UROTHELIAL LINED CYSTOPLASTY IN A SHEEP MODEL

and

Clinical Application of these and Related Procedures

A Thesis for the Degree of Doctor of Medicine
in the University of Adelaide

PA DEWAN

MBBS BMedSc FRACS

ACKNOWLEDGEMENTS

Many people have assisted me with this project. The idea was developed from a respect for urothelial lining for urine storage, a lesson taught to me by Mr Phillip Ransley. With that thought in mind, and the recent development of autoaugmentation and paediatric gastrocystoplasty, the study was formulated during time spent with Dr Riccardo Gonzales in Minneapolis. Riccardo, thanks for the beer and the stimulus to think about bladder enlargement! Mr Robert Fowler and Professor Villis Marshall have contributed many helpful comments at various stages of the project and have provided assistance with funding applications.

Julie Goldfinch and Kylie Maddison, at the Children's Hospital animal house, have tolerated many long Friday afternoons and have cared for the sheep extremely well; the radiographers of the Women's and Children's Hospital and the technicians of the Histopathology Department have provided technical assistance, as have the staff at the WAITE institute.

The project would not have been possible without the help and involvement of Dr Roger Byard at the Women's and Children's Histopathology Department; he has provided detailed reports on the histology of the bladders. Valuable support and practical assistance has been provided by the two research fellows working in the Women's and Children's Hospital Urology Unit during the time of the study: my many thanks to Christian Lorenz and Wojciech Stefanek for their energy and assistance.

No such project can be completed by a husband and father without the support of his wife and family. I, therefore, acknowledge the contribution of Brigid, and my children, Emily, Rachael and Simon, to what is hopefully significant Paediatric Urology research.

Funding was obtained from the Women's and Children's Hospital Foundation for the computer facility and the costs of the colonic component of the study. The Clive and Vera Ramaciotti Foundation funded the urodynamic equipment. The animals and equipment for the gastric and autoaugmentation phases were donated by the Spina Bifida Association of South Australian and the Edwardstown Rotary Club (administered through the Australian Brain Foundation).

Last, but not least, I would like to pay tribute to those parents and children who had sufficient trust and confidence in me to allow the newly developed bladder augmentation technique to be used clinically.

SUMMARY

This study looks at the laboratory development and clinical use of new techniques for bladder augmentation, all of which result in a neo-bladder lined by urothelium. The combination of autoaugmentation and demucosalised enterocystoplasty was explored in a sheep model, using both the stomach and colon. These results were then compared with a control group, and animals after demucosalised enterocystoplasty without autoaugmentation and autoaugmentation alone. In addition, the clinical application of the laboratory developed approach was studied. As well, patients who had either a ureterocystoplasty or diverticulocystoplasty were followed.

Sheep experiments

The sheep experiments have demonstrated the feasibility of demucosalisation of the sheep fourth stomach, the usual survival of the urothelium under the gastric patch and the ability to produce an augmented bladder. It appears that the urothelium of an autoaugmentation does not always survive, and when urine is in contact with the denuded muscle, through a defect in the autoaugmentation, poor urodynamic results are seen. However, the autoaugmentation gastrocystoplasty was the only group with a significantly larger bladder at six months. The numbers of animals at 12 months were too small for statistical significance to be achieved, but the trends appeared to persist. The colon bladders failed, due to the inability of the delicate colon to tolerate the dissection necessary to remove the mucosa, and demucosalised enterocystoplasty failed to improve the bladder capacity because of the slow ingrowth of the urothelium over the muscle allowed for the development of fibrosis. The autoaugmentation alone produced an unsatisfactory bladder, probably secondary to the overlying fat being poorly compliant. Variability in the control group and those operated on was a notable feature.

The animal bladders were assessed radiologically, urodynamically, macroscopically and histologically.

Patient Application

Ureterocystoplasty has been used in five boys and diverticulocystoplasty in one, with improvement in the bladder capacity in all. Concurrently, these procedures were successful in reducing the predisposition to urinary tract infection and pyelonephritis. An additional advantage to each of these operations is the ability to use them in the first year of life, thus preventing the need for urine diversion.

The autoaugmentation enterocystoplasty has been used in nine children, five using the stomach and four using colon as the source of muscle, with improvement in the bladder function in all. These operations take longer than a routine enterocystoplasty, and are much more difficult to perform. Both the bladder and bowel dissections are tedious and time consuming, however, the effort seems worth the investment, given the long-term complications that are avoided. No mucosal regrowth has been evident in any of the patients, nor in any animals where removal of the submucosa, with the mucosa, was performed.

The results are encouraging, but, obviously, on-going surveillance is needed to ensure that a new set of complications is not generated by these procedures. With careful attention to operative detail and post-operative care, the "urothelial lined" approach to cystoplasty will hopefully provide those who need a bladder augmentation with a better future. On-going extensive animal studies and careful clinical follow-up is required to ensure appropriate use of this new concept.

CONTENTS

SHEEP RESULTS

Clinical Application of Urothelial Bladder Augmentation

MATERIALS AND METHODS

OPERATIONS

RESULTS

Discussion

SHEEP STUDIES

CLINICAL APPLICATION

CONCLUSION

INTRODUCTION

Overview

Any operation with a significant number of complications stimulates the development of alternative approaches. Bladder augmentation has had many alternatives tested in the laboratory, but few have been used to any great extent clinically.

Detubularised full thickness bowel segments are currently the most common material used for bladder augmentation, but are increasingly recognised to be accompanied by many potential complications [1-4]. Consequently, the following materials do not reliably produce a satisfactory urinary reservoir when used to replace or enlarge the bladder.

Autologous:

bowel muscle [5-10],
submucosa [11]
omentum [12]
peritoneum or myoperitoneum [13-15]
fascia [16,17]
gall bladder [18]

Biodegradable:

amnion [19]
dura [20,21]
pericardium [22,23]

Synthetic:

teflon [24]
gelatin [25]
polyvinyl sponge [26]
silastic [27,28]

Most of these procedures have been developed in animals, but have not been extensively used in humans. Regrowth of transitional epithelium across bladder substitute material within the bladder and regeneration of bladder muscle have both been recorded, however, urothelial regenerative methods generally fail to produce a consistently adequate reservoir in large animals and humans as does autoaugmentation which produces a wide-mouthed diverticulum [29-38]. The neo-bladder is covered with a layer of fibrous tissue and is only applicable to patients with a moderate sized bladder initially [31,39].

In an attempt to avoid the metabolic, mucous and malignancy risk complications of small or large bowel the stomach has been used [40-43]. The secretion of acid is of benefit in renal failure [43,44], but produces a 'haematuria-dysuria' syndrome in a significant number of patients. Also, metaplasia is probably of no lesser risk than when small and large bowel are used [45].

Large bladder diverticula and the oversized, refluxing ureters [46-48] have also been advocated as available sources of urothelial lined tissue for bladder augmentation, but their use is limited to appropriate patients.

This study is not the first to combine autoaugmentation and demucosalised enterocystoplasty, but it is the first to use the stomach muscle for the purpose, and it is the most extensive follow-up work produced, and the first to be published. It includes the subsequent clinical application of techniques developed in animal experiments, and shows that lessons from the sheep bladder, stomach and colon are not directly applicable to humans.

It would appear that an exciting new technique of bladder augmentation has been explored in this study with encouraging results.

History of Bladder Augmentation Procedures

Bladder augmentation has a long history which is well worth recounting. Enterocystoplasty commenced more than 100 years ago when in 1888 Tizzoni and Foggi reported the results of their animal experiments [49]. Rutkowski [50] and Mikulizc [51] subsequently recorded a clinically successful operation, integrating a detubularised segment of the small intestine into the bladder wall. Both patients were older children with bladder exstrophy; Rutkowski performed a one stage ileocystoplasty, and Mikulicz used a delayed, two-stage operation. Each operation was similar to the procedures currently practiced. Statements made by these two authors are still widely held; Rutkowski wrote (22.4.1899) - "A bowel wall patch, pedicled on the mesentry, meets all these requirements; with it we, therefore, have the ideal material for a cystoplasty" [50]; and Mikulizc (3.6.1899) cautioned that "the value of it (*the operative technique*) is finally, however, only dependent on the subsequent function of the created bladder" [51].

Many technical variations have been advocated since the initial work of Rutkowski and Mikulicz, and the clinical application of the different modifications has been much debated [52-57].

In the search for alternatives to routine enterocystoplasty, Sinaiko (1956) used a segment of stomach on a vascularised pedicle to create an isolated gastric pouch urinary reservoir initially in dogs [58] and subsequently in humans [59]. The pouch used was similar to that designed by the German physiologist R.P.H. Heidenhain (1834-1897) for the study of gastric secretions. In 1962, D.C.Martin *et al.* [60] reported the first successful gastrocystoplasty in dogs by adapting the gastric pedicle to allow the segment to reach the orthotopic bladder. The part of the stomach used,

and the method of fashioning both the segment and its blood supply, have since been further studied [45,61-63].

In the 1950's, to avoid the number of complications attributed to the gastrointestinal tract mucosa, attempts were made to remove the mucosa from detubularised intestinal segments for bladder augmentation [64-66]. In their dog model, Shoemaker *et al.* reported that the peritoneal surface of the bowel became lined with urothelium within 2 to 3 weeks. They also found the two-layered muscular architecture of the intestine to interlace into a plexiform network, indistinguishable from the normal detrusor muscle. However, regrowth of bowel epithelium was noted if the submucosa was not removed with the mucosa [10,67].

In the demucosalised enterocystoplasty the ingrowth of urothelium occurs within 3 to 6 weeks in most situations, depends on the size of remaining bladder and the species used. This slow ingrowth seemingly allows inflammation and fibrosis of the muscle patch, resulting in shrinkage and the formation of calculi. The mucosa is difficult to remove from the small and large bowel in animals, increasing the chances of regrowth of the gastrointestinal epithelium. Never-the-less, Blandy [10] developed a reliable technique for mucosal removal, but found regeneration of the urothelium to be slower than reported by Shoemaker's group [68].

Campbell [9] was the first to perform a de-epithelialised intestinocystoplasty in a patient. He claimed a satisfactory result, but there were no urodynamic recordings, and the published cystogram was that of an unsatisfactory bladder. Shoemaker *et al.* published four cases in 1957, including a 9 year old girl; the bladder volumes were generally small in all four patients, and no urodynamic results were given [69]. Heeg *et al.* suggested and tried the novel approach of attaching the serosal surface of the sigmoid colon to a resection defect at the back of a bladder, producing a urothelial lined augmentation [70]. Subsequent animal work, using

different parts of ileum or colon, with either the serosal or denuded external wall covering the inner surface of the bladder, have shown mixed results [6-8,71]. Recently a seromuscular bowel flap has been used for a combined bladder augmentation and repair of a vesico-vaginal fistula with success [72].

Various alternatives have been used to produce an epithelial lined urinary reservoir, including omentum [12], peritoneum or myoperitoneum [13-15,73], fascia [16] amnion [19], dura [20,21], pericardium [22,23], and many synthetic substances [24-27]. The most extensively used of these is dura; Kelâmi reported on duracystoplasty in 34 patients in 1975 [21].

Autoaugmentation is an alternative to covering enteric segments by urothelial ingrowth. It involves creating a large-mouth bladder diverticulum. In 1917, Neuhof reported the results of animal experiments by Kostenko, Rubaschew, and himself [17]. Their attempts to use fascia as a substitute for the wall of the bladder (they also studied other hollow viscera) showed that it was essential to preserve the continuity of the urothelium. Similarly, Huggins in 1931 [16] described removal of a patch of bladder muscle, covering the defect with fascia; when the urothelium was preserved it prevented the bone formation seen where the graft came into direct contact with urine.

The more recent studies of preservation of an intact urothelium resulted in the coining of the terms Autoaugmentation [29,30,35], Detrusorectomy [32], Autocystoplasty [74] or Seromuscular Myotomy [34]. The incision in the bladder muscle is similar to the routine clam cystoplasty, but does not breach the bladder mucosa. The bladder mucosa is left to bulge through the muscle incision as a wide mouthed diverticulum. Cartwright and Snow were the first to report their results in dogs [30] and then in a series of patients [29] - in fact the first patient procedure occurred before the dog experiments had been conducted (Cartwright and Snow -

personal communication).

The long-term outcome of autoaugmentation have been well documented in investigations of dogs, 4-6 weeks after operation. The histology showed scarring over the area where the detrusor had been resected, but the urothelial layer, the lamina propria and network of small vessels were intact, although surrounded by a thin layer of collagen and a layer of hypercellular fibrous tissue. Shrinking of the urothelial bulge with time has meant that the long-term results of this technique have been less favourable, with bladder dynamic improvements in only 50% of cases in some series [37-39]. Small trabeculated bladders respond less well to autoaugmentation and there appears to be a risk of vesicoureteric reflux and bladder perforation. Nevertheless, Moorehead *et al.* [32] and Gordon *et al.* [74] reported good results in a number of children.

Complications of Current Enterocystoplasty

Unfortunately, several clinical problems are seen with the use of intestinal segments in the urinary tract. These include excessive mucous production, recurrent urinary tract infection, reflux or obstruction at the vesicoureteric junction, metabolic changes (acidosis, ammonaemia) and electrolyte shifts (hyperchloraemia, hypercalcuria) [2,75-78]. More recently, spontaneous bladder perforation, haematological changes and growth retardation have been recognised [79-82], along with the risk of malignancy, bone demineralisation, chronic vitamin deficiency, urinary stone formation, cholelithiasis, and fibrosis and bone formation within the intestinal segments [1,3,77,83-89]. The reported incidence of complications related to the use of intestinal segments vary widely with age, basic disease, type of enteroplasty and renal function. All patients require long-term monitoring for the complications of the enterocystoplasty.

Extensive work has been carried out to look at the potential and real risks of gastrocystoplasty, including:- serum gastrin changes and their relationship to the specific portion of the stomach and the effect of distension, the effect of acid output on metabolism and the remaining bladder, mucus production, stone formation; and the development of bladder ulceration [45,60,90-93]. The expected benefits of acid secretion in the urine have to some degree been overshadowed by adverse effects of the acid urine in early animal experiments [60,94,95], and, to date, marked symptoms from acid in the bladder and urethra are the single most important gastrocystoplasty complication [43,44]. Many of those with symptoms need to have both systemic H_2 receptor antagonists and bladder irrigations with buffer solutions. More recently a combination of stomach and small bowel has been used to overcome the metabolic complications of each [96,97].

Investigations of gastrocystoplasty bladders in rats suggest that the risk of metaplasia is significant in both the adjacent urothelium and the incorporated segment of gastric mucosa [45,98,99].

Autoaugmentation Enterocystoplasty

Blandy in 1964 [10] summarised the remarkable properties of urothelium: it is almost waterproof allowing only minimal movement of water and ions - making it perfect for lining a urinary reservoir. It was the recognition of these properties, and the complications of each of the alternatives, that helped foster further attempts to find a urothelial lined bladder augmentation. L.S.J. Martin [5] was the first to report the application of urothelial lined ileal segments for bladder replacement in dogs. He covered the inner surface of seromuscular ileal grafts with epithelium, which they had removed from the resected bladder, work which was also conducted by Gilbert [100]. Compared to bladder substitutes with uncovered seromuscular grafts the epithelial grafts appeared to hasten the uroepithelisation of the ileal bladder. Unfortunately, the epithelial regeneration was uneven and epithelial cysts formed at the mucosal edge.

Pompino *et al.* [101] cite Russian authors (Golub, Kimbarovskaja, Mochort, Savtschenko) who used seromuscular grafts in children with a neurogenic bladder. Reinnervationplasty, Vesicopexy or Autocystoduplication were names used to describe their attempts to attach a seromuscular ileal patch to the back wall of the bladder after removal of its serosa. Even though a number of children were treated successfully, Pompino *et al.* [101] could not confirm the optimistic results obtained by the Russians. All these studies were mainly aimed at reinnervation of the bladder.

Mau [102] created a neuropathic bladder in pigs and later removed two thirds of the spastic and trabeculated bladder muscle, leaving the urothelial layer intact. A detubularised seromuscular ileal segment was then sewn over the urothelium, producing a urothelial lined ileal graft. Histological investigations showed an intact transitional epithelium attached to the muscular layer of the ileal patch in most

specimens with only mild inflammation between the two layers. The results were considered unfavourable because the bladder muscle did not become reinnervated. The author, however, demonstrated encouraging bladder capacity and compliance results. His study of the functional aspects of the bladder were less detailed than in this work, and the results were never published outside his Berlin University Library.

In this work a number of experiments were performed to look at the efficacy of both stomach and colon as the muscle covering to an autoaugmentation. When it appeared that stomach was the acceptable source of enteric muscle the first patient underwent an autoaugmentation gastrocystoplasty (AAGC) and he, and the subsequent four children, had acceptable bladder results. Unfortunately three had poor tolerance of large meals initially. Therefore, the next four children had an autoaugmentation colocystoplasty (AACC) when, with the permission of the Women's and Children's Hospital ethics committee, demucosalisation of the sigmoid colon was attempted and found to be satisfactory. The early results indicate that the bladder can be at least as good as the AAGC, with a shorter incision and less morbidity. The broader application of the principle of producing a urothelial lined bladder augmentation has allowed six other patients to undergo a new form of bladder augmentation using either ureter or paraureteric diverticula.

AIMS AND HYPOTHESES

AIMS

Bladder

To confirm that bladder muscle can be separated from part of the bladder mucosa (autoaugmentation) in the living sheep with survival of the urothelium.

To study the rate of growth of urothelium on the under surface of denuded stomach and colon which has been used for a demucosalised clam cystoplasty.

Stomach

To confirm that gastric mucosa can be separated from its muscle in the living sheep.

To confirm survival of urothelium on the under surface of denuded gastric muscle in the *AAGC*.

To study the histology, upper renal tract status, and urodynamic function of the neo-bladder in animals with an *AAGC*.

To compare *AAGC* with demucosalised gastrocystoplasty (DMGC), autoaugmentation omentoplasty, and a control group, both histologically and urodynamically.

Colon

To confirm that colonic mucosa can be separated from its muscle in the living sheep.

To confirm survival of urothelium on the under surface of denuded colonic muscle in the *AACC*.

To study the histology, upper renal tract status, and urodynamic function of the neo-bladder in animals with an *AACC.*

To compare *AACC* with demucosalised colocystoplasty (DMCC), autoaugmentation omentoplasty (AAOC), and a control group, both histologically and urodynamically.

To compare *AACC* with the *AAGC*, *DMGC*, and *AAOC* both histologically and urodynamically.

Clinical

To confirm that both human gastric and colonic muscle can tolerate removal of its mucosa.

To study the serum gastrin response to *AAGC* in children.

