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The Consequences of Enterocystoplasty

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Introduction

The use of bowel in the urinary tract has become an important means of reconstruction in the ureter, bladder and rarely, the urethra. This chapter concentrates on bladder reconstruction. It is important to be clear about terminology; augmentation cystoplasty is expansion of the existing bladder capacity using a segment of bowel whilst substitution cystoplasty is the loss or removal of the bladder with the creation of a complete reservoir-using bowel.

The history of enterocystoplasty is well documented–suffice to say that it was popularized in the 1980's following Bramble's paper suggesting success in a group of 15 patients with enuresis and urge incontinence.[1] Prior to this there had been limited use in patients with small shrunken bladders since the 1950's with chronic inflammatory conditions–including tuberculosis.[2] Alternative techniques for urinary diversion have been used including ileal conduit, cutaneous ureterostomy (still used in paediatric practice) and a ureterosigmoidostomy or latterly a Mainz II diversion where a rectosigmoid pouch is created in continuity with the bowel, the ureters are anastomosed to the pouch thus the faecal and urinary streams are combined and passed out through the anal canal. An awareness of these alternatives may have both practical and intellectual application but the concentration of this chapter is on the expansion or creation of a bladder or reservoir using bowel segments.

Surgical and Bowel Consequences

Whether augmentation or substitution cystoplasty is used surgical complications are similar. The most catastrophic early complication would be that of anastomotic leak cited as 1%-5% in Farnham's review relating to urinary diversion.[3] Other complications include small bowel obstruction requiring laparotomy 3%-5.7%, significant wound infection in 5%-6.4% and up to 3% reoperation rate for bleeding[4] when this occurs it is often from the harvested bowel mesentery. Fistulae also occur–early series have described a rate of nearly 30%[5] Greenwell's review suggests a lower rate in more recent series and their own institutional rate of 0.4%[4] re-operation for any reason will increase this rate.

The use and method of ureteric reimplantation remains a controversial topic. An augmentation cystoplasty is unlikely to require ureteric re-implantation unless there is a pre-existing ureteric abnormality. Substitution cystoplasty in which the trigone is removed must include a ureteric anastomosis. There are many methods to achieve this but a simple breakdown to refluxing and non-refluxing will highlight the major concerns. A non-refluxing anastomosis is said to be important in a heterotopic cystoplasty (where there is no anastomosis to the urethra) as there is no 'pop-off' valve other than the upper tracts if the bladder pressure rises. In those who have an anastomosis to a normal urethra a refluxing anastomosis may be used. The benefit of a refluxing anastomosis may be a reduced rate of ureteric stricture.[4]

Bowel disturbance is also reported with cystoplasty-the precise mechanism is unclear in those patients that are theoretically left with an adequate functional length of bowel. This may relate to factors including bile salt handling, altered water absorption or a change in bowel commensals.[6]

The most significant and potentially disastrous long-term consequence is that of spontaneous perforation with any form of cystoplasty. This is a rare complication with an incidence estimated at 1.5%[7]–the rate increases in neuropaths–with a mortality reported of up to 25%[8] and appears to happen most commonly at the site of the junction between the bowel and native bladder, where this exists. Greenwell's review identifies predispositions alongside neuropathy including a competent bladder outlet, self catheterization and recurrent urinary tract infections.[4] During overdistension, local ischaemia[9] or microvascular occlusion are postulated to occur and probably create an area of weakness that gives way with a transient rise in pressure resulting in extravasation of urine.[10] It is not safe to regard this as sterile urine or to treat such a perforation conservatively. Diagnostic imaging is generally unhelpful with a false negative rate of up to 60%[4] thus if the diagnosis is suspected–and a high index of suspicion is the key–surgical intervention is the only safe course of action. At the time of surgery it is often impossible to safely close a perforation–it may also be very difficult to safely identify the precise location of a hole as there are often dense adhesions and very friable bowel associated with urinary peritonitis thus a risk of attempted closure is to make the defect bigger. The procedure involves insertion of large (18 Ch)

catheters into the reservoir and widespread abdominal drainage. The expectation is that the drainage prevents the accumulation of infected urine in the abdominal cavity whilst the catheters allow the bladder to heal and close. This is an unnerving scenario–patients need to be counseled about this risk as part of their preoperative preparation for cystoplasty so that they understand the importance of early presentation. Ideally, emergency laparotomy would be performed by a surgeon familiar with cystoplasty–however this is a potentially life-threatening situation and treatment should not be delayed if immediate transfer is not available.

Metabolic Consequences

The metabolic outcome of cystoplasty will vary with the segment of bowel used–see Table 1.

