter during voiding.

In addition to standard fill and void cystometry, the electrical activity of the external urinary sphincter (electromyography; EMG) and the intraurethral pressure (urethral pressure profile; UPP) can be measured. EMG, performed with either needle or surface electrodes, facilitates the diagnosis of disorders of the external sphincter especially detrusor sphincter dyssynergia. The behaviour of the external sphincter may be deduced from the appearance of the bladder neck mechanism during the VCU, although simultaneous external sphincter EMG improves the diagnostic accuracy.⁵ The UPP is the measurement of the passive resistance of a particular point within the urethra to stress and is calculated by the controlled withdrawal of a specially designed catheter. Such studies may be of particular use in children who have undergone bladder neck reconstruction allowing assessment of outflow obstruction.

Indications for cystometry

Neurologically normal children with urinary incontinence account for a major portion of paediatric urological practice. Cystometric and VCU studies are not indicated in the vast majority of children with monosymptomatic nocturnal enuresis as almost all have normal bladder function.⁶⁻⁸

Children with persistent daytime urinary incontinence may be divided into two groups. Firstly, those in whom normal micturition takes place at a socially inappropriate time and place while awake, asleep, or both. There is no history of urinary tract infections and the upper tracts are non-dilated with complete bladder emptying after voiding. There is a slight male preponderance in this group⁹ and non-invasive urodynamic investigations are invariably normal. These children do not require cystometry.

The second group may be referred to as dysfunctional voiders, a condition that has been defined by Van Gool and associates as any form of wetting caused by non-neuropathic bladder sphincter dysfunction.¹⁰ A history of

urgency is not uncommon and staccato or interrupted voiding may be noted on uroflometry. Once these abnormal voiding patterns have formed incomplete bladder emptying and urinary tract infections may develop. In contrast to the first group, dysfunctional voiding occurs much more commonly in girls.⁹ In a small group of females who are persistently wet, and have never been dry, despite voiding normally, it is important to exclude an ectopic ureter.

Dysfunctional voiders who are noted to have upper tract dilatation and/or urinary tract infections need micturating cystourethrography (MCU) to exclude vesicoureteric reflux and urethral pathology. This is particularly important in the male who may have posterior urethral valves. However, controversy exists as to which children should proceed to cystometry. We believe that invasive urodynamic studies such as cystometry must not be considered as routine for every case. Allen has recommended that this be reserved for those who exhibit structural damage of the urinary tract or who prove refractory to treatment.¹¹

The treatment of dysfunctional voiding is multidisciplinary combining pharmacological and non-pharmacological measures. The latter may include the development of biofeedback programmes based on the cystometric findings and psychological counselling. Incontinent children with simple urgency, non-dilated upper tracts, complete bladder emptying, and no urinary tract infections do not require more invasive studies and can initially be treated by toilet training with or without anticholinergic medication.

Cystometry is indicated in the spinal dysraphism group of disorders such as myelomeningocele and sacral agenesis.¹² The nature of the vesicourethral dysfunction frequently does not correlate with either the level of the spinal/vertebral abnormality or the other neurological signs.¹³ There is now strong evidence to suggest that cystometry should be carried out early in the first year of life in all children with spinal abnormalities to allow a rational therapeutic regimen for lower urinary tract management.¹⁴ Early changes in bladder behaviour may be related to a tethered cord that may respond to surgical untethering. The pattern of bladder behaviour will determine the frequency with which the studies should be repeated.

Urodynamic parameters that may predispose to upper tract dilatation include high leak point pressures (40 cm H₂O),¹⁵ detrusor sphincter dyssynergia,¹⁶ poor bladder compliance, and high pressure vesicoureteric reflux. Cystometry in the older myelodysplastic child frequently determines the aetiology of their urinary incontinence. Preoperative and postoperative urodynamic studies are recommended in children undergoing spinal surgery such as for the tethered cord syndrome¹⁷ and for lipomyelomeningocele permitting the establishment of baseline values and assessing the effects of surgery.¹⁸ Urodynamic assessment and surveillance is mandatory in the management of the urinary tract in the patient with myelomeningocele and is vital in lower tract assessment before and after bladder reconstruction.

Cystometry is indicated in those children with major anatomical conditions that predispose to incontinence (see the table).¹⁹ As in the management of neurogenic bladder dysfunction such studies will determine bladder compliance, detect instability, and assess outflow resistance. Appropriate measures, whether conservative or surgical,

Major anatomical abnormalities that predispose to urinary incontinence

Classic bladder exstrophy	Cloacal abnormalities
Primary epispadias	Prune-belly syndrome
Genitourinary sinus	Imperforate anus

may then be taken both to achieve urinary continence and to preserve upper tract function. The common surgical procedures carried out include bladder neck reconstruction, bladder augmentation, and the placement of the artificial urinary sphincter. Perioperative urodynamic studies in children undergoing such procedures are standard practice in most major centres.

End stage renal disease in children requiring renal transplantation is associated with lower urinary tract obstruction in as many as 25%. Pretransplant urodynamics in these children will allow, if necessary, the construction of a urinary tract that will not prejudice renal function in the engrafted kidney.^{20 21} Cystometry is indicated in children with reflux where bladder dysfunction is suspected, especially if reimplantation surgery is contemplated, as a relationship may exist between severe vesicoureteric reflux and abnormal bladder activity.²²

Cystometry and videocystometry are invasive studies, the latter involving exposure to radiation. Recent advances include the availability of extended night time cystometry,²³ with so called physiological filling of the bladder with the patient's own urine.²⁴ More recently ambulatory urodynamics involving a Holter type principle has permitted the recording of bladder pressure over many hours while the child goes about his or her normal activities.²⁵ These studies provide a more sensitive index of lower urinary tract function than conventional cystometry and are of particular use in infants and younger children (such as those under the age of 5 years) who are often unable to cooperate with the more traditional techniques.

Urodynamic studies in general, and cystometric investigations in particular, are fundamental to the initial and on-going management of many children with urological abnormalities, particularly those with neuropathic bladder dysfunction. The value of these studies in children depends on careful patient selection together with sympathetic management of the child during the study.

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Dietary management in nephrotic syndrome

Nephrotic syndrome is characterised by heavy proteinuria, hypoalbuminaemia, and oedema with hyperlipidaemia.¹ The majority of children with nephrotic syndrome have a steroid sensitive condition that is associated with minimal histological changes in the glomeruli (MCNS). The initial management involves the control of oedema and prevention of infection while awaiting the response to corticosteroids.

If the child does respond to prednisolone with infrequent relapses, then there are likely to be a few long term dietary problems.² However, children who frequently relapse and are steroid dependent may require long term dietary advice to monitor and maintain nutritional status and prevent obesity. Growth and endocrine function are important issues in the long term management of such patients.³

Initial advice

Growth parameters should always be recorded and dry weight estimated, as surface area is used to calculate the prednisolone dosage. A dietitian should be involved in the initial management both to review the dietary history as well as advising on the practicalities of the moderate fluid restriction that is often required in the initial oedematous phase while awaiting the response to steroids.

The basic advice is a 'healthy eating' diet for all the family. It should provide adequate energy based on the estimated average requirement for children of the same chronological age.⁴ A protein intake of 1-2 g/kg body weight/day should be adequate for most children.

In the past diets containing increased intakes of protein (3-4 g/kg/body weight/day) were prescribed in the belief