To study the gastric complications of *AAGC* in children.

To study the urodynamic and clinical outcome of bladders in children who have an *AAGC* and *AACC.*

To apply the principles of ureterocystoplasty and diverticulocystoplasty to appropriate children.

HYPOTHESES

Sheep

The urothelium of an autoaugmented bladder survives under stomach and colonic muscle, and under omentum.

The muscle of the sheep fourth stomach tolerates demucosalisation better than does the sigmoid colon and the presence of muscle on an autoaugmented

bladder improves the quality of the augmentation. Therefore, the histologic, radiographic and urodynamic results for the *AAGC* should be superior to the *AACC* and *AAOC*.

Ingrowth of urothelium under stomach (*DMGC*) and colonic (*DMCC*) muscle is associated with a greater degree of fibrosis than when autoaugmentation of the bladder is an added part of the procedure, thereby giving less favourable urodynamic results than for the *AAGC* and *AACC* procedures.

Clinical

The serum gastrin is unaffected by the *AAGC* in children.

The human stomach and colon are able to tolerate removal of the mucosa and submucosa.

AAGC and *AACC* can produce a satisfactory urodynamic and clinical result for bladder augmentation in children.

Ureterocystoplasty reduces the risk of urinary tract infection, while improving the bladder dynamics in children with large ureters, high grade vesicoureteric reflux and a high pressure, small volume bladder.

Diverticulocystoplasty reduces the risk of urinary tract infection and improves the bladder dynamic function in children with a neuropathic bladder and large paraureteric diverticula.

MATERIALS AND METHODS FOR SHEEP EXPERIMENTS

Anaesthesia, Analgesia and Antibiotics

General anaesthesia was induced with intravenous thiopentone via the jugular vein after the neck wool had been clipped. The sheep was then intubated and allowed to breath nitrous oxide, halothane and oxygen spontaneously. Intramuscular antibiotics of Gentamicin 2mg/kg and Penicillin 25mg/kg, or cephtriaxone later in the study, were administered prior to the incision and maintained for three days. The animals were given intramuscular pethidine as required, and animals that became unwell were sacrificed early and usually included in the bladder assessment for the stage they had reached at the time of their demise.

Operations

General Information

The abdominal wall was opened through a midline incision. The gastric or colonic component was prepared, then the bladder. At the end of the augmentation a bladder catheter was exited through a stab incision and the wound closed in layers with vicryl and catgut sutures. The suprapubic catheter was left in situ draining dependently for ten days. Normal feeding was instigated as tolerated by the animals. Adequate hydration was usually maintained by a supplement of 1000ml of saline intravenously during the procedure.

Autoaugmentation Gastrocystoplasty (Figure 1)

The fourth stomach was delivered and a length of the greater curve mobilised as a vascularised flap on the right gastro-epiploic vessels, having divided the proximal branches. After preparing the vessels the isolated segment was clamped and incised, and removed from the remainder of the stomach, which was closed. The gastric mucosa of the isolated segment was then dissected from its muscle with diathermy. Next, the bladder muscle was partly separated from the bladder mucosa via a midline incision extending from the anterior to the posterior bladder neck region, resulting in herniation of the bladder mucosa. At the end of the procedure, approximately one third of the bladder muscle remained in contact with the bladder mucosa. The autoaugmentation of the bladder was performed in the same manner in the gastric, colonic and omental reinforced groups. The gastric muscle flap was then sutured to the free edge of the bladder muscle, thus covering the exposed bladder mucosa. The bladder mucosa was, therefore, left intact with both bladder and stomach muscle covering it.

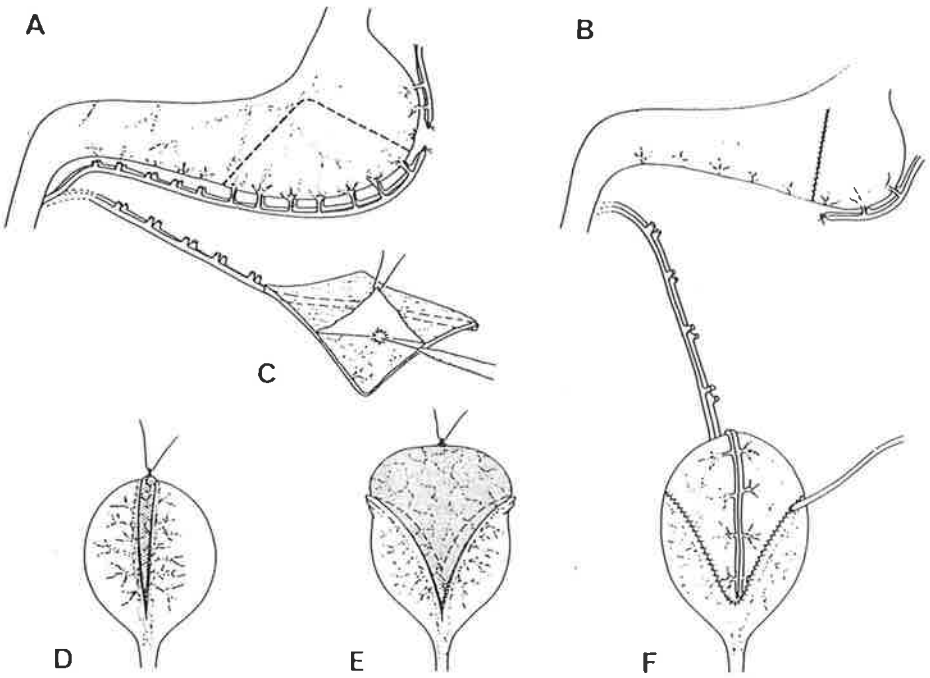


Figure 1 (A-F). The principle steps in the operation of Autoaugmentation Gastrocystoplasty. A: A wedged shaped segment of the greater curve was mobilised on a vascular pedicle of the right gastroepiploic vessels. B: The stomach was closed by continuous suture, and the pedicle mobilised more proximally if required. C: The mucosa was removed from the gastric pouch by diathermy dissection. D: A stay suture was placed in the dome of the bladder and the muscle and mucosa of the bladder separated by sharp dissection. E: The bladder layers were separated until a large, wide-mouth diverticulum was created. F: The denuded surface was laid over the submucosal layer of the bladder and sutured in place, during which a suprapubic catheter was inserted.

Demucosalised Clam Gastrocystoplasty

The stomach was mobilised in the same manner as for the AAGC, and the mucosa similarly denuded. The bladder was opened through all layers from the anterior bladder neck to just above the ureters posteriorly. The denuded gastric muscle was then sewn edge to edge with the full thickness of the bladder, resulting in the denuded surface of the stomach patch coming to lie in contact with urine.

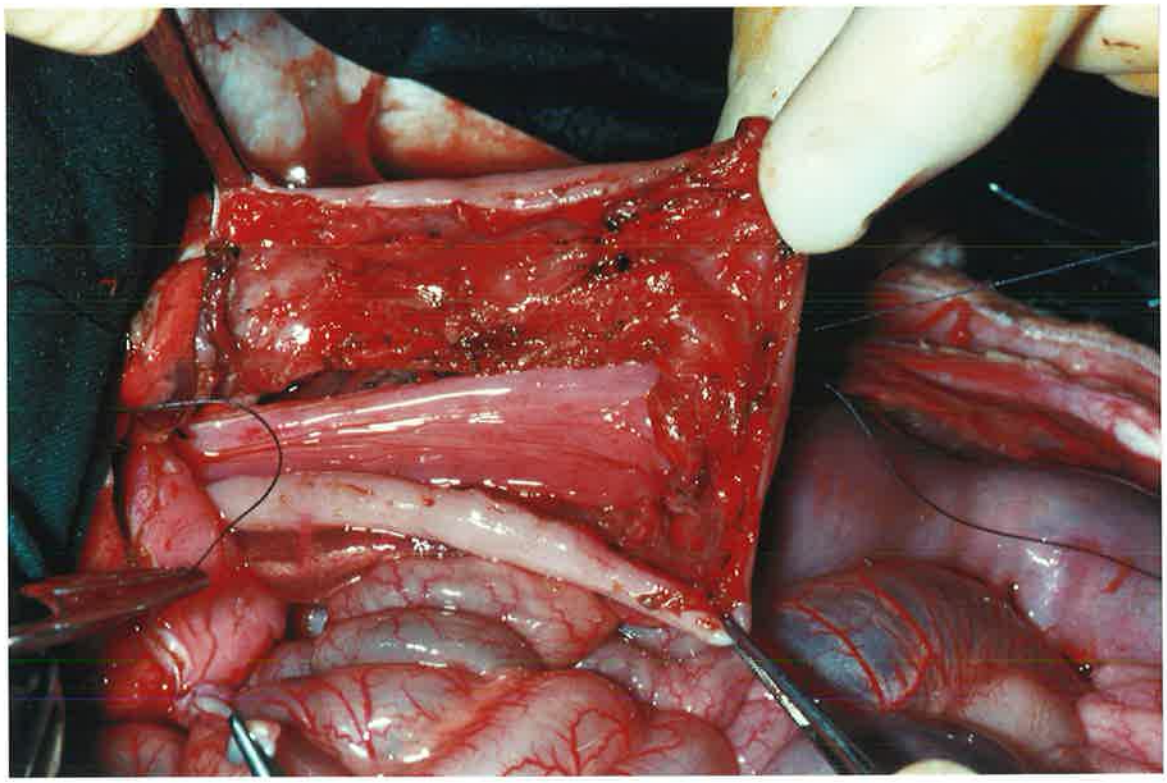


Figure 2A. The partially completed DMGC - denuded gastric muscle adjacent to urothelium.

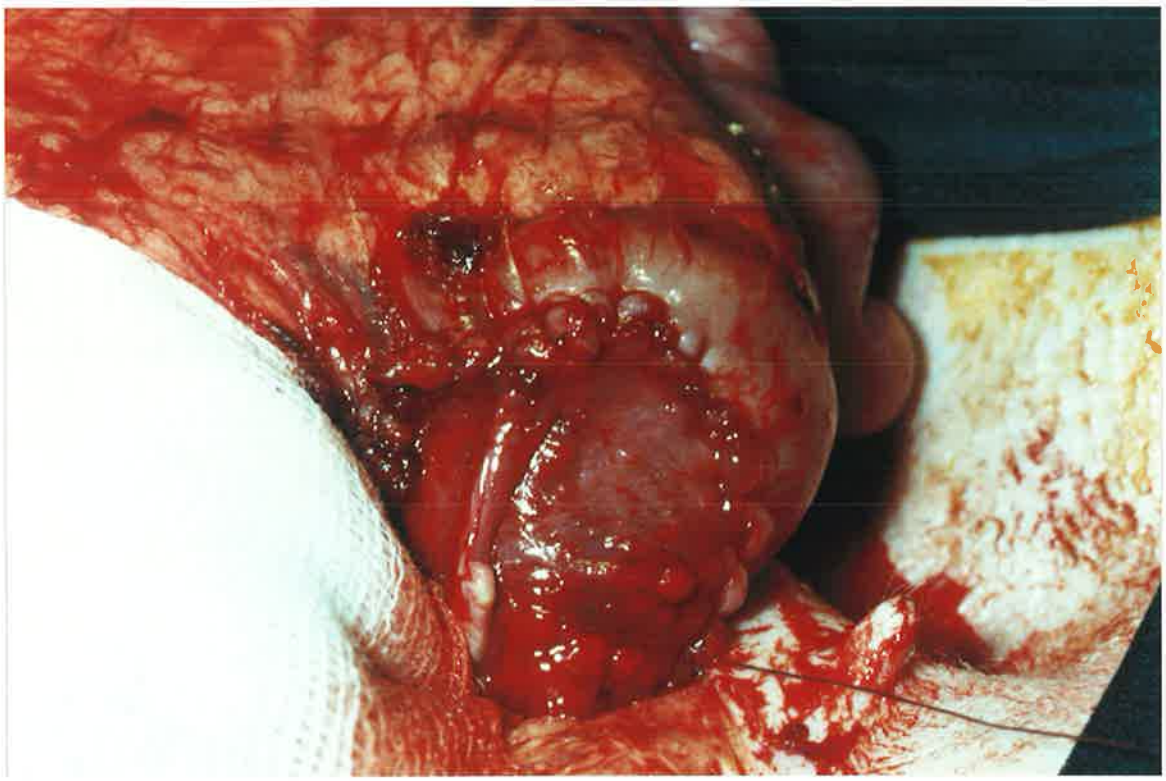


Figure 2B. The completed DMGC and AAGC have the same external appearance.

Autoaugmentation

The omentum was mobilised on a vascular pedicle, down to the bladder which was prepared by stripping the detrusor from the underlying mucosa in the manner used for the AAGC. The omentum was sutured to the bladder and a suprapubic catheter was introduced through the suture line and into a stab incision in the underlying mucosa, around which was placed a purse string suture. The omentum was therefore lying in contact with the submucous layer of that portion of the bladder where the muscle had been stripped from the urothelium.

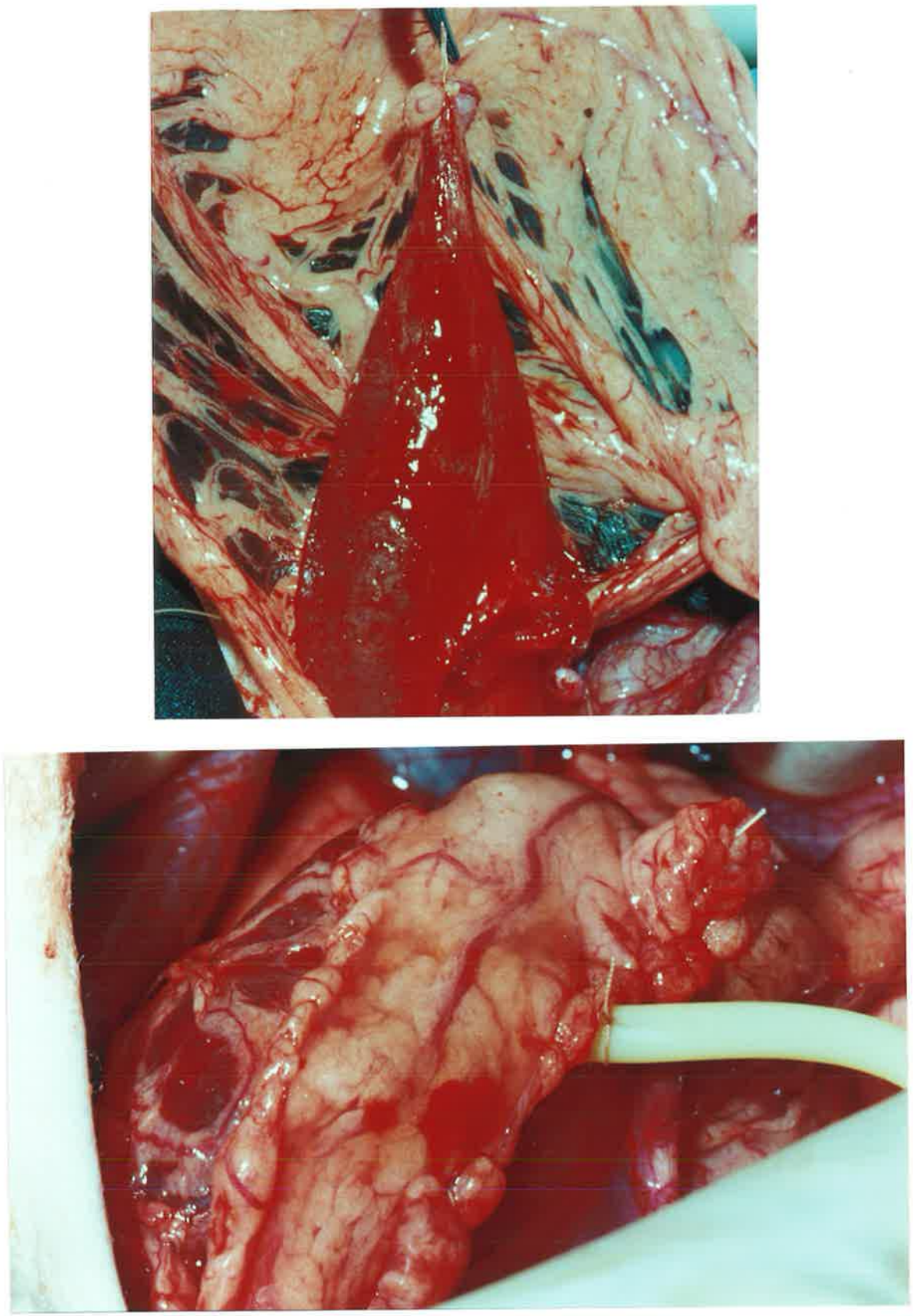


Figure 3A+B. The omentum being positioned over the urothelium and a completed AAOC with the suprapubic catheter in place.

Autoaugmentation Colocystoplasty (Figure 4)

The sigmoid colon was mobilised on its vascular pedicle, the bowel continuity restored with a continuous vicryl suture. The segment was opened along its antimesenteric border and a combination of diathermy dissection, saline injection and stripping with forceps was used to remove the mucosa, while attempting to preserve the integrity of the colonic muscle. This was an extremely tedious dissection, and not always denuded with the complete confidence felt when removing the gastric mucosa.

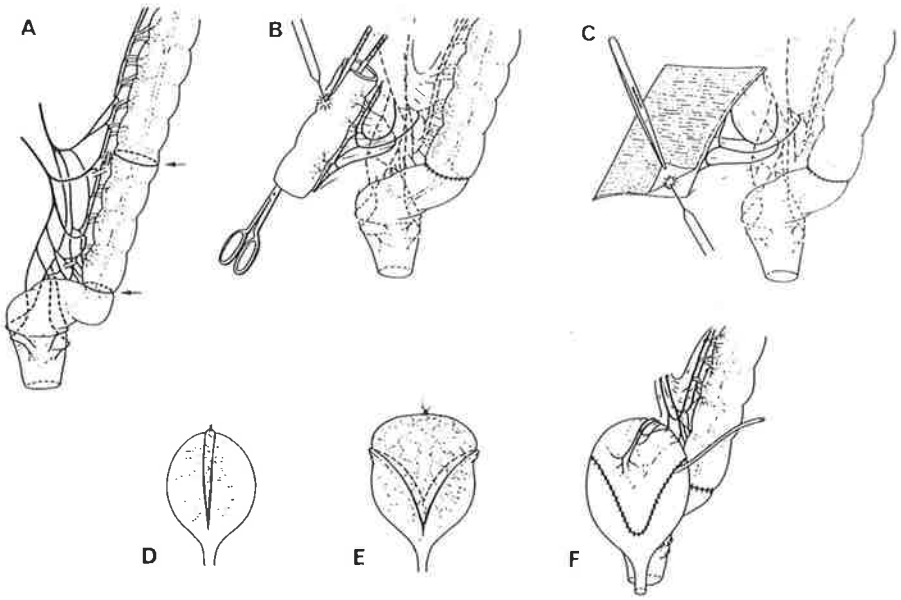


Figure 4: The steps involved in the Autoaugmentation Colocystoplasty. A: A segment of sigmoid colon was mobilised on its vascular pedicle. B: The colon was opened along the antimesenteric border. C: The mucosa was removed from the colonic segment by diathermy dissection. D: Dissection of the muscle from the bladder mucosa was commenced along the anterior wall. E: The bladder layers were separated until a wide-mouth diverticulum was created. F: The denuded colonic surface was laid over the submucosal layer of the bladder and sutured in place.