TABLE 1. The Relationship Between Bowel Segment and Metabolic Anomaly

Bowel Segment	Systemic Metabolic Abnormality	Significance
Stomach	Hypochloraemic, metabolic alkalosis	Rarely significant if renal function normal
Jejunum	Hyponatraemic, hyperchloraemic, hyperkalaemic, metabolic acidosis	Common, may be serious-vomiting, lethargy dehydration. 'Jejunal conduit syndrome'
Ileum/ Colon	Hyperchloraemic metabolic acidosis	May relate to length of bowel used and/or renal function

The most widely available and, in the majority, of circumstances the most versatile and easy to harvest is ileum. Many patients will develop an acidosis as a result of having bowel in contact with urine. The metabolic basis for the acidosis is a net loss of bicarbonate with chloride retention (to maintain electroneutrality) and the absorption of ammonium (NH_4^+)–creating a hyperchloraemic metabolic acidosis (Fig. 1). Jejunum is not used in clinical practice as the resulting 'jejunal conduit sydrome' may be fatal. With stomach the hypochloraemic metabolic alkalosis is only usually significant if combined with impaired renal function–stomach is rarely used as it is also associated with dysuria that may be very unpleasant for patients.

Aside from the bowel segment used, renal function and the ability of the kidneys to excrete acid may be a factor. In his experiments using dogs Kristjansson showed that a GFR above 55 ml/min/1.73 m^2 is sufficient to deal with this. A further important finding of his study suggests that there is little difference in renal deterioration with either a refluxing or non-refluxing anastomosis.[11] Other authors have suggested that is the length of bowel rather than its type that affects the acid base balance in patients.[12]

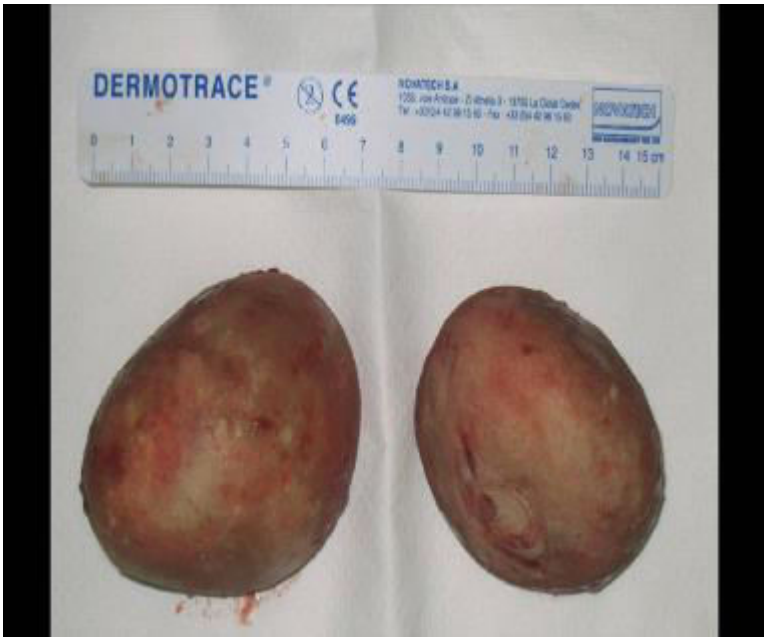

Fig. 1. Bladder stones removed from a patient who had undergone enterocystoplasty as a child

The increased ammonia load presented to the body by this exchange appears to be controlled and dealt with by an adaptive hepatic metabolism. The ammonia passes into the portal circulation and in normal individuals with no disturbance to liver function this increased solute load is dealt with. It is incorporated into the ornithine cycle and converted to urea. This is supported by the fact that in these patients the urinary levels of ammonia remain high but plasma levels to not appear to rise.[13] Hyperammonaemic states may present–these are rare but are most often seen in ureterosigmoidostomy[14] but have also been reported in patients with ileal conduit diversion. These may be due to an alteration in liver function and in caring for these patients the most important steps are to optimize urinary drainage–minimising contact time with bowel and reduce dietary protein load–patients are given neomycin to decrease ammonia load from the GI tract, systemic antibiotics should be given to treat urease positive bacteria and a hepatologist should be consulted to ensure there is no hepatic anomaly.[15]

There is little value in following patients' ammonia levels unless there is a clinical indication to do so as it is a cumbersome process with no clinical benefit. Biochemical follow-up including bicarbonate, chloride, creatinine and urea levels on an annual basis is our practice. As many of our patients come from a wide area and it is often difficult to be precise about which bowel segments may have been used we will routinely check vitamin B_{12} as the consequences of abnormally low levels are so significant and will result in irreversible neurological damage if not corrected. Some authors have suggested that as levels are found to reduce within 4 years it may simply be cheaper and just as effective to simply give empirical vitamin B_{12} replacement to all cystoplasty patients rather than routinely measure levels.[16]