Demucosalised Clam Colocystoplasty

The bladder was incised through all layers, from the anterior to the posterior bladder neck. The demucosalisation technique was usually by stripping with forceps in these animals; the muscle tolerated this technique better than the diathermy used for the AACC animals. The denuded colonic muscle was sutured to the bladder with the inner surface of the colon in contact with urine. The colonic and gastric demucosalised clam procedures were essentially the same for the stomach and the colon.

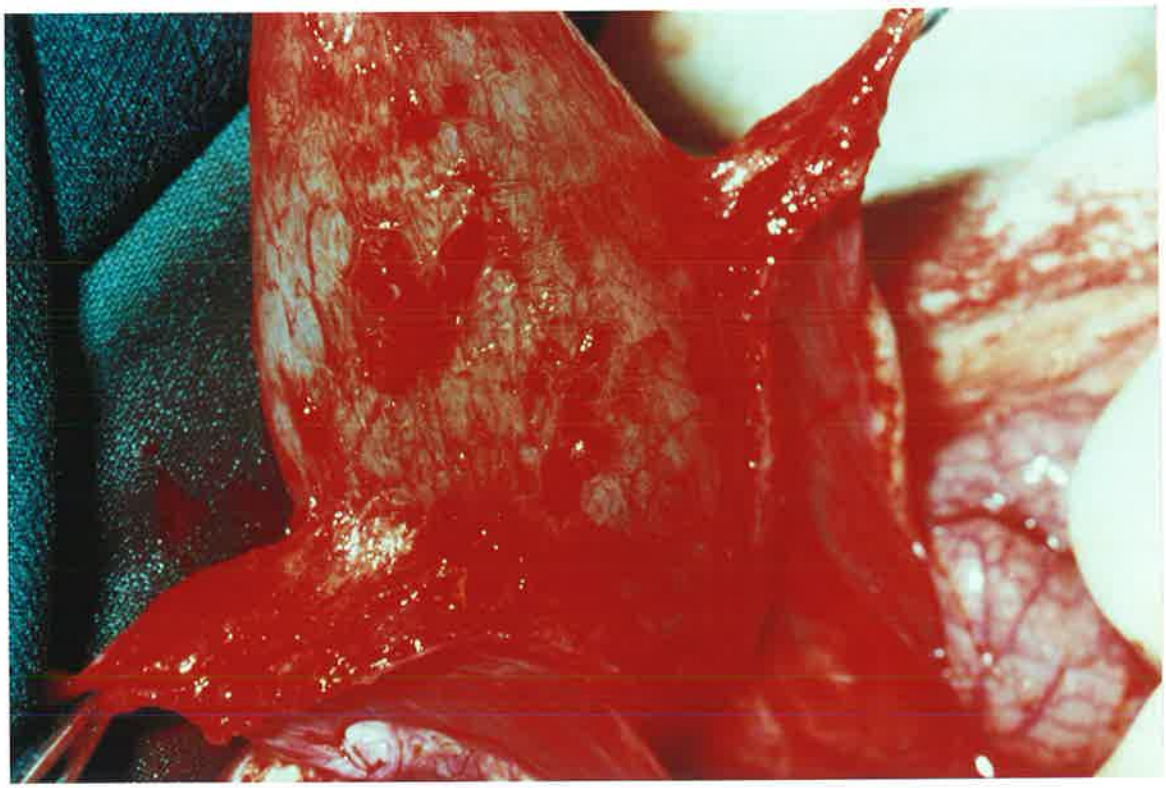


Figure 5A. An autoaugmented bladder prior to an AACC.

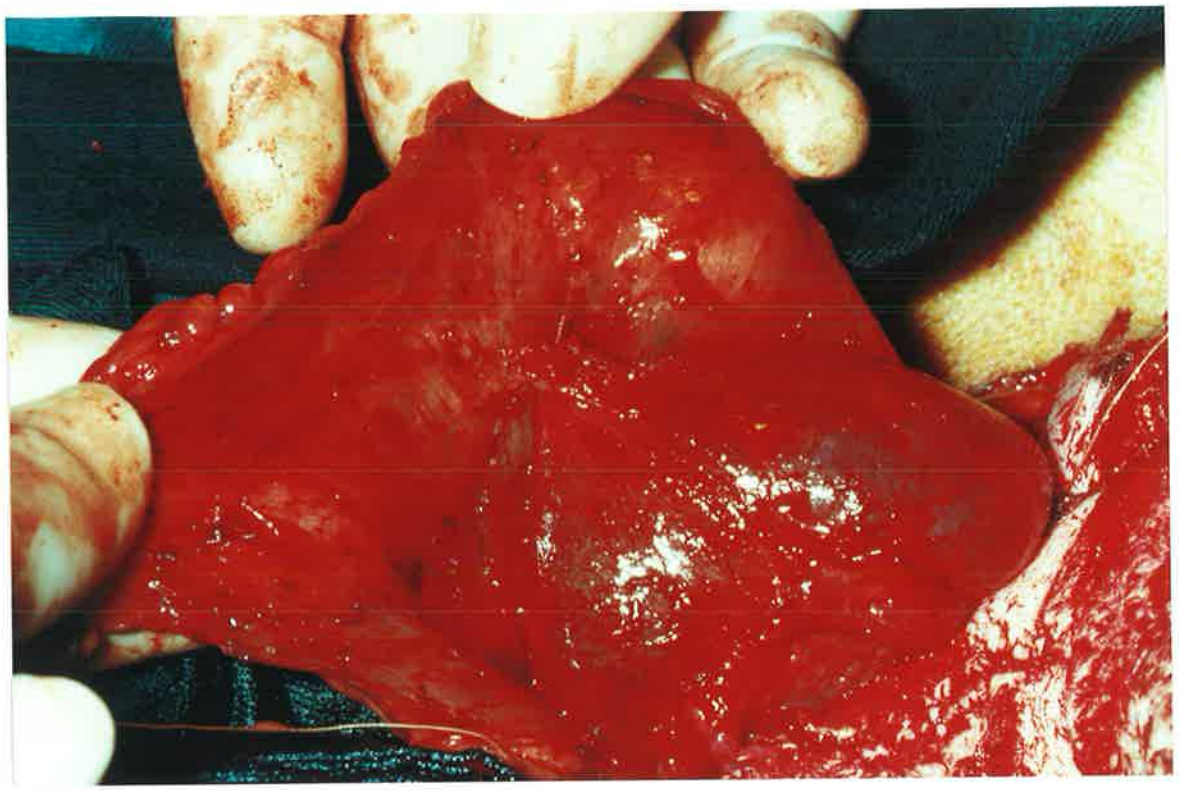


Figure 5B. The denuded segment of colon against the autoaugmented bladder.

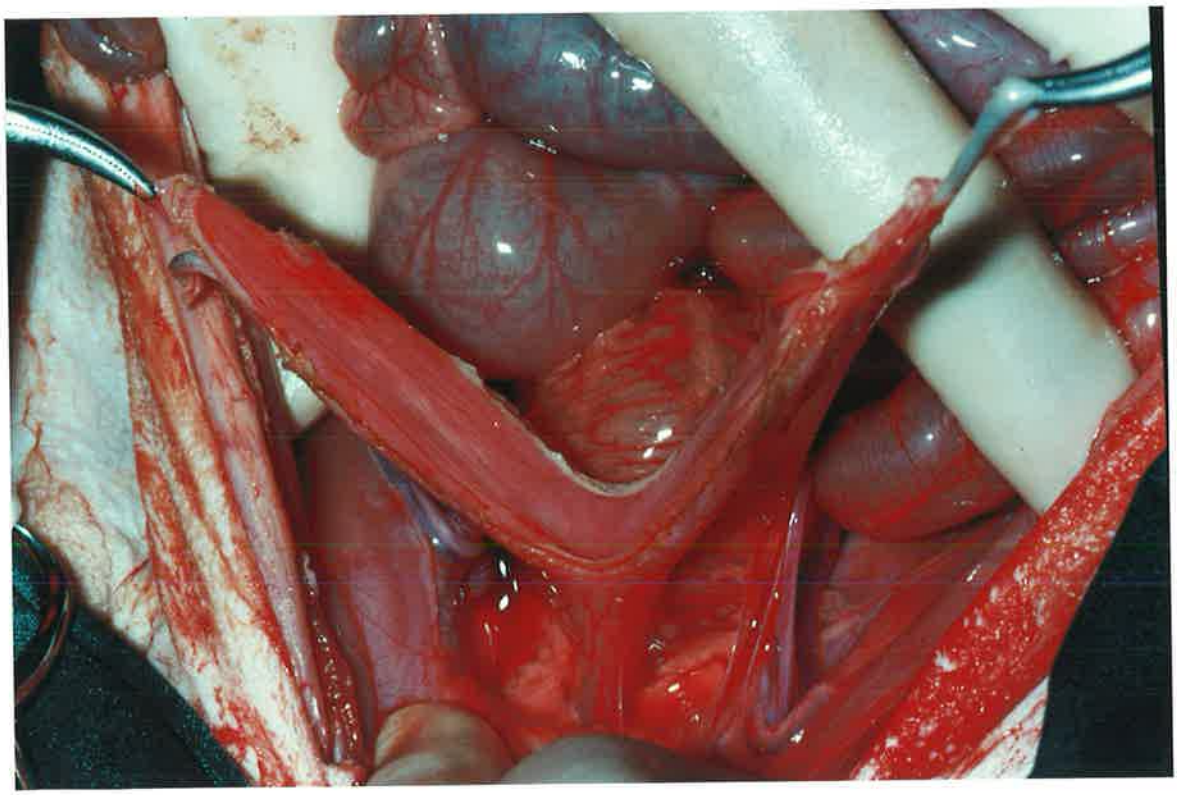


Figure 5C. The bladder opened in sagittal plane for a DMCC.

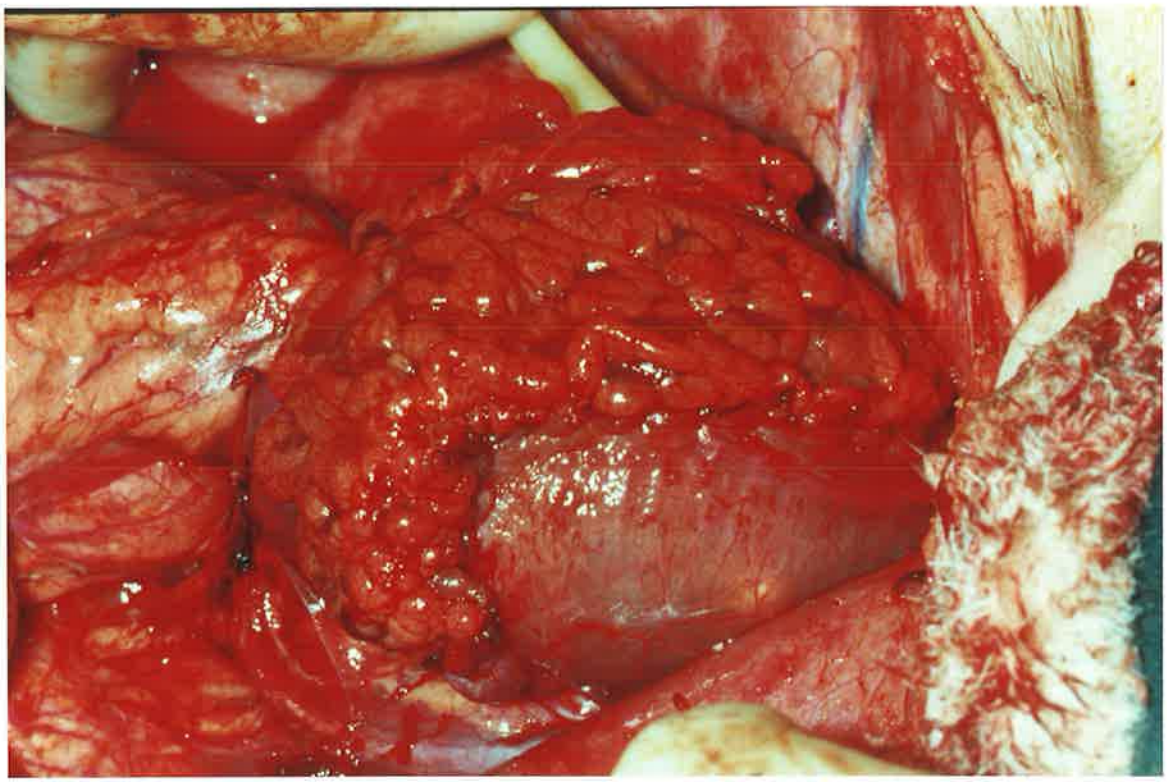


Figure 5D. External appearance which is similar for the DMCC and AACC.

Urodynamics

The urodynamic studies were performed through a double lumen suprapubic catheter [103] inserted under ultrasound control, with the animals under a light general anaesthetic of halothane, nitrous oxide and oxygen. The bladder was filled with warmed saline at a rate of 30ml/min. The data was collected on urodynamic specific Apple Macintosh software (Uromac), and printed at the end of the study to store as hard copy. All studies were stored on hard disc and reviewed at the time of any follow-up studies in the same animal.

When the results of the bladder filling were difficult to interpret, the bladder was emptied and a further filling phase recorded. The study was considered terminated when there was a rise in the bladder pressure associated with the passage of urine. The pressure at the end of filling and the volume at 20cm H_20 were noted. A cystogram was taken at the end of the study, after the saline used for the cystometry had been replaced with 15% urografin.

	6 months	12 months
AAGC	13	6
DMGC	5	3
AAOC	7	4
AACC	6	6
DMCC	5	5
Control	23	6
Total	59	30

Table 1: The number and timing of the urodynamic studies in each group.

Radiology

A cystogram was performed on a total of 120 occasions, which included a urodynamic study in all those performed at six and 12 months. For those with a cystogram alone up to 100ml of 15% urografin was instilled via the suprapubic catheter, with the sheep awake. Films were taken in the antero-posterior and lateral projections. Details were recorded on the volume of the bladder, the shape, the presence of leak and the presence of vesicoureteric reflux.

An intravenous pyelogram was performed in the awake sheep in all the study animals that survived to three weeks, and then again at three months. This was done to ensure the well-being of the animals, and that unexpected renal consequences of the procedure had not occurred. Fifty millilitres of 30% urografin was injected into the internal jugular vein and three views of the kidneys and bladder were taken. This gave information on the function and drainage of the kidneys, and the configuration of the bladder. The numbers of radiological studies in each of the groups are given in Tables 2 & 3.

At the time of the urodynamic study at six and 12 months, the bladder was imaged after the urodynamic study to assess the shape and regularity of the bladder outline. The volume of contrast used for the studies was determined by the bladder volume during the urodynamic study.

	10 days	6 months	12 months
AAGC	15	13	6
DMGC	7	5	3
AAOC	8	6	4
AACC	7	6	6
DMCC	10	5	5
Control	-	23	6
Total	47	58	30

Table 2: The numbers of cystograms performed in each group.

	3 weeks	3 months
AAGC	16	12
DMGC	6	5
AAOC	9	6
AACC	6	5
DMCC	6	6
Control	-	-
Total	43	34

Table 3: The numbers of intravenous pyelograms performed in each group.

Histology

Following sacrifice, the urinary bladder, ureters, kidneys and gastric or colonic muscle pedicle, were removed and fixed in 10% buffered formalin. The bladder was filled to capacity with formalin after it had been removed from the animal. Sections were taken from the bladder to include mucosa, subepithelial connective tissue, gastric muscle, bladder muscle, and the suture line joining the two, so that mucosa and muscularis propria were fully examined in each case. Routine staining was performed with haematoxylin and eosin. Histology was only obtained on 56 of 67 animals because of difficulties in accessing some of the animals after death at the farm or where material was thought unlikely to contribute to interpretation of results.

The kidneys, stomach and colon were examined macroscopically in all animals, but histologically in only a selected few.

Animal usage and Timing of Sacrifice

All study animals were between 8-10 wks at the time of the bladder augmentation, and all the animals that survived to assessment of their bladder function were male.

Autoaugmentation Gastrocystoplasty

A total of 27 lambs had an AAGC; there were two groups in this part of the study. The first *seven* animals were used to assess the feasibility of the AAGC procedure and the urothelial survival. *Two* animals were culled at the end of the procedure to ensure feasibility of the technique, *an additional* animal was sacrificed at one week and *one* at one month for assessment of the welfare of the animals as judged by the

state of the bladder at that early stage. After radiological assessment *three* further animals were sacrificed at two months.

The subsequent *20* animals were used to compare with the longer-term results of the other animal groups. This was the first study group to be operated on, and only after the operation had been shown to be possible and likely to be successful was the group expanded. The other limbs of the study were then instigated. Of these 20 AAGC animals, *one* died in the early post operative period from non-surgical complications, *four* animals developed adhesions and/or sepsis, and were sacrificed. *One* was sacrificed at four months and *one* other died without an autopsy. *Five* were sacrificed after the urodynamic study at six months and one died of urosepsis. *Seven* had an attempted urodynamic study at 12 months, of which one failed because the suprapubic catheter could not be inserted.

Demucosalised Clam Gastrocystoplasty

Eleven animals had a DMGC. *Two* of the DMGC animals were culled at seven days after operation. *Two* sheep died shortly after surgery: one on day five, because of bladder leak, one on day 10 because of bowel obstruction. All were examined histologically as part of the assessment of the urothelial ingrowth onto the denuded gastric muscle segment. Of the remaining *seven* animals, *one* was sacrificed at 14 days and *one* 21 days after surgery, to further study the urothelial ingrowth. Combined urodynamic and cystogram studies were performed in these five animals at six months at which time *two* were sacrificed. The last *three* sheep had follow-up investigations at 12 months.

Autoaugmentation

Ten lambs had an autoaugmentation omentocystoplasty (AAOC). *Three* were sacrificed at seven, 56 and 112 days, to study the survival of the underlying urothelial graft and the early histological response. *Two* animals died while awaiting a urodynamic study. No pathological information is available on these animals. *Five* sheep had cystometry at six months of which *one* was sacrificed. The remaining animals had a urodynamic study at 12 months.

Autoaugmentation Colocystoplasty

Nine animals had an AACC, of which *three* were sacrificed prior to six months; two at seven days and one at one month. Their bladders were examined histologically to assess the survival of the urothelial graft under the colonic muscle. *Six* have had urodynamic studies at six and 12 months.

Demucosalised Clam Colocystoplasty

Ten lambs had a DMCC of which *five* were culled at up to six months; four at weekly intervals for four weeks to study growth of the urothelium over the colonic muscle, and one sacrificed at 25 weeks due to an unexplained gut infarction. The remaining *five* had a urodynamic study at six and 12 months.

Control group

Twenty-three, six month old male sheep, of similar weights to the study animals,

formed the control group. A further six control animals had a urodynamic study at 12 months of age.

Table 4

AAGC	27
DMGC	11
AAOC	10
AACC	9
DMCC	10
Control	29
Total	96

Table 4: Summary of the animals used in each study group.

Statistics

The Mann-Whitney μ test (also known as the Wilcoxon Rank Sum test) was used to analyse the urodynamic data. This test was chosen because of the small sample size, where the distribution was unknown. This test can handle non-parametric data, and does so by ranking the data rather than taking its magnitude into account.

SHEEP RESULTS

Urodynamics

The urodynamic results (Tables 5-16) have been grouped, for each operation type, into those at six months and those at 12 months. The mean and standard deviation of the volume and compliance at 20 cmH_2O bladder pressure, and mean and standard deviation for the pressure, volume and compliance at the end of fill are given for each of the groups, and these calculations are grouped in Tables 17 and 18, for ease of comparison. As the numbers in many of the groups are small the medians and ranges are also given and listed in Tables 19 and 20.

In Figures 6 through to 9, the volume and compliance values for all those animals studied have been plotted for each of the animal groups, and charted for the six and twelve month urodynamic investigations.

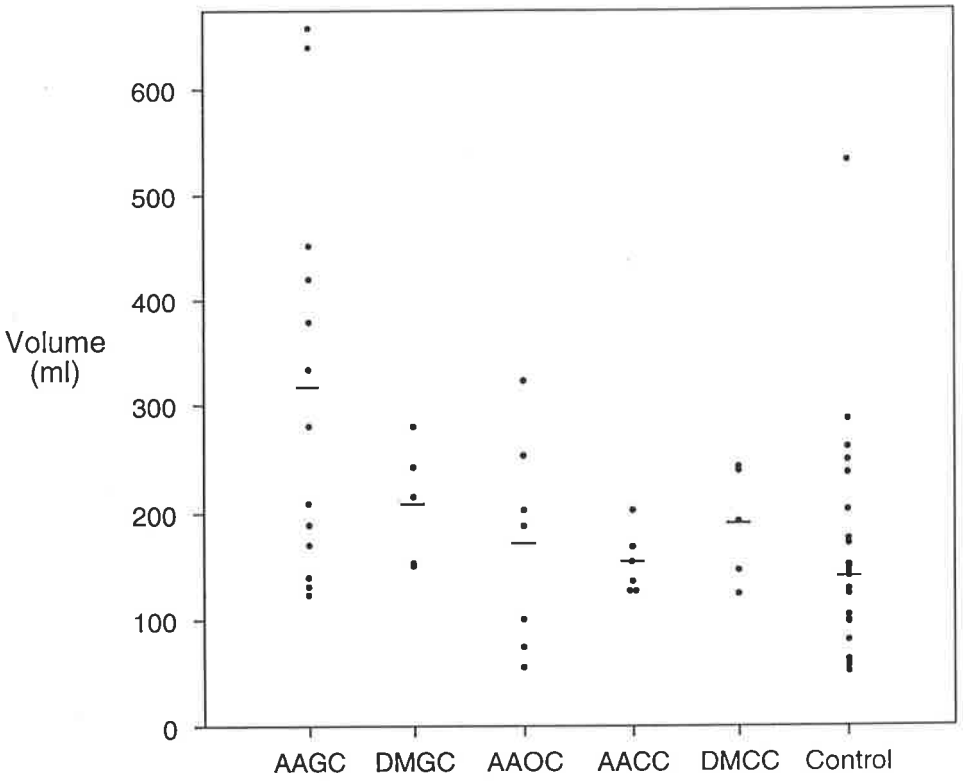


Figure 6: The values and medians (-) for ***sheep bladder volumes*** at ***six*** months, grouped according to the type of operation performed.

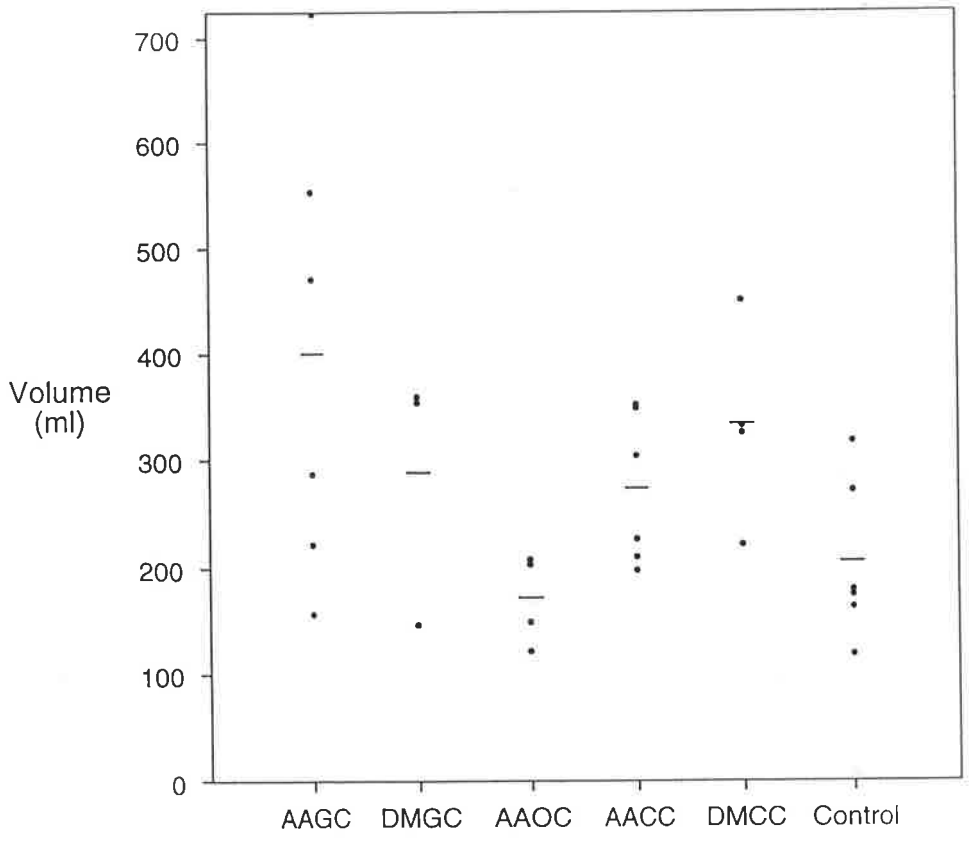


Figure 7: The values and medians (-) for ***sheep bladder volumes*** at ***twelve*** months, grouped according to the type of operation performed.

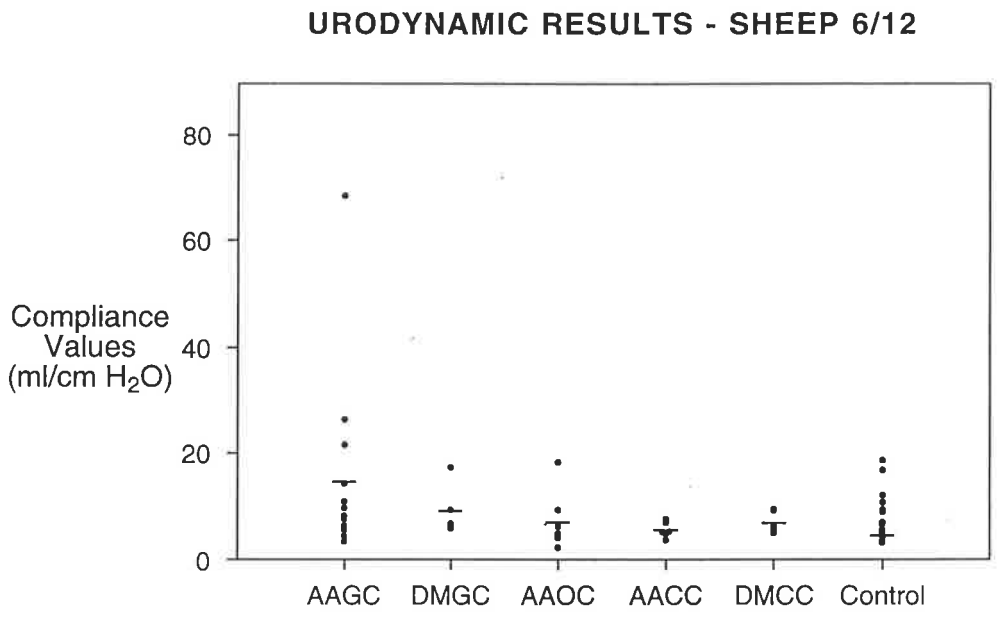


Figure 8: The values and medians (-) for ***compliance values*** at ***six*** months, grouped according to the type of operation performed.

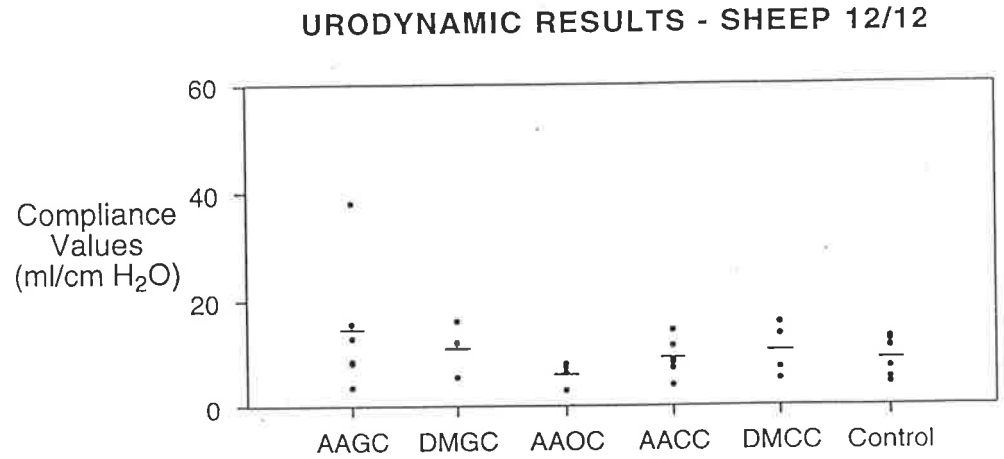


Figure 9: The values and medians (-) for ***compliance values*** at ***twelve*** months, grouped according to the type of operation performed.

Table 5: Autoaugmentation Gastrocystoplasty - Six months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	4-330	43	250	12.5	279	28.5	9.8
2.	5-426	40	158	7.9	208	47.4	4.4
3.	0-151	45	-	-	130	17.0	7.7
4.	5-284	40	-	-	380	17.6	21.6
5.	6-390	47	-	-	420	6.1	68.6
6.	7-36	37	107	5.4	170	49.6	3.4
7.	72-271	45	292	14.6	336	41.5	8.1
8.	72-277	37	334	16.7	453	32.0	14.2
9.	7-392	34	59	3.0	124	20.1	6.2
10.	7-50	35	312	15.6	638	58.3	10.9
11.	7-89	33	120	6.0	140	25.4	5.5
12.	7-125	36	105	5.3	189	53.3	3.5
13.	7-37	?	533	26.7	656	24.8	26.4
		Mean	**227**	**11.4**	**317**	**32.4**	**14.6**
		S.D.	**146**	**7.3**	**184**	**16.2**	**17.6**
		Median	**204**	**10.2**	**279**	**32.0**	**7.9**
Range		**Low**	**59**	**3.0**	**124**	**6.1**	**3.4**
		High	**533**	**26.7**	**656**	**58.3**	**68.6**

Table 6: Autoaugmentation Gastrocystoplasty - Twelve months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	5-284	?	720	36.0	725	18.8	38.6
2.	6-390	?	-	-	552	15.9	15.5
3.	72-277	?	137	6.9	219	25.9	8.5
4.	7-392	38.4	202	10.1	286	33.1	8.6
5.	7-89	25.6	128	6.4	156	39.6	3.9
6.	7-37	43.6	382	19.1	472	36.9	12.8
		Mean	**314**	**15.7**	**401**	**28.4**	**14.7**
		S.D.	**223**	**11.2**	**120**	**8.9**	**11.3**
		Median	**202**	**10.1**	**378**	**29.5**	**10.7**
Range		**Low**	**128**	**6.4**	**156**	**15.9**	**3.9**
		High	**720**	**36.0**	**725**	**39.6**	**38.6**

Wt. in Kilograms; Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20; Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 7: Demucosalised Clam Gastrocystoplasty - Six months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	72-288	32	-	-	242	14.0	17.3
2.	72-290	37	208	10.4	219	24.1	9.1
3.	72-292	33	119	6.0	152	22.8	6.7
4.	72-293	39	128	6.4	150	24.4	6.1
5.	7-391	32	189	9.5	280	49.5	5.7
		Mean	**161**	**8.1**	**209**	**27.0**	**9.0**
		S.D.	**44**	**2.2**	**57**	**13.3**	**4.8**
		Median	**159**	**7.9**	**219**	**24.1**	**6.7**
Range		**Low**	**119**	**6.0**	**150**	**14.0**	**5.7**
		High	**208**	**10.4**	**280**	**49.5**	**17.3**

Table 8: Demucosalised Clam Gastrocystoplasty - Twelve months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	72-288	32.5	130	6.5	146	26.4	5.5
2.	72-290	42.6	326	16.3	353	29.4	12.0
3.	7-391	36.8	276	13.8	359	22.0	16.3
		Mean	**244**	**12.2**	**286**	**25.9**	**11.3**
		S.D.	**102**	**5.1**	**121**	**3.7**	**5.4**
		Median	**276**	**13.8**	**353**	**26.4**	**12.0**
Range		**Low**	**130**	**6.5**	**146**	**22.0**	**5.5**
		High	**326**	**16.3**	**359**	**29.4**	**16.3**

Wt. in Kilograms; Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20;
Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 9: Autoaugmentation - Six months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	72-260	33.0	-	-	55	13.6	4.0
2.	72-287	38.0	263	13.2	322	35.5	9.1
3.	72-289	34.0	-	-	253	13.9	18.2
4.	72-294	37.0	133	6.7	189	39.6	4.8
5.	7-389	32.0	59	3.0	101	21.9	4.6
6.	72-274	23.8	39	2.0	73	34.6	2.1
7.	70-580	30.0	83	4.2	201	38.8	5.2
		Mean	**115**	**5.8**	**171**	**28.3**	**6.9**
		S.D.	**90**	**4.5**	**99**	**11.5**	**5.4**
		Median	**83**	**4.2**	**201**	**34.6**	**4.6**
Range		**Low**	**39**	**2.0**	**73**	**13.6**	**2.1**
		High	**263**	**13.2**	**322**	**39.6**	**18.2**

Table 10: Autoaugmentation - Twelve months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	72-287	45.6	134	6.7	148	23.5	6.3
2.	72-289	38.8	165	8.3	207	25.3	8.2
3.	72-294	40.0	174	8.7	202	28.0	7.2
4.	7-389	35.6	105	5.3	122	38.4	3.2
		Mean	**145**	**7.3**	**170**	**28.8**	**6.2**
		S.D.	**31**	**1.6**	**42**	**6.7**	**2.2**
		Median	**150**	**7.5**	**175**	**26.6**	**6.8**
Range		**Low**	**105**	**5.3**	**122**	**23.5**	**3.2**
		High	**174**	**8.7**	**207**	**38.4**	**8.2**

Wt. in Kilograms; Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20; Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 11: Autoaugmentation Colocystoplasty - Six months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	70-588	27.8	114	5.7	128	27.4	4.7
2.	80-538	27.0	108	5.4	128	25.0	5.1
3.	80-527	?	51	2.6	135	35.6	3.8
4.	80-537	29.0	146	7.3	155	21.4	7.3
5.	80-533	30.4	141	7.1	173	34.1	5.1
6.	8-45	29.2	175	8.0	203	24.6	7.5
		Mean	**123**	**6.1**	**154**	**28.0**	**5.7**
		S.D.	**42.5**	**2.1**	**30**	**5.6**	**1.7**
	Median		**128**	**6.3**	**145**	**26.2**	**5.1**
Range		**Low**	**51**	**2.6**	**128**	**21.4**	**3.8**
		High	**175**	**8.0**	**203**	**35.6**	**7.5**

Table 12: Autoaugmentation Colocystoplasty - Twelve months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	70-588	42.0	322	16.1	350	24.0	14.6
2.	80-538	43.0	294	14.7	351	31.1	11.3
3.	80-527	48.0	101	5.1	224	55.1	4.1
4.	80-537	52.0	167	8.4	197	22.0	9.0
5.	80-533	53.0	190	9.5	210	27.9	7.5
6.	8-45	52.0	237	11.9	305	35.6	8.6
		Mean	**218**	**10.9**	**273**	**32.6**	**9.2**
		S.D.	**83**	**4.1**	**71**	**12.1**	**3.5**
	Median		**214**	**10.8**	**265**	**35.5**	**8.8**
Range		**Low**	**101**	**5.1**	**197**	**22.0**	**4.1**
		High	**322**	**16.1**	**351**	**55.1**	**14.6**

Wt. in Kilograms; Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20; Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 13: Demucosalised Clam Colocystoplasty - Six months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	80-524	27.3	116	5.8	127	24.0	5.3
2.	80-549	32.6	230	11.5	240	25.8	9.3
3.	8-43	27.2	219	11.0	239	26.4	9.1
4.	8-46	29.4	132	6.6	151	31.4	4.8
5.	8-44	29.8	165	8.3	192	32.6	5.9
		Mean	**172**	**8.6**	**190**	**28.0**	**6.9**
		S.D.	**51**	**2.5**	**51**	**3.7**	**2.2**
	Median		**165**	**8.3**	**192**	**26.4**	**5.9**
Range		**Low**	**116**	**5.8**	**127**	**24.0**	**4.8**
		High	**230**	**11.5**	**240**	**32.6**	**9.3**