Infections and Bacteriuria

The presence of bacteria in urine taken from an augmented bladder is so common and well documented it should be regarded as a normal finding unless it is found in the presence of persistent symptoms consistent with a urinary tract infection. Urinary tract infections are a consequence of cystoplasty in up to 43 % a wide variation in rates has been reported.[4] Many symptoms are attributed by patients and 'non-urologists' to infection such as mucus, smelly urine, malaise and increased back pain. The use of antibiotics on the basis of symptoms alone or a urine dipstick test is not sufficient to make a diagnosis in these patients. The correlation of symptoms with a urine culture allows precise diagnosis and targeted treatment.

Stone Formation in Enterocystoplasty

Formation of stones in patients who have had enterocystoplasty is common and the incidence rises with the length of follow-up–see Fig. 1. Up to 53% of all patients will suffer and may present with symptoms such as an increase in urinary tract infections, voiding symptoms, pain or difficulty in catheterization. Many are also found as part of routine follow-up–either by imaging or screening endoscopy (the role of which will be discussed subsequently). The principle physical risk factor is the need for abdominal catheterisation and non-dependant drainage.[17,18,19] Hensle identified that the incidence could be significantly reduced incomparable groups by the use of a fastidious regime of bladder washouts. Their group published a reduction in stone incidence from 43% to 7%. This forms an important message in patient education. (Fig. 1 Near here)

Hamid *et al* identified metabolic factors which may create a predisposition to form stones when the group compared those who formed stones to those who did not. Significant differences, between the two groups were found in urinary citrate, calcium and 24-hour urine volume with a calculated significant increase in stone forming risk for calcium oxalate and calcium phosphate stones in stone formers. Hyperoxaluria is found in many of these patients–they postulate that this may be due to altered absorption secondary to small bowel resection or the change in gut flora and eradication of Oxalobacter formigenes as a side effect of antibiotic treatment for urinary tract infections. This bacteria is known to metabolise oxalate in the colon and its absence destroys this ability leading to increased plasma absorption and hence passage into the urine. This may, in part, explain the increased risk for calcium oxalate stones with high urinary pH and hypocitraturia contributing to the risk of calcium citrate stones.[20] Urinary tract infections have themselves been identified as an independant risk factor for the development of stones.[21]

In treating reservoir stones it is important to consider access to the bladder. Although much rarer, stones do occur in patients who drain via a native urethra clearly these are amenable to established, endoscopic means of stone fragmentation and removal. However, any residual fragments must be seen as a considerable risk for the formation of new stones and hence in the case of large stones open removal should be considered. The need for complete removal of all fragments prevents treatment down a mitrofanoff channel from being a practical option. In patients who rely on abdominal drainage a percutaneous approach can be useful for stones that can be 'picked' out through a nephroscope without fragmentation. Larger stones (> 1cm) may still be treatable percutaneously if the correct equipment for suction of fragments is available, if not or if the stone is much larger (>2cm) open removal is likely to be necessary.

Consequences in Pregnancy

The diagnosis of pregnancy in the presence of an enterocystoplasty requires a mention. In patients using over the counter urinary pregnancy tests a 57% false positive rate was found in patients with enterocystoplasty–this probably relates to an unidentified factor in the mucus as urinary hCG was not raised in any of these patients.[22] It does not take a great deal of imagination to think of scenarios where such a result could cause considerable upset–the take home message is that in these patients pregnancy must be confirm using a serum hCG test.

As a unit we have recently examined data relating to female exstrophy patients and their outcomes in pregnancy–the majority of these patients have had an enterocystoplasty. We found a stillbirth/neonatal death rate much higher than the national average–neonatal deaths were exclusively in patients delivered by emergency caesarian section outside our unit where delivery was significantly delayed (Deans/Creighton–unpublished data). This, above all, emphasizes the need for shared care and elective caesarian section delivery in this group of exstrophy patients-in other patients with cystoplasty the mode of delivery should be considered, as discussed below. We would advocate that all patients who have undergone significant urological reconstruction should be under the shared care of an urologist and obstetrician. This allows for monitoring of upper tracts and intervention when required, combined treatment of urinary tract infections, should they arise, and management of issues relating to mitrofanoff channels, where they are present.