Table 14: Demucosalised Clam Colocystoplasty - Twelve months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	80-524	48	Failed catheter insertion				
2.	80-549	60	321	16.1	333	20.6	16.2
3.	8-43	47	350	17.5	452	32.9	13.7
4.	8-46	47	191	9.6	221	40.9	5.4
5.	8-44	54	280	14.0	327	44.8	7.3
		Mean	**286**	**14.3**	**333**	**34.8**	**10.7**
		S.D.	**69**	**3.5**	**94**	**10.7**	**5.1**
	Median		**301**	**15.1**	**330**	**36.9**	**10.5**
Range		**Low**	**191**	**9.6**	**221**	**20.6**	**5.4**
		High	**350**	**17.5**	**452**	**44.8**	**16.2**

Wt. in Kilograms; Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20; Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 15: Control - Six months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	1	43.0	-	-	203	12.2	16.6
2.	6-381	47.4	249	12.5	287	26.3	10.9
3.	5-294	40.8	254	12.7	260	21.4	12.1
4.	5-289	35.8	128	6.4	148	34.3	4.3
5.	7-41	40.5	450	22.5	532	28.6	18.6
6.	7-245	35.8	-	-	175	19.0	9.2
7.	7-246	36.0	204	10.2	237	34.3	6.9
8.	8-160	48.6	228	11.4	249	26.8	9.3
9.	453	31.2	81	4.0	99	25.5	3.9
10.	473	32.0	118	5.9	124	20.4	6.1
11.	454	29.0	119	6.0	145	32.0	4.5
12.	472	17.0	56	2.8	171	26.6	6.4
13.	474	16.8	33	1.7	98	32.0	3.1
14.	796	29.8	104	5.2	151	33.3	4.5
15.	795	22.6	96	4.8	104	21.3	4.9
16.	39	26.4	68	3.4	104	37.4	2.8
17.	542	25.0	70	3.5	62	18.8	3.3
18.	52	30.0	146	7.3	55	16.9	3.3
19.	146	31.4	51	2.5	80	22.5	3.6
20.	643	-	58	2.9	50	19.5	2.6
21.	17	19.6	58	2.9	58	20.0	2.9
22.	one	31.2	99	5.0	141	23.0	6.2
23.	2	33.0	-	-	128	32.9	3.9
		Mean	**134**	**6.7**	**159**	**25.4**	**6.5**
		S.D.	**100**	**5.0**	**106**	**6.7**	**4.4**
		Median	**102**	**5.1**	**141**	**25.5**	**4.5**
Range		**Low**	**33**	**1.7**	**50**	**12.2**	**2.6**
		High	**450**	**22.5**	**532**	**37.4**	**18.6**

Wt. in Kilograms; Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20; Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 16: Control - Twelve months

			p=20		Leak Point		
No.	Name	Wt.	Vol.	Comp.	Vol.	Pres.	Comp.
1.	642	53	-	-	164	14.4	11.4
2.	640	53	-	-	177	14.0	12.6
3.	641	52	220	11.0	270	35.3	7.6
4.	643	48	34	1.7	118	26.9	4.4
5.	644	54	57	2.9	178	31.6	5.6
6.	645	52	299	15.0	317	25.1	13.0
		Mean	**152**	**7.6**	**205**	**24.6**	**9.1**
		S.D.	**128**	**6.4**	**77**	**8.8**	**3.7**
		Median	**137**	**7.0**	**178**	**26.0**	**9.5**
Range		**Low**	**34**	**1.7**	**118**	**14.0**	**4.4**
		High	**299**	**15.0**	**317**	**35.3**	**13.0**

Wt. in Kilograms; Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20; Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 17: Overall Urodynamic mean and standard deviations - Six months

	p=20		Leak Point		
	Vol.	Comp.	Vol.	Pres.	Comp.
AAGC	227±146	11.4±7.3	317±184	32.4±16.2	14.6±17.6
DMGC	161±44	8.1±2.2	209±57	27.0±13.3	9.0±4.8
AAOC	115±90	5.8±4.5	171±99	28.3±11.5	6.9±5.4
AACC	123±43	6.1±2.1	154±30	28.0±5.6	5.7±1.7
DMCC	172±51	8.6±2.5	190±51	28.0±3.7	6.9±2.2
Control	134±100	6.7±5.0	159±25	25.4±6.7	6.5±4.4

Table 18: Overall Urodynamic mean and standard deviations - Twelve months

	p=20		Leak Point		
	Vol.	Comp.	Vol.	Pres.	Comp.
AAGC	314±223	15.7±11.2	401±120	28.4±8.9	14.7±11.3
DMGC	244±102	12.2±5.1	286±121	25.9±3.7	11.3±5.4
AAOC	145±31	7.3±1.6	170±42	28.8±6.7	6.2±2.2
AACC	218±83	10.9±4.1	273±71	32.6±12.1	9.2±3.5
DMCC	286±69	14.3±3.5	333±94	34.8±10.7	10.7±5.1
Control	152±128	7.6±6.4	205±77	24.6±8.8	9.1±3.7

Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20;
Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 19: Overall Urodynamic ***medians*** - Six months

	p=20		Leak Point		
	Vol.	Comp.	Vol.	Pres.	Comp.
AAGC	204	11.4	317	32.4	14.6
DMGC	159	7.9	219	24.1	6.7
AAOC	83	4.2	201	34.6	4.6
AACC	128	6.3	145	26.2	5.1
DMCC	165	8.3	192	26.4	5.9
Control	134	6.7	159	25.4	6.5

Table 20: Overall Urodynamic ***medians*** - Twelve months

	p=20		Leak Point		
	Vol.	Comp.	Vol.	Pres.	Comp.
AAGC	202	10.1	378	29.5	10.7
DMGC	276	13.8	353	26.4	12.0
AAOC	150	7.5	175	26.6	6.8
AACC	214	10.8	265	35.5	8.8
DMCC	301	15.1	330	36.9	10.5
Control	137	7.0	178	26.0	9.5

Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20;
Pres. = pressure in cmH_20; p = 20 i.e. pressure = 20 cmH_20.

Table 21: Mann-Whitney comparisons of the pressure, volume and compliance results at the leak point for ***six month*** studies. All t values of 2.0000 or greater have been highlighted and the p values given.

Comparison (sample size)	Sum Ranks μm	μn	$E(\mu)$	SD	t
AAGC vs Control (m=13) vs (n=23)					
Volume ***(p < 0.01)***	338.5	327.5	425.5	30.36	**2.8653**
Pressure	396.0	270.0			0.9716
Compliance ***(p < 0.05)***	363.0	303.0			**2.0584**
DMGC vs Control (m=5) vs (n=23)					
Volume	304.0	102.0	333.5	16.67	1.7696
Pressure	335.0	71.0			0.0900
Compliance	309.5	97.5			1.4396
AAOC vs Control (m=7) vs (n=23)					
Volume	348.5	116.5	356.5	20.39	0.3923
Pressure	336.0	129.0			1.0052
Compliance	352.0	113.0			0.2207
AACC vs Control (m=6) vs (n=23)					
Volume	333.5	101.5	345.0	18.57	0.6191
Pressure	326.5	108.5			0.9960
Compliance	335.0	100.0			0.5384
DMCC vs Control (m=5) vs (n=23)					
Volume	311.5	94.5	333.5	16.67	1.3197
Pressure	321.0	85.0			0.7498
Compliance	317.5	88.5			0.9598

Comparison (sample size)	Sum Ranks μm	Sum Ranks μn	E(μ)	SD	t
AAGC vs DMGC (m=13) vs (n=5)					
Volume	131.0	40.0	123.5	10.14	0.7393
Pressure	133.0	38.0			0.9364
Compliance	126.0	45.0			0.2464
AAGC vs AAOC (m=13) vs (n=7)					
Volume	159.5	50.5	136.5	12.62	1.8226
Pressure	144.0	66.0			0.5943
Compliance	154.0	56.5			1.3868
AAGC vs AACC (m=13) vs (n=6)					
Volume ***($p < 0.07$)***	153.0	37.0	130.0	11.40	**2.0172**
Pressure	134.0	56.0			0.3508
Compliance	148.0	42.0			1.5787
AAGC vs DMCC (m=13) vs (n=5)					
Volume	135.0	36.0	123.5	10.14	1.1336
Pressure	125.0	46.0			0.1479
Compliance	132.0	39.0			0.8379

Comparison (sample size)	Sum Ranks μm	Sum Ranks μn	$E(\mu)$	SD	t
DMGC vs AAOC (m=5) vs (n=7)					
Volume	37.0	41.0	32.5	6.16	0.7308
Pressure	33.0	45.0			0.0812
Compliance	41.5	36.5			1.4616
DMGC vs AACC (m=5) vs (n=6)					
Volume	39.0	27.0	30.0	5.48	1.6432
Pressure	24.0	42.0			1.0954
Compliance	39.0	27.0			1.6432
DMGC vs DMCC (m=5) vs (n=5)					
Volume	31.0	24.0	27.5	4.79	0.7311
Pressure	22.0	33.0			1.1489
Compliance	31.5	23.5			0.8356
AAOC vs AACC (m=7) vs (n=6)					
Volume	50.0	41.0	49.0	7.00	0.1429
Pressure	51.0	40.0			0.2857
Compliance	48.0	43.0			0.1429
AAOC vs DMCC (m=7) vs (n=5)					
Volume	43.0	35.0	45.5	6.16	0.4060
Pressure	48.0	30.0			0.4060
Compliance	38.0	40.0			1.2180
AACC vs DMCC (m=6) vs (n=5)					
Volume	31.0	35.0	36.0	5.48	0.9200
Pressure	36.0	30.0			0.0000
Compliance	29.0	37.0			1.2780

Table 22: Mann-Whitney comparisons of the pressure, volume and compliance results at the leak point for ***twelve month*** studies. All t values of 2.0000 or greater have been highlighted and the p values given.

Comparison (sample size)	Sum Ranks μ_m	μ_n	E(μ)	SD	t
AAGC vs Control (m=6) vs (n=6)					
Volume	29.0	49.0	39.0	6.25	1.6013
Pressure	33.0	45.0			0.9608
Compliance	34.0	44.0			0.8006
DMGC vs Control (m=3) vs (n=6)					
Volume	26.0	19.0	30.0	3.87	1.0328
Pressure	30.0	15.0			0.0000
Compliance	28.0	17.0			0.5164
AAOC vs Control (m=4) vs (n=6)					
Volume	35.0	20.0	33.0	4.69	0.4264
Pressure	30.0	25.0			0.6396
Compliance	38.0	17.0			1.0660
AACC vs Control (m=6) vs (n=6)					
Volume	28.0	50.0	39.0	6.25	1.7614
Pressure	33.0	45.0			0.9608
Compliance	40.0	39.0			0.1601
DMCC vs Control (m=4) vs (n=6)					
Volume ***($p < 0.07$)***	23.0	32.0	33.0	4.69	**2.1320**
Pressure	26.0	29.0			1.4924
Compliance	30.0	25.0			0.6396

Comparison (sample size)	Sum Ranks μm	Sum Ranks μn	$E(\mu)$	SD	t
AAGC vs DMGC (m=6) vs (n=3)					
Volume	33.0	12.0	30.0	3.87	0.7746
Pressure	31.0	14.0			0.2582
Compliance	30.0	15.0			0.0000
AAGC vs AAOC (m=6) vs (n=4)					
Volume ***($p < 0.07$)***	43.0	12.0	33.0	4.69	**2.1320**
Pressure	33.0	22.0			0.0000
Compliance	42.0	13.0			1.9188
AAGC vs AACC (m=6) vs (n=6)					
Volume	44.0	34.0	39.0	6.25	0.8006
Pressure	37.0	41.0			0.3203
Compliance	42.5	35.5			0.5604
AAGC vs DMCC (m=6) vs (n=4)					
Volume	34.0	21.0	33.0	4.69	0.2132
Pressure	28.0	27.0			1.0660
Compliance	34.0	21.0			0.2132

Comparison (sample size)	Sum Ranks μm	Sum Ranks μn	E(μ)	SD	t
DMGC vs AAOC (m=3) vs (n=4)					
Volume	15.0	13.0	12.0	2.83	1.0607
Pressure	11.0	17.0			0.3536
Compliance	15.0	13.0			1.0607
DMGC vs AACC (m=3) vs (n=6)					
Volume	18.0	27.0	15.0	3.87	0.7746
Pressure	11.0	34.0			1.0328
Compliance	18.0	27.0			0.7746
DMGC vs DMCC (m=3) vs (n=4)					
Volume	12.0	16.0	12.0	2.83	0.0000
Pressure	9.0	19.0			1.0607
Compliance	13.0	15.0			0.3536
AAOC vs AACC (m=4) vs (n=6)					
Volume **($p < 0.07$)**	12.0	43.0	22.0	4.69	**2.1320**
Pressure	21.0	34.0			0.2132
Compliance	14.0	41.0			1.7056
AAOC vs DMCC (m=4) vs (n=4)					
Volume ***($p < 0.05$)***	10.0	26.0	18.0	3.46	**2.3094**
Pressure	15.0	21.0			0.8660
Compliance	14.0	22.0			1.1547
AACC vs DMCC (m=6) vs (n=4)					
Volume	29.0	26.0	23.0	4.69	0.8528
Pressure	31.0	24.0			0.4264
Compliance	32.0	23.0			0.2132

Radiology

No upper tract dilatation was shown for any of the IVP's performed at three weeks or three months in the study animals. The control group did not have IVP's, because they were largely performed to establish the well-being of the animals that had been operated on.

The size, shape and appearance of the bladder for each of the animal groups is shown in Tables 24-28, and representative views of low volume, and high volume bladders are given for the principle groups in Figures 10-19.

Table 24 Autoaugmentation Gastrocystoplasty - *Cystograms*

	10 d	6 mths	12 mths
Shape			
Irregular	9	0	0
Normal	6	13	5
Size			
Small	15	0	0
Medium	0	8	3
Large	0	5	2
VUR			
No	7	12	3
Unilateral	4	1	0
Bilateral	4	0	2

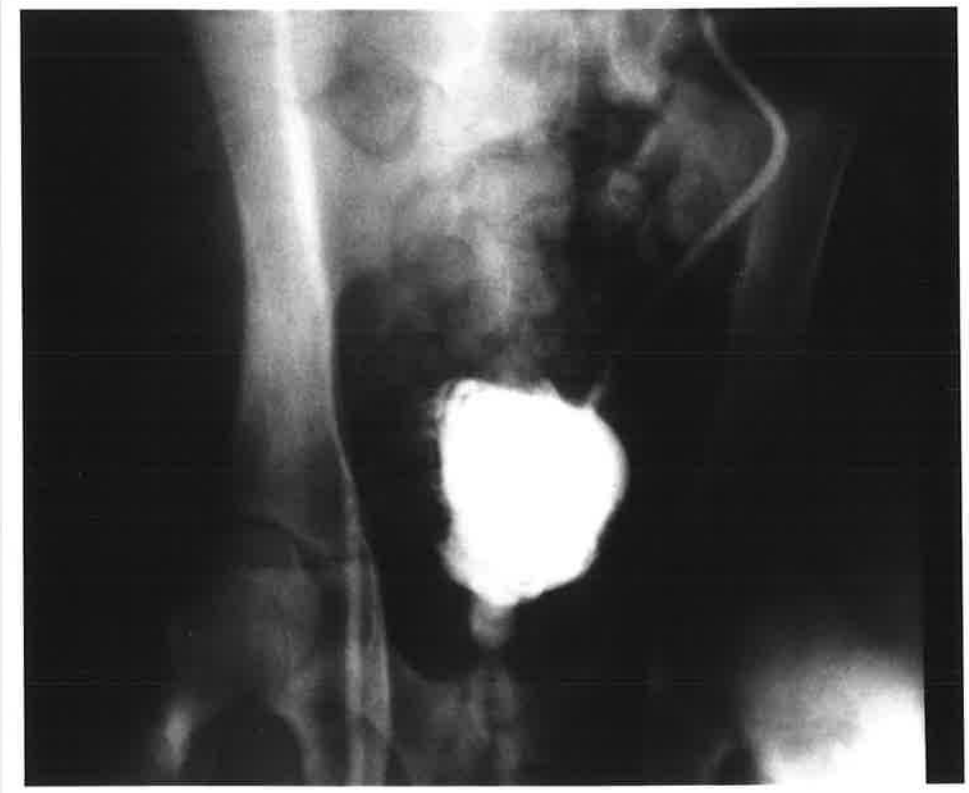


Figure 10A: An ***AAGC*** bladder (# 5-284) with ***good*** function shown on cystogram at <u>10 days</u>.

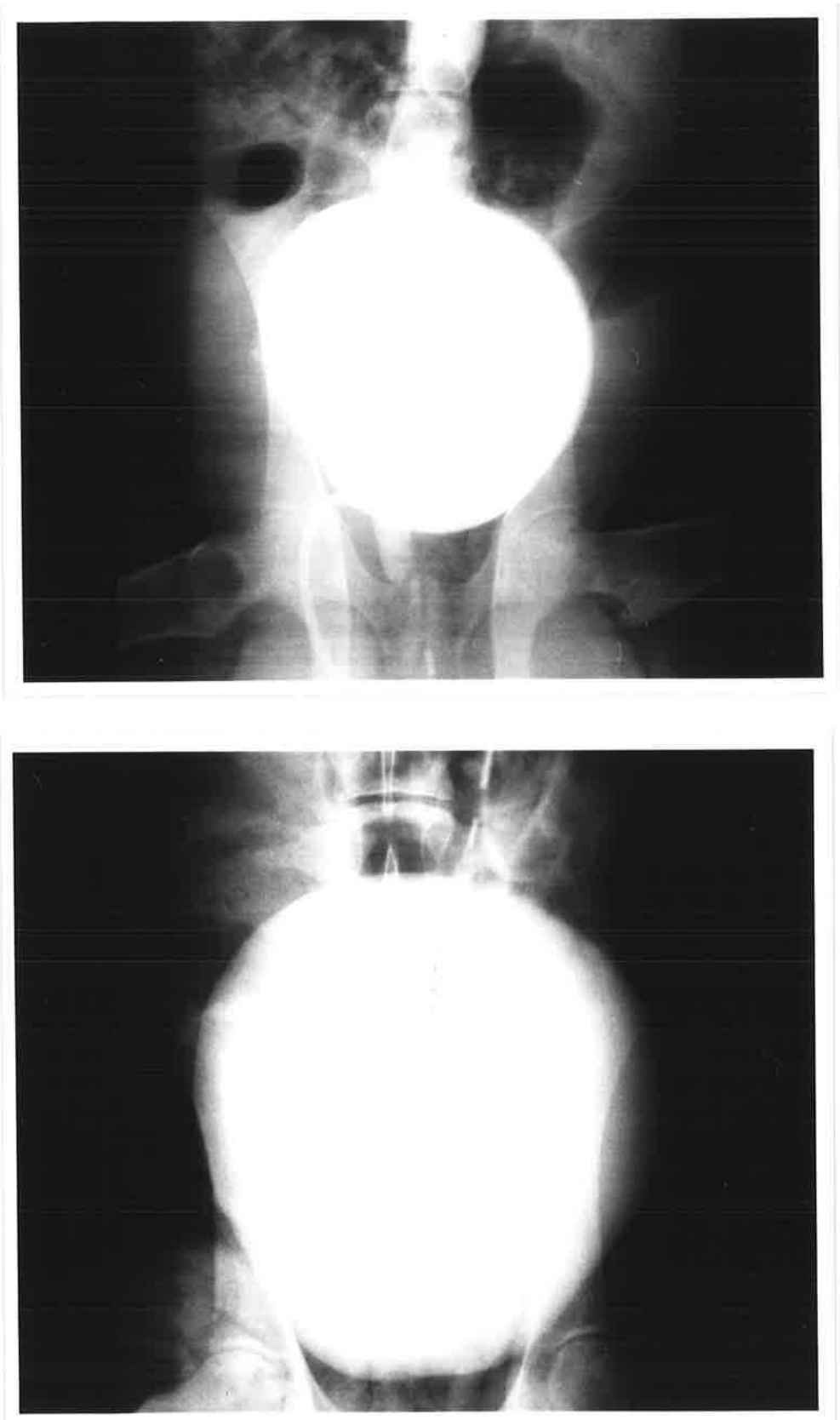


Figure 10B+C: An ***AAGC*** bladder (# 5-284) with ***good*** function shown on cystogram at 6 and 12 months (Volume = 725 ml: Compliance = 38.6 ml/cmH_2O @ 12 months).

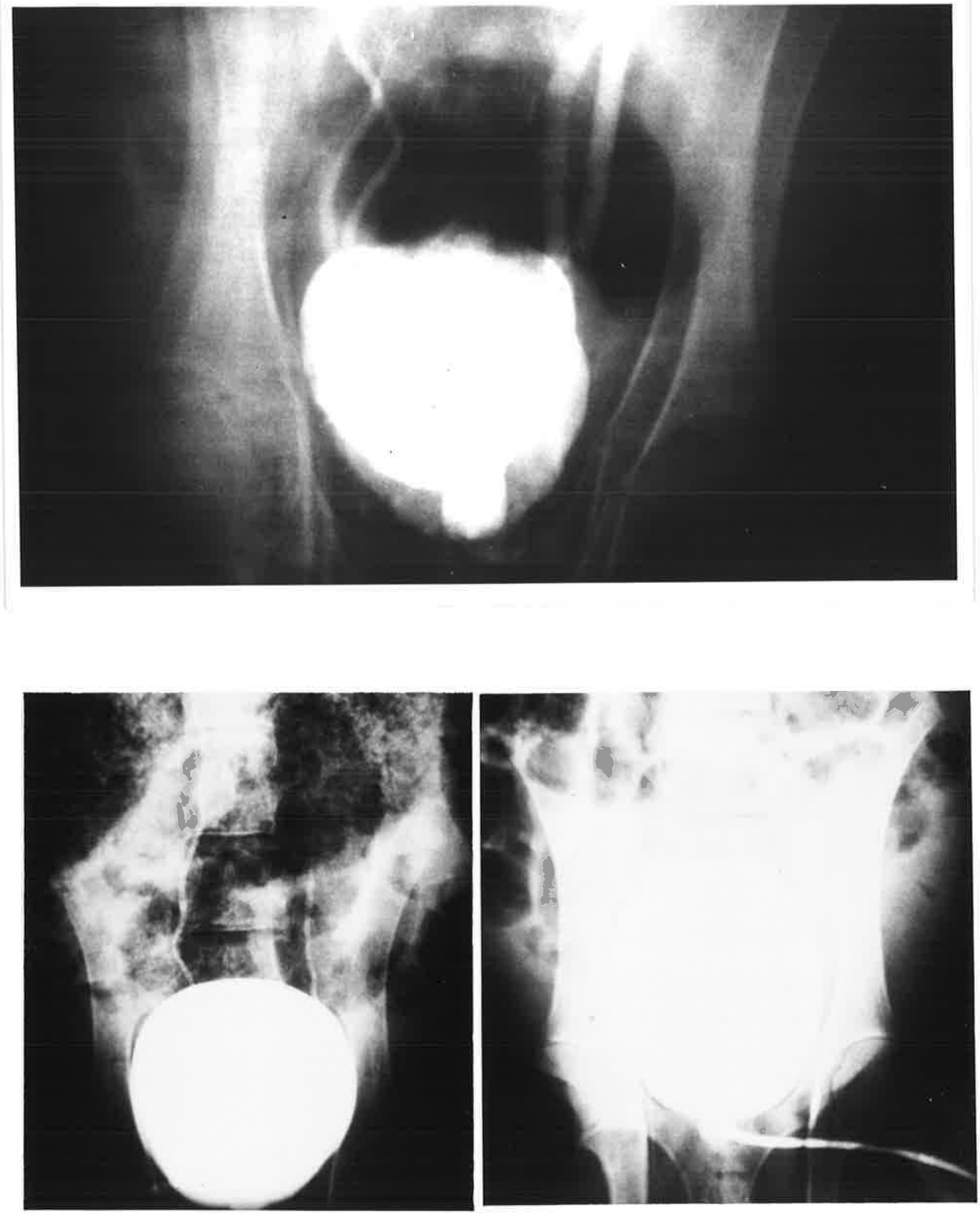


Figure 11A,B+C: An ***AAGC*** bladder (# 7-89) with ***bad*** function shown on cystogram at 10 days, 6 and 12 months (Volume = 156 ml: Compliance = 3.9 ml/cmH_2O @ 12 months).

Table 25 Demucosalised Clam Gastrocystoplasty - *Cystograms*

	10 d	6 mths	12 mths
Shape			
Irregular	5	0	1
Normal	2	5	2
Size			
Small	6	0	0
Medium	1	4	2
Large	0	1	1
VUR			
No	3	5	3
Unilateral	2	0	0
Bilateral	2	0	0

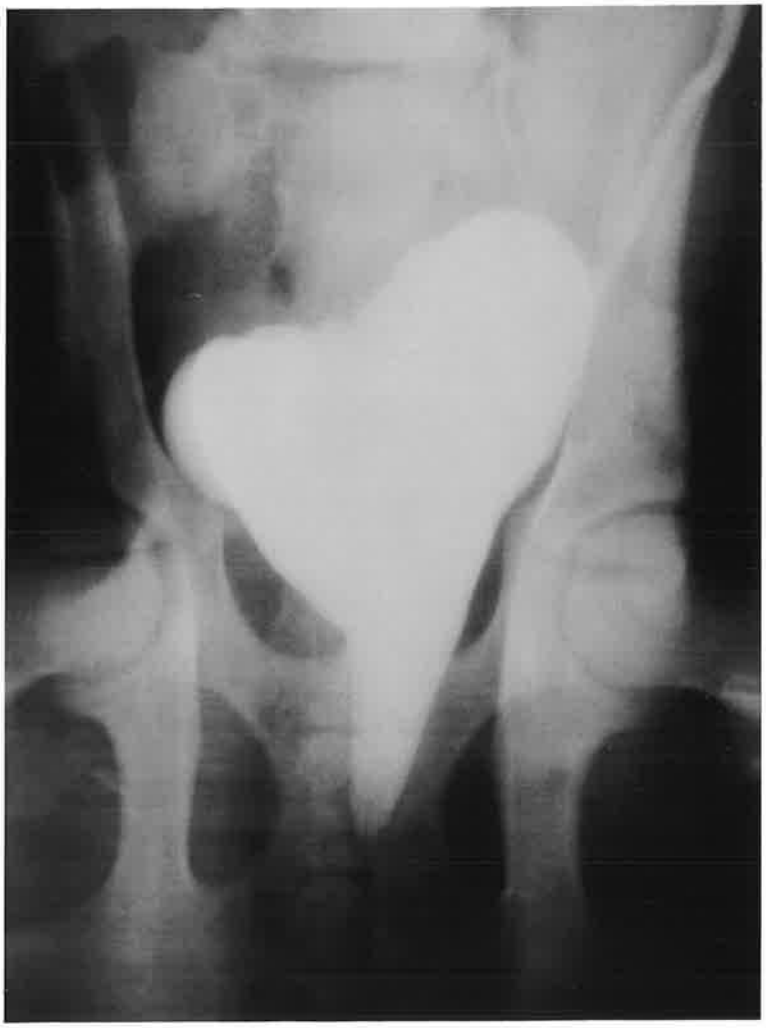
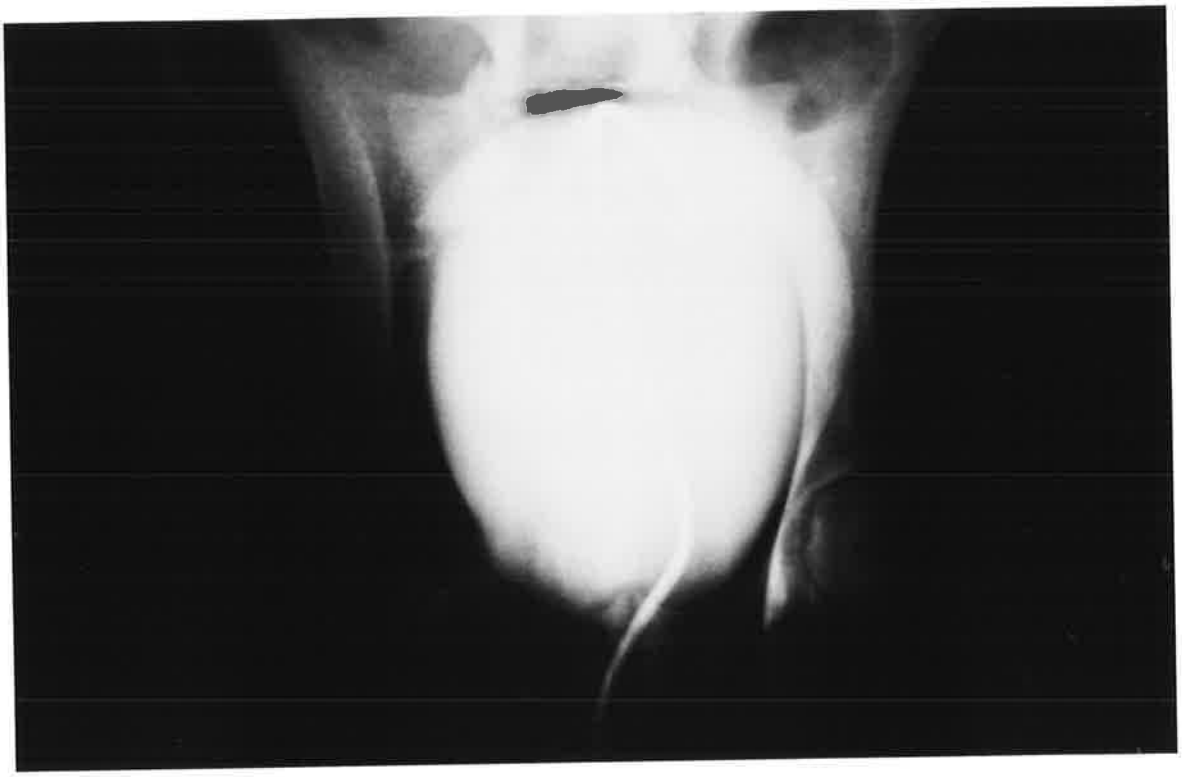


Figure 12A: A ***DMGC*** bladder (#72-290) with ***good*** function shown on cystogram at <u>10 days</u>.



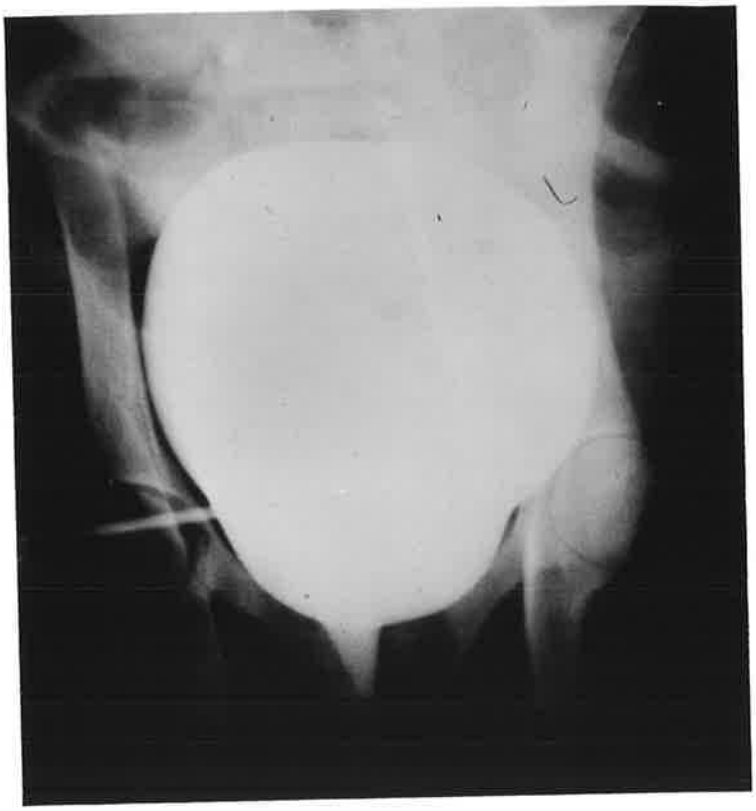


Figure 12B+C: A ***DMGC*** bladder (#72-290) with ***good*** function shown on cystogram at 6 and 12 months.(Volume = 353 ml: Compliance = 12.0 ml/cmH_2O @ 12 months).

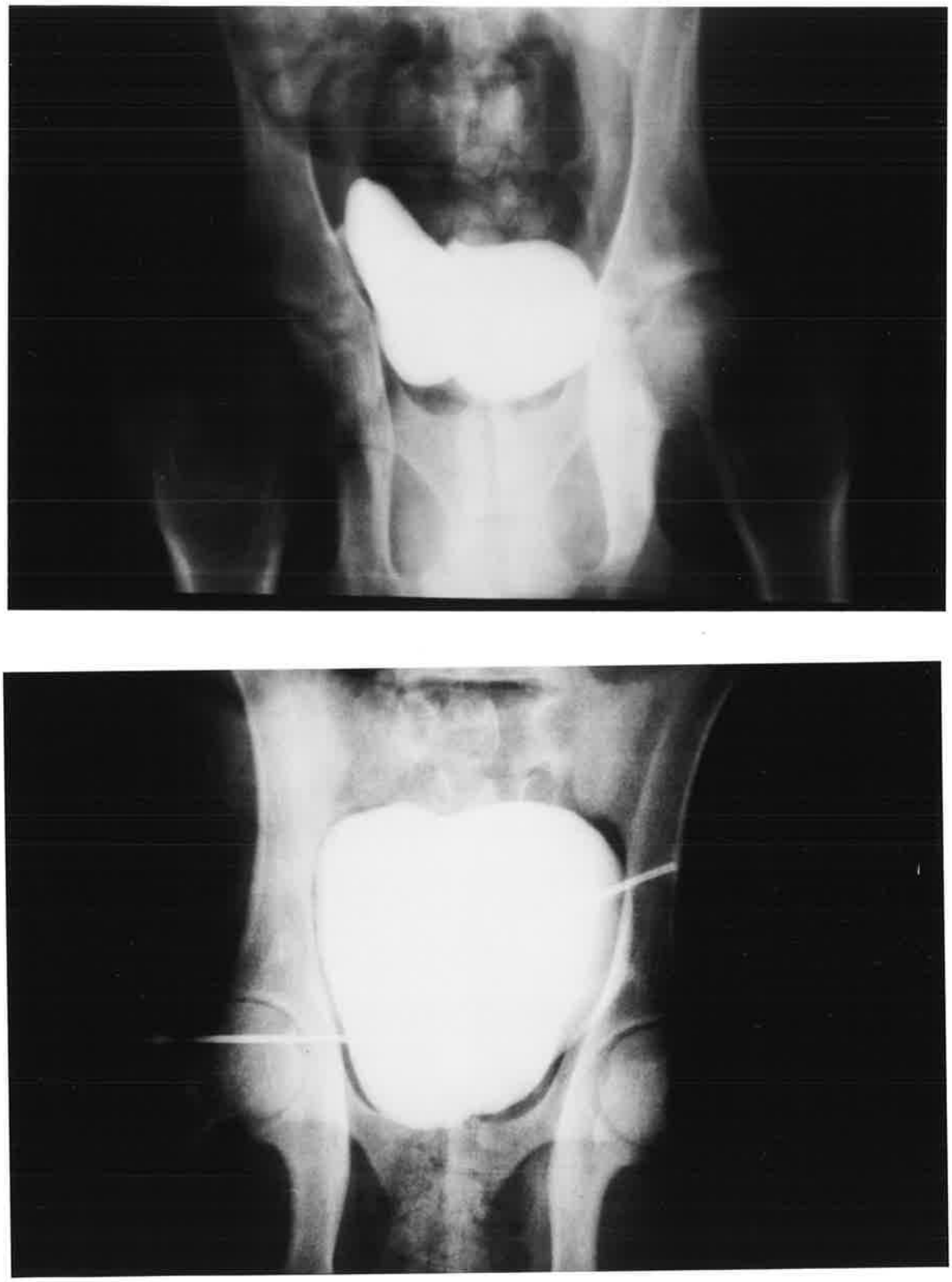


Figure 13A+B: A ***DMGC*** bladder (#72-288) with ***bad*** function shown on IVP at 3 weeks and on cystogram at 6 months.