Data suggests that in a wider group of patients successful obstetric outcomes can be expected although problems including urinary tract infections, upper tract obstruction, difficulty in catheterising a mitrofanoff may be encountered.[23,24]

Urinary tract infections were found to be at a much higher rate (52%-91%) in both studies – these should be treated with prophylactic antibiotics–this may be coupled with the need to leave an indwelling catheter in the mitrofanoff which may become difficult to catheterize.[23,24] The majority of patients in both these studies were delivered by caesarian section before term. However, some did achieve vaginal delivery 34%[23] vs 25%,[24] as a management principle–the worst of all possible situations is an out of hours emergency caesarian section when appropriate support cannot be obtained. Therefore, in cases where there has been previous urological reconstruction a low threshold for arranging an elective caesarian section should be maintained.

In his paper Hensle describes the fact that the urological recontrsuction can easily be moved aside in order to gain access to the uterus. This is usually the case with first time deliveries–although cannot be relied upon and sharp dissection in order to achieve adequate access to the uterus may be necessary to minimize risk to any reconstruction and its pedicle.

The upper tracts can be a problem with 10% requiring insertion of a percutaneous nephrostomy.[23] There appears to be little correlation between the type of reconstruction and any form of reliable prediction as to the risk of upper tract issues. Hence our practice is to scan the upper tracts once per month from approximately 20 weeks (earlier if significant symptoms arise). Close discussion with experienced radiology colleagues is essential to make this effective as the indications to intervene and the imaging modalities required will vary with individuals.

Malignancy

The risk of malignancy in enterocystoplasty is frequently discussed; on last review approximately 150 cases of malignancy have been indentified in patients with bowel in the urinary system. Long term follow up has suggested that the incidence might be as high as 4.3% at 30 years.[25] In patients who have had a ureterosigmoidostomy the risk of neoplasia (adenoma and adenocarcinoma) is 24% at 20 years.[26] The natural history of a benign adenoma in these patients is to progress to malignancy and therefore, when identified these need exicision and reforming of the anastomosis. It is important to remember that in these patients the combination of urothelium in contact with bowel mucosa, urine and faeces appears to create the risk for, in the absence of any one of these factors in the reported incidence declines dramatically.[4]

However rare, when cancer is diagnosed in a reconstructed bladder it can be a devastating situation–the concern is how to ensure early identification and resultant curative treatment. This remains a dilemma and very difficult to achieve. Data suggests that risks include a history of chronic inflammatory disease,[27] tobacco use, previous renal transplant[25] and bladder exstrophy.[28] Our own unit looked at the benefit of annual surveillance cystscopy and found that it was not an effective way of screening for malignancy.[29] As with many other units we have moved away from annual cystoscopic reviews and our follow-up consists of annual bloods and imaging with escalation to endoscopy only when symptoms have changed. Triggers for endoscopy would include a new history of recurrent urinary tract infection, suprapubic pain or haematuria. It has remained a concern of the author that views along a mitrofanoff may be falsely reassuring as in the face of difficult access, mucus and debris adequate views may be impossible to achieve using a paediatric cystoscope or a flexible cystoscope. If there is doubt about the views obtained or imaging suggests a lesion which has not been seen we would proceed to a percutaneous cystoscopy-creating a track and passing a cystoscope or nephroscope into the bladder to improve visualization. Many tumours occur at the junction between the bowel and urothelium and the tendency is for them to be adenocarcinoma although other types have been reported.[25,30]

Summary

Enterocystoplasty remains important for a reconstructive urologist to use the in the management of incontinence, preservation of upper tracts, following extirpative surgery or as treatment for congenital anomalies. It has lifelong consequences that require careful and specialist follow-up coupled with patient support. Patients need to understand these risks before they commit to such surgery and to take an active part in their own long-term management.

Reference:

1. Bramble, F.J., The treatment of adult enuresis and urge incontinence by enterocystoplasty. *Br J Urol,* 54(6): 693-696, 1982.
2. Couvelaire, R., [The “little bladder” of genito-urinary tuberculosis; classification, site and variants of bladder-intestine transplants]. *J Urol Medicale Chir*, 56(6): 381-434, 1950.
3. Farnham, S.B. and M.S. Cookson, Surgical complications of urinary diversion. *World J Urol*, 22(3): 157-167, 2004.
4. Greenwell, T.J., S.N. Venn, and A.R. Mundy, Augmentation cystoplasty. *BJU Int*, 88(6): 511-525, 2001.

5. Kuss, R., *et al*: Indications and early and late results of intestino-cystoplasty: a review of 185 cases. *J Urol,* 103(1): 53-63, 1970.
6. N'Dow, J., *et al*: Bowel dysfunction after bladder reconstruction. *J Urol,* 159(5): 1470-1474, discussion 1474-1475, 1998.
7. Mansson, W., *et al*: Perforation of continent urinary reservoirs. Scandinavian experience. *Scand J Urol Nephrol,* 31(6): 529-532, 1997.
8. Elder, J.S., *et al*: Perforation of the augmented bladder in patients undergoing clean intermittent catheterization. *J Urol,* 140(5 Pt2): 1159-1162, 1988.
9. Essig, K.A., *et al*: Elevated intravesical pressure causes arterial hypoperfusion in canine colocystoplasty: a fluorometric assessment. *J Urol,* 146(2 (Pt 2): 551-553, 1991.
10. Slaton, J.W. and K.A. Kropp, Conservative management of suspected bladder rupture after augmentation enterocystoplasty. *J Urol,* 152(2 Pt 2): 713-715, 1994.
11. Kristjansson, A., *et al*: Long-term renal morphology and function following enterocystoplasty (refluxing or anti-reflux anastomosis): an experimental study. *Br J Urol,* 78(6): 840-846, 1996.
12. Racioppi, M., *et al*: Acid-base and electrolyte balance in urinary intestinal orthotopic reservoir: ileocecal neobladder compared with ileal neobladder. *Urology,* 54(4): 629-635, 1999.
13. Diamond, D.A., *et al*: Ammonia levels in paediatric ureterosigmoidostomy patients: a screen for hyperammonaemia. *Br J Urol*, 67(5): 541-544, 1991.
14. Mishra, V.C.S., D.; Nethercliff, J.; Wood, D.; Woodhouse, C.R.J., Hyperammonaemic encephalopathy 60 years after ureterosigmoidostomy: Case report and clinicopathological correlations. *British Journal of Medical and Surgical Urology*, 3: 116-117, 2010.
15. McDougal, W.S., Metabolic complications of urinary intestinal diversion. *J Urol*, 147(5): 1199-1208, 1992.
16. Gerharz, E.W., *et al*: Metabolic and functional consequences of urinary reconstruction with bowel. *BJU Int*, 91(2): 143-149, 2003.
17. Blyth, B., *et al*: Lithogenic properties of enterocystoplasty. *J Urol*, 148(2 Pt 2): 575-577, discussion 578-579, 1992.
18. Nurse, D.E., *et al*: Stones in enterocystoplasties. *Br J Urol*, 77(5): 684-687, 1996.
19. Woodhouse, C.R. and G.N. Lennon, Management and aetiology of stones in intestinal urinary reservoirs in adolescents. *Eur Urol,* 39(3): 253-259, 2001.
20. Hamid, R., W.G. Robertson, and C.R. Woodhouse, Comparison of biochemistry and diet in patients with enterocystoplasty who do and do not form stones. *BJU Int,* 101(11): 1427-1432, 2008.
21. DeFoor, W., *et al*: Bladder calculi after augmentation cystoplasty: risk factors and prevention strategies. *J Urol,* 172(5 Pt 1): 1964-1966, 2004.
22. Nethercliffe, J., *et al*: False-positive pregnancy tests in patients with enterocystoplasties. *BJU Int,* 87(9): 780-782, 2001.
23. Greenwell, T.J., *et al*: Pregnancy after lower urinary tract reconstruction for congenital abnormalities. *BJU Int*, 92(7): 773-777, 2003.
24. Hensle, T.W., *et al*: The urological care and outcome of pregnancy after urinary tract reconstruction. *BJU Int*, 93(4): 588-590, 2004.
25. Husmann, D.A. and S.R. Rathbun, Long-term follow up of enteric bladder augmentations: the risk for malignancy. *J Pediatr Urol*, 4(5): 381-385, discussion 386, 2008.
26. Woodhouse, C.R., Guidelines for monitoring of patients with ureterosigmoidostomy. *Gut,* 51 Suppl 5: V15-6, 2002.
27. Stone, A.R., N. Davies, and T.P. Stephenson, Carcinoma associated with augmentation cystoplasty. *Br J Urol*, 60(3): 236-238, 1987.
28. Smeulders, N. and C.R. Woodhouse, Neoplasia in adult exstrophy patients. *BJU Int*, 87(7): 623-628, 2001.
29. Hamid, R., *et al*: Routine surveillance cystoscopy for patients with augmentation and substitution cystoplasty for benign urological conditions: is it necessary. *BJU Int,* 104(3): 392-395, 2009.
30. Lane, T. and J. Shah, Carcinoma following augmentation ileocystoplasty. *Urol Int*, 64(1): 31-32, 2000.