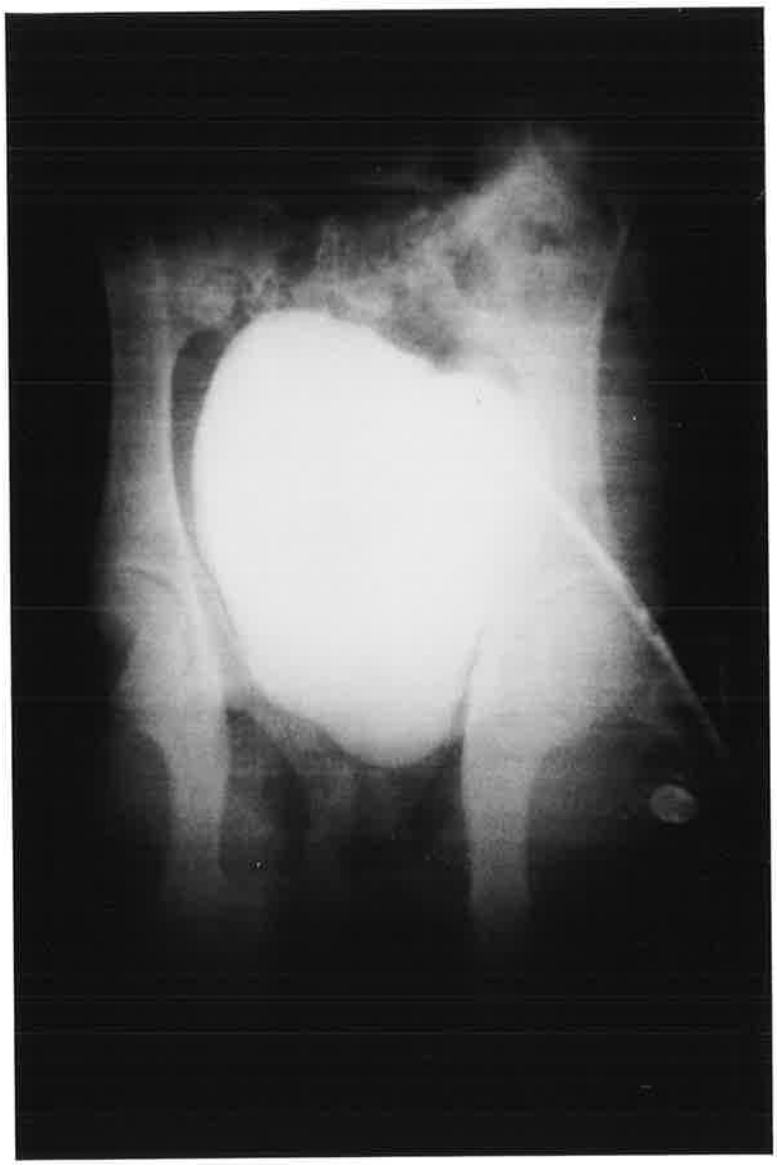


Figure 13C: A ***DMGC*** bladder (#72-288) with ***bad*** function shown on cystogram at 12 months (Volume = 146 ml: Compliance = 5.5 ml/cmH_2O @ 12 months).

Table 26 Autoaugmentation - *Cystograms*

	10 d	6 mths	12 mths
Shape			
Irregular	2	1	0
Normal	6	5	4
Size			
Small	7	0	0
Medium	1	5	3
Large	0	1	1
VUR			
No	7	5	3
Unilateral	1	0	1
Bilateral	0	1	0

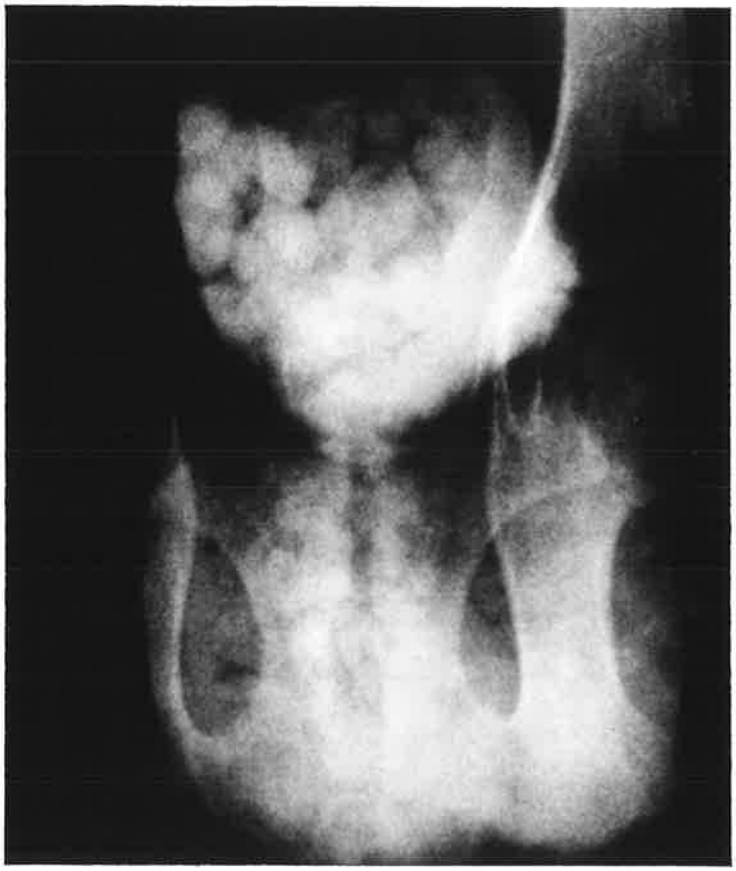


Figure 14A: An ***AAOC*** bladder (#72-294) with ***good*** function shown on IVP at 3 weeks.

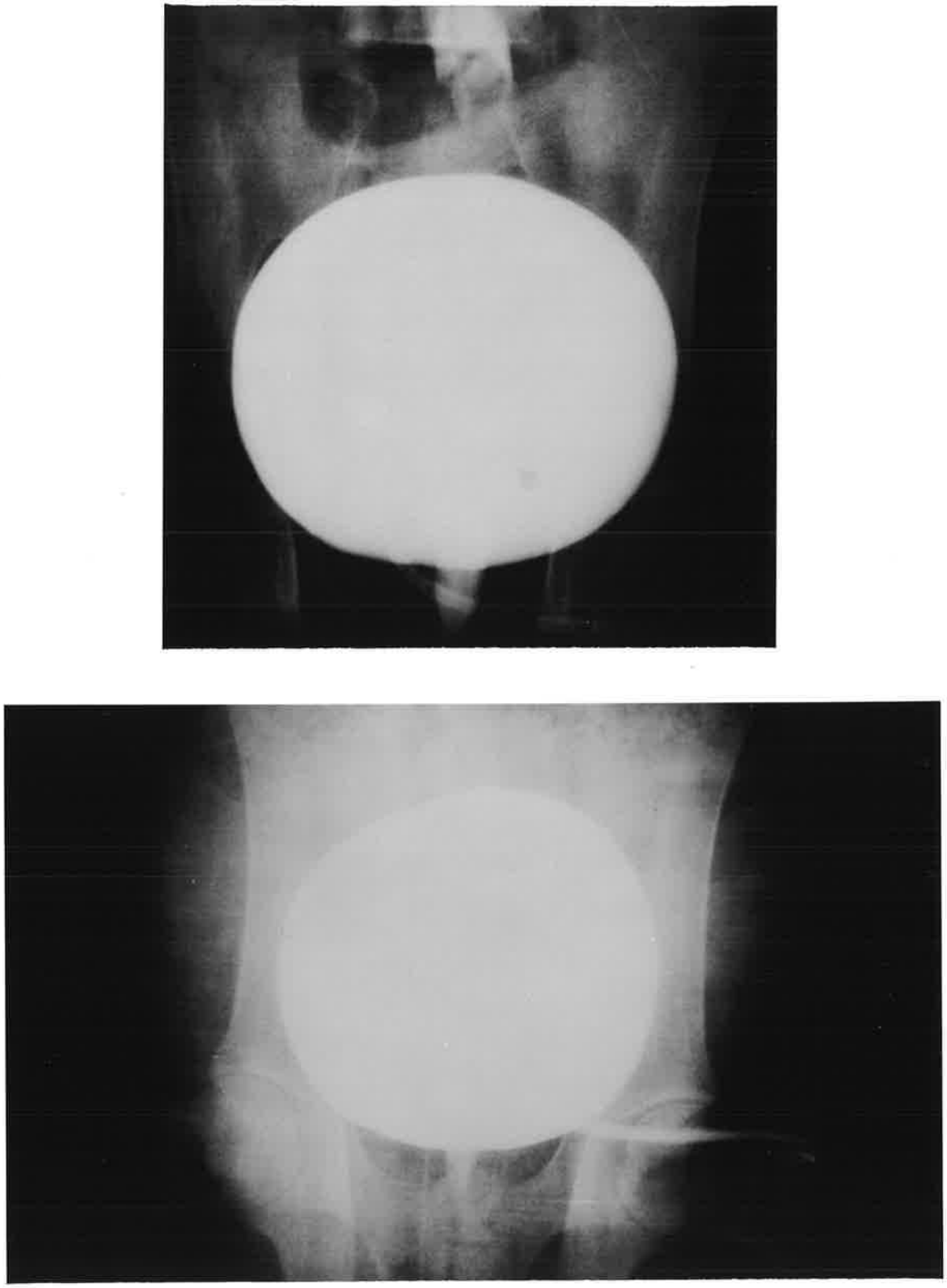


Figure 14B+C: An ***AAOC*** bladder (#72-294) with ***good*** function shown on cystogram at 6 and 12 months (Volume = 253 ml: Compliance = 18.2 ml/cmH_2O @ 12 months).

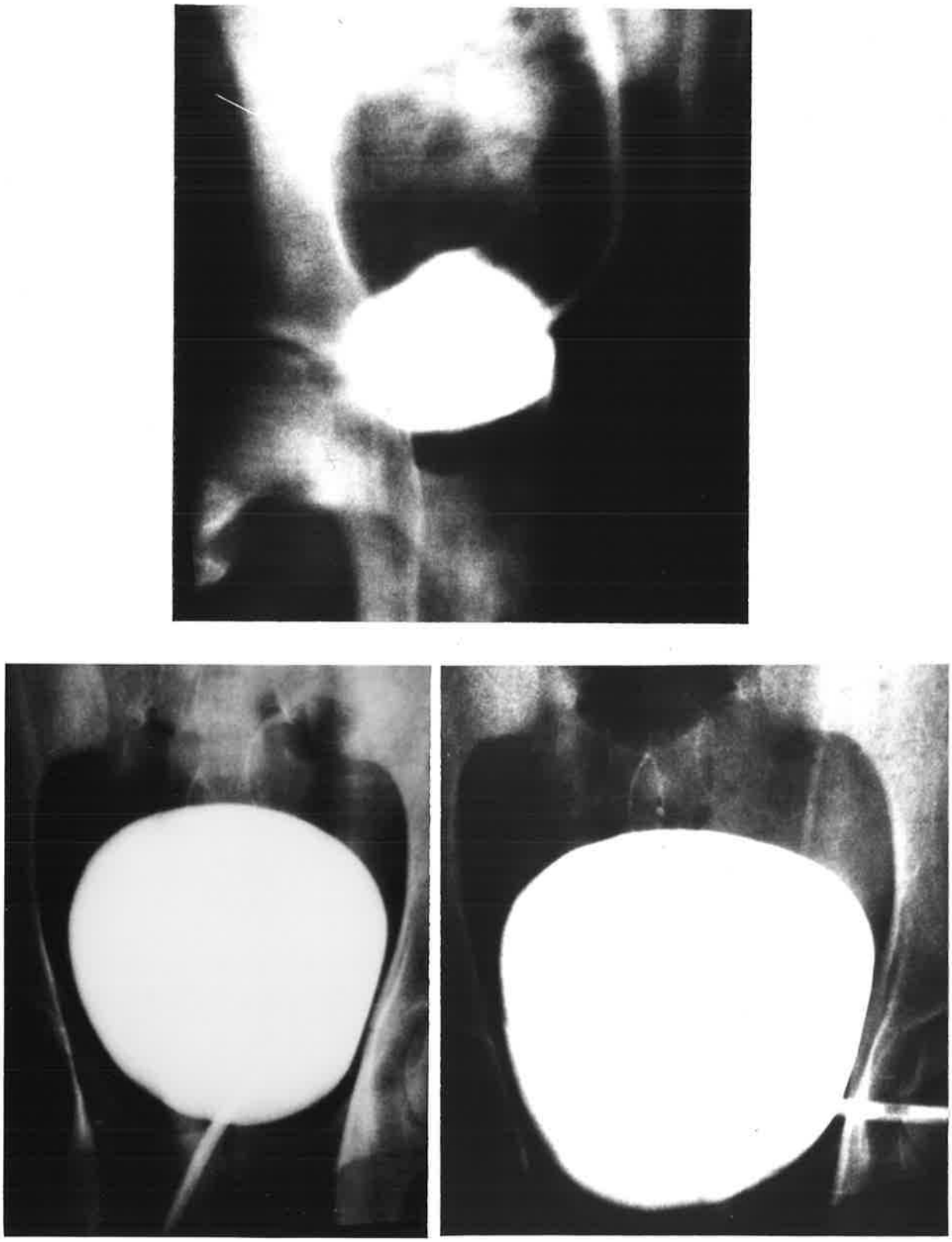


Figure 15: An ***AAOC*** bladder (#7-389) with ***bad*** function shown on cystogram at 10 days, 6 and 12 months (Volume = 122 ml: Compliance = 3.2 ml/cmH_2O @ 12 months).

Table 27 Autoaugmentation Colocystoplasty - *Cystograms*

	10 d	6 mths	12 mths
Shape			
Irregular	3	6	1
Normal	4	0	5
Size			
Small	6	0	0
Medium	1	6	2
Large	0	0	4
VUR			
No	3	6	6
Unilateral	0	0	0
Bilateral	4	0	0

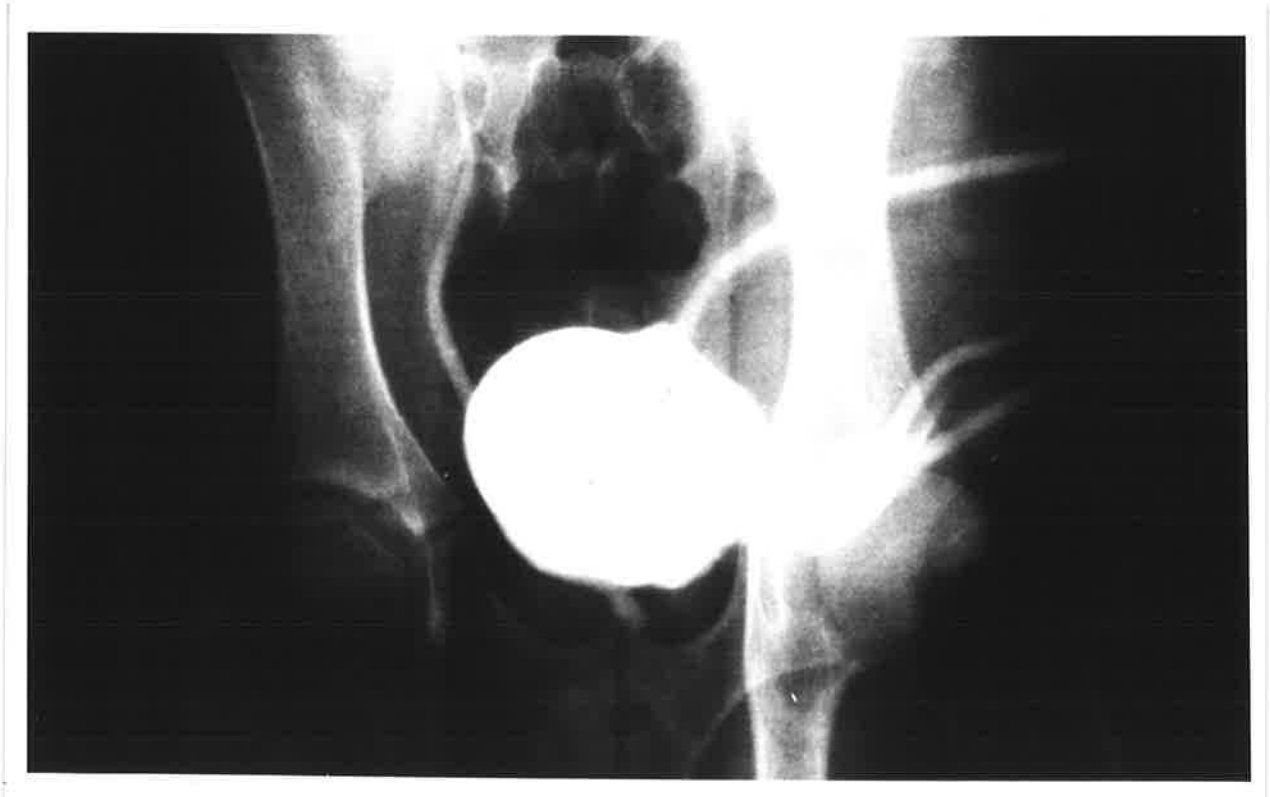


Figure 16A: An ***AACC*** bladder (#70-588) with ***good*** function shown on cystogram at 10 days.

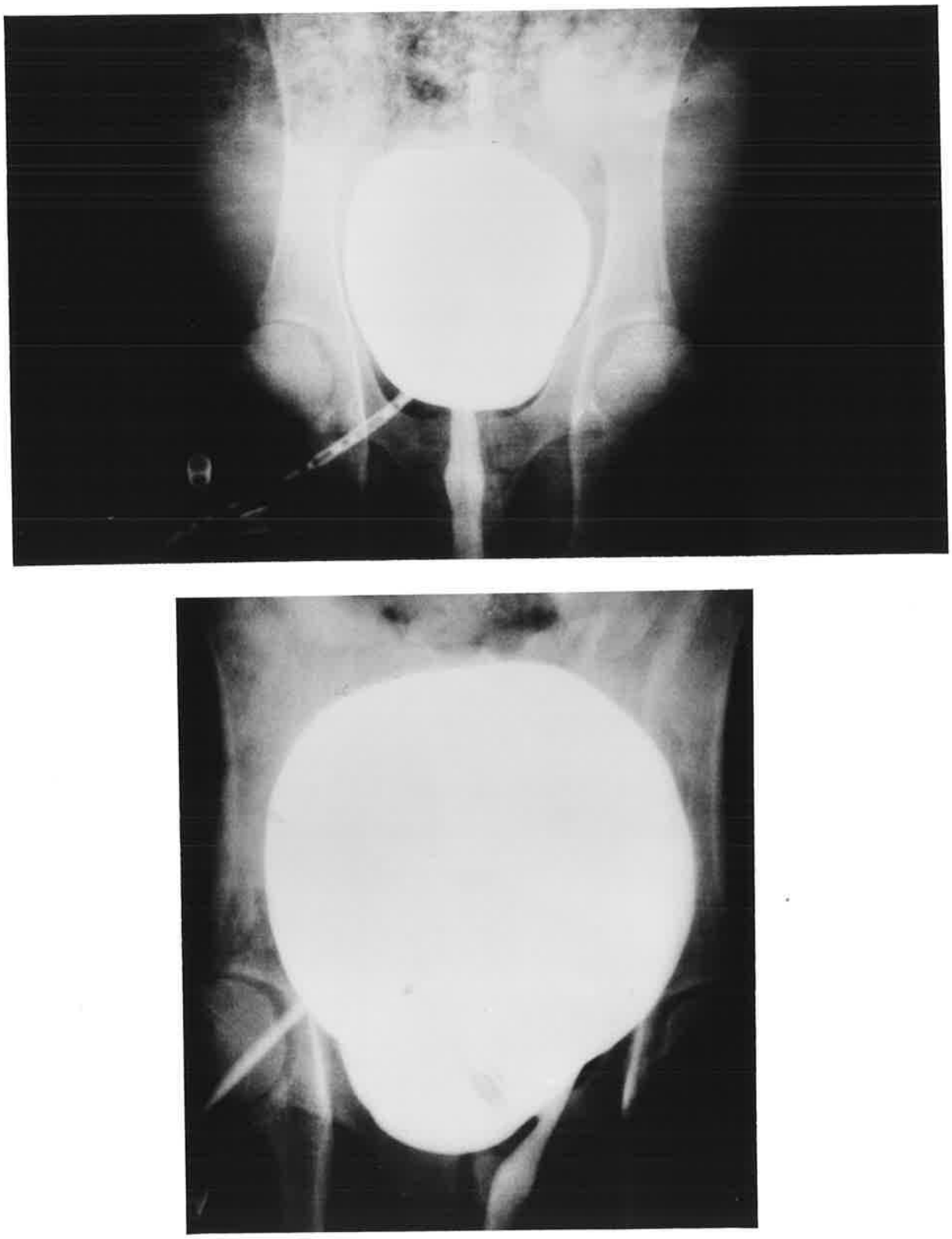


Figure 16B+C: An ***AACC*** bladder (#70-588) with ***good*** function shown on cystogram at <u>6 and 12 months</u> (Volume = 350 ml: Compliance = 14.6 ml/cmH_2O @ 12 months).

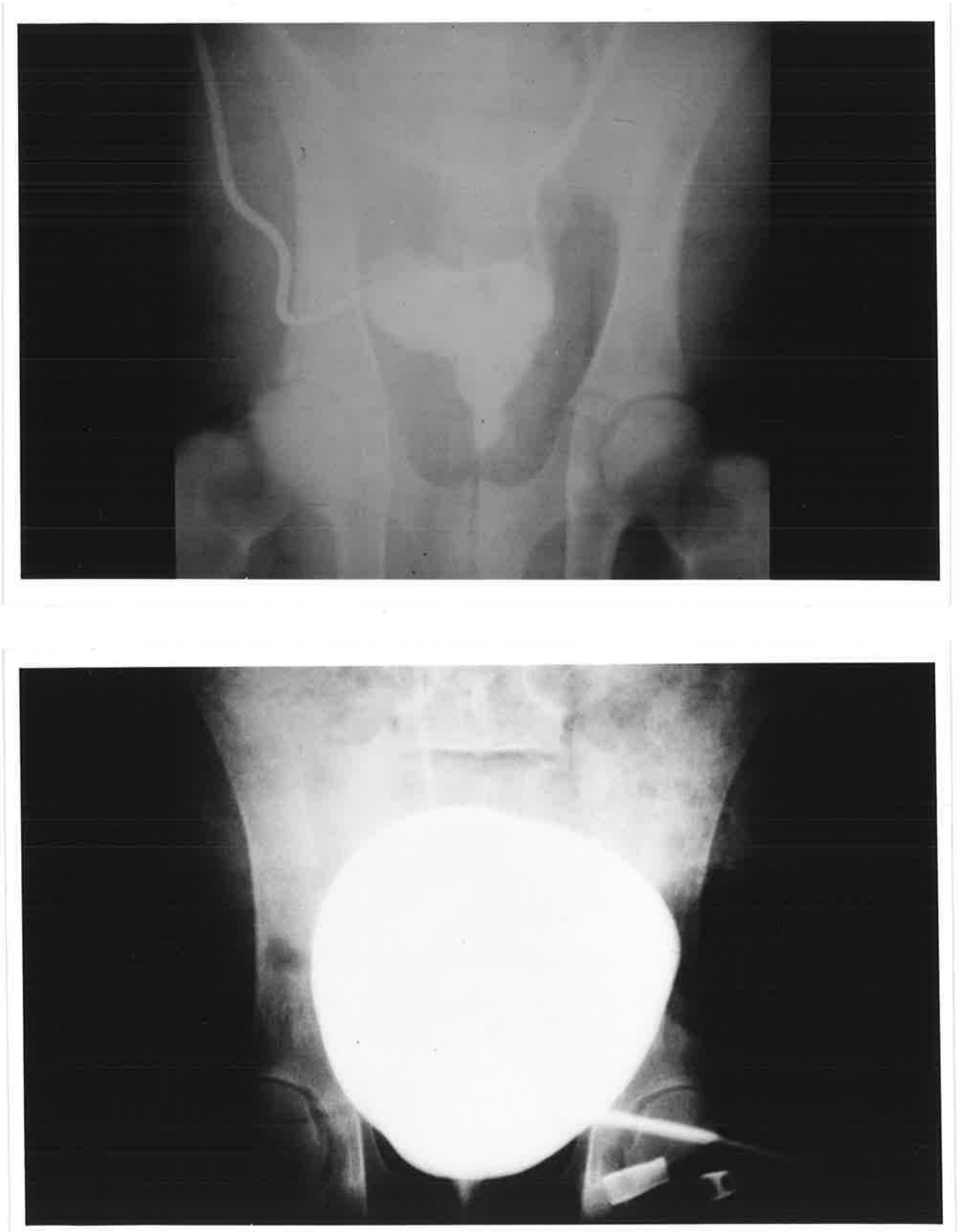


Figure 17A+B: An ***AACC*** bladder (#80-537) with ***bad*** function shown on cystogram at 10 days and 6 months.

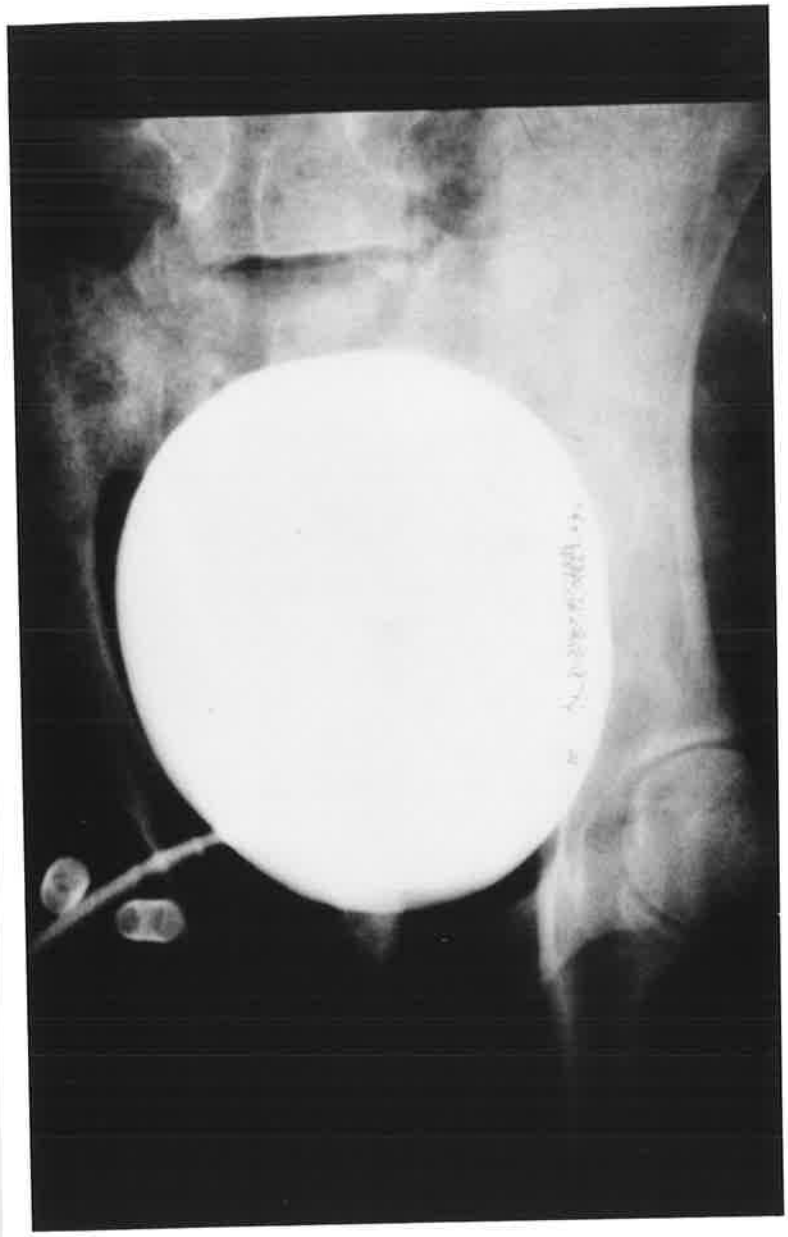


Figure 17C: An ***AACC*** bladder (#80-537) with ***bad*** function shown on cystogram at 12 months (Volume = 197 ml: Compliance = 9.0 ml/cmH_2O @ 12 months).

Table 28 Demucosalised Clam Colocystoplasty - *Cystograms*

	10 d	6 mths	12 mths
Shape			
Irregular	5	3	2
Normal	5	2	3
Size			
Small	4	0	0
Medium	6	5	2
Large	0	0	3
VUR			
No	6	5	5
Unilateral	0	0	0
Bilateral	4	0	0

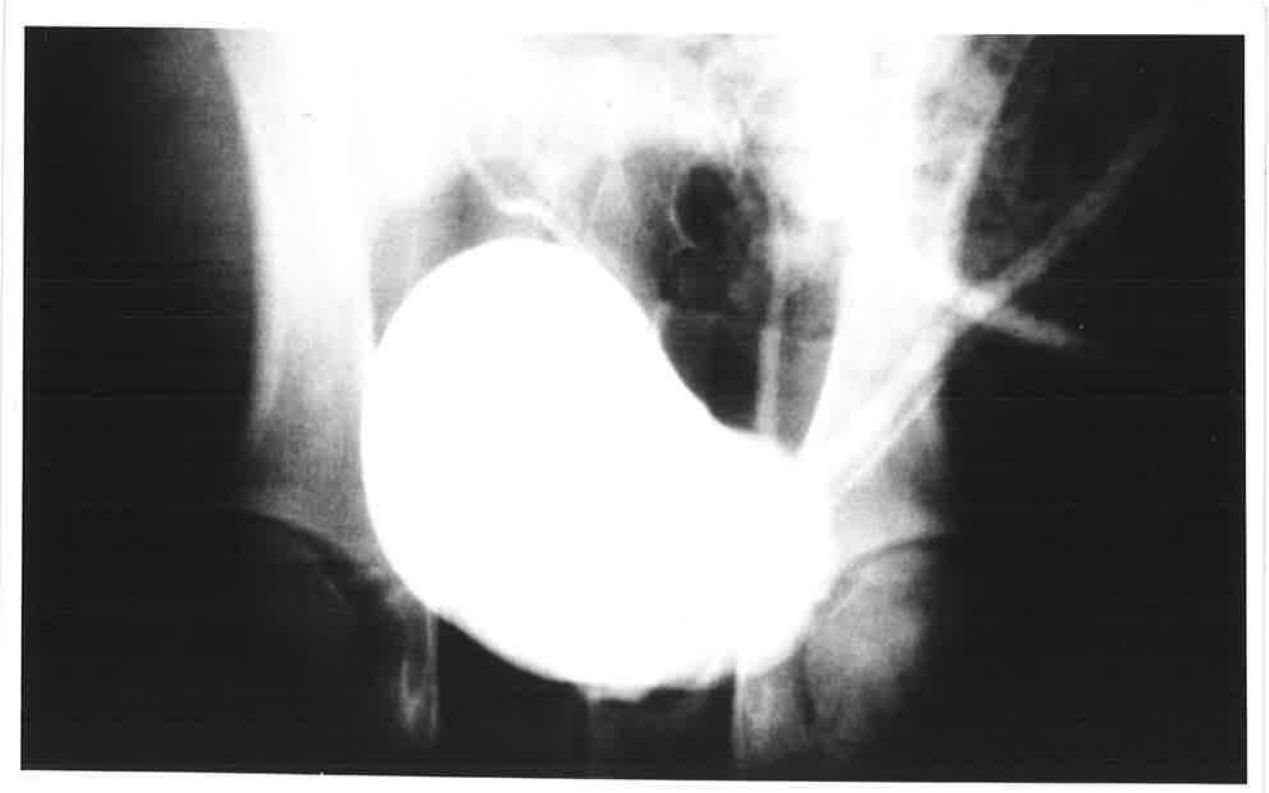


Figure 18A: A ***DMCC*** bladder (#80-549) with ***good*** function shown on cystogram at <u>10 days</u>.

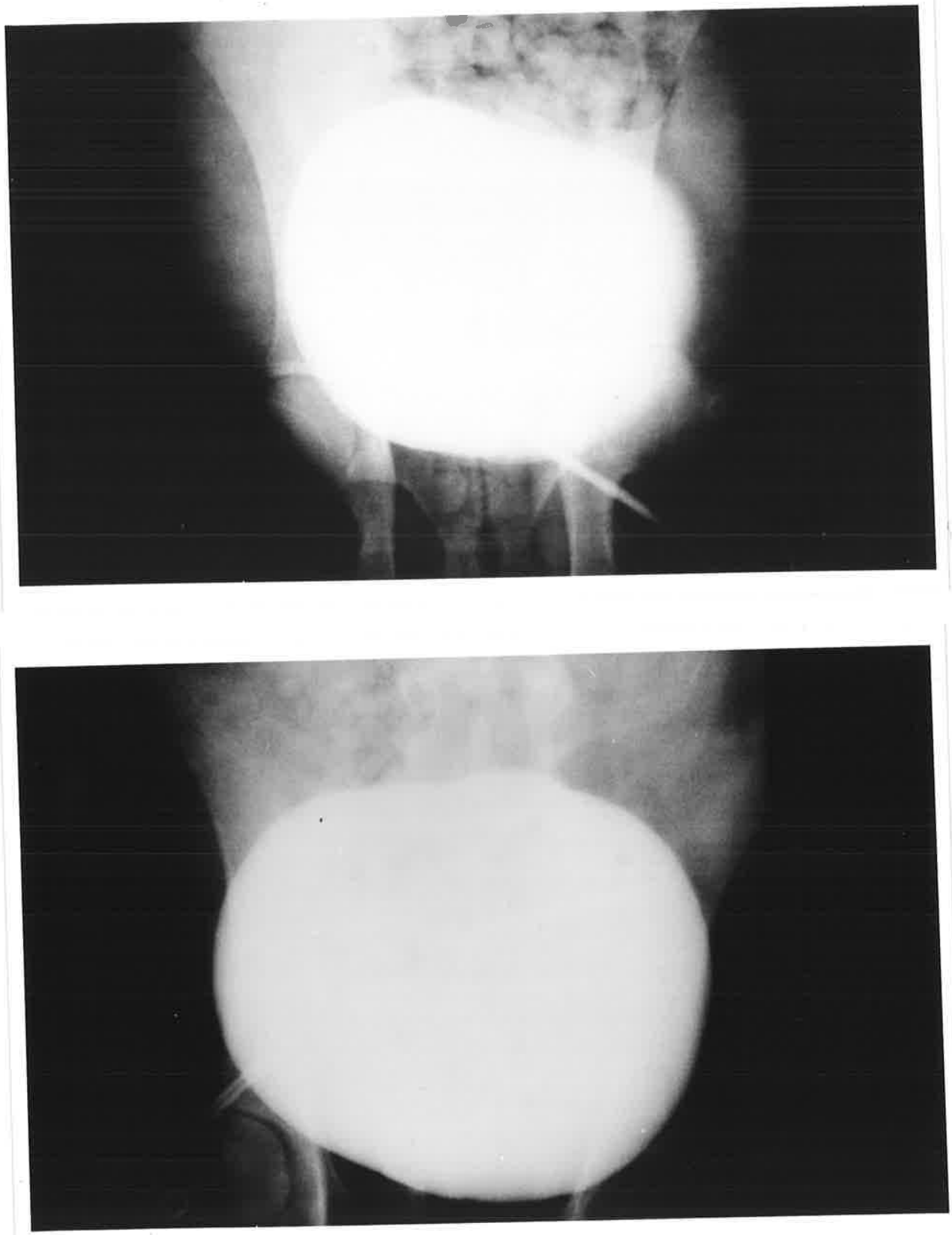


Figure 18B+C: A ***DMCC*** bladder (#80-549) with ***good*** function shown on cystogram at 6 and 12 months (Volume = 542 ml: Compliance = 13.7 ml/cmH_2O @ 12 months).

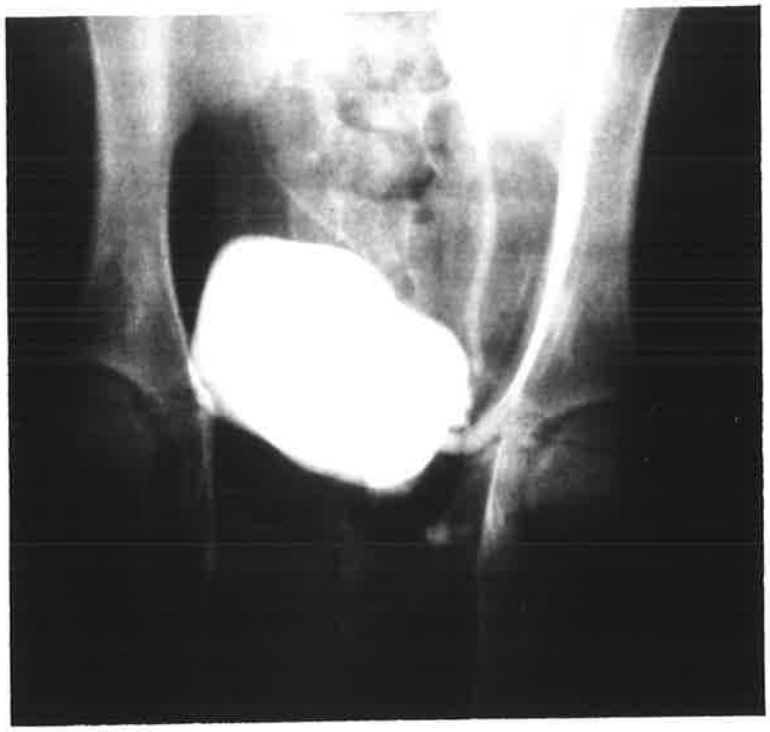


Figure 19A: A ***DMCC*** bladder (#8-46) with ***bad*** function shown on cystogram at 10 days (Volume = 221 ml: Compliance = 5.4 ml/cmH_2O @ 12 months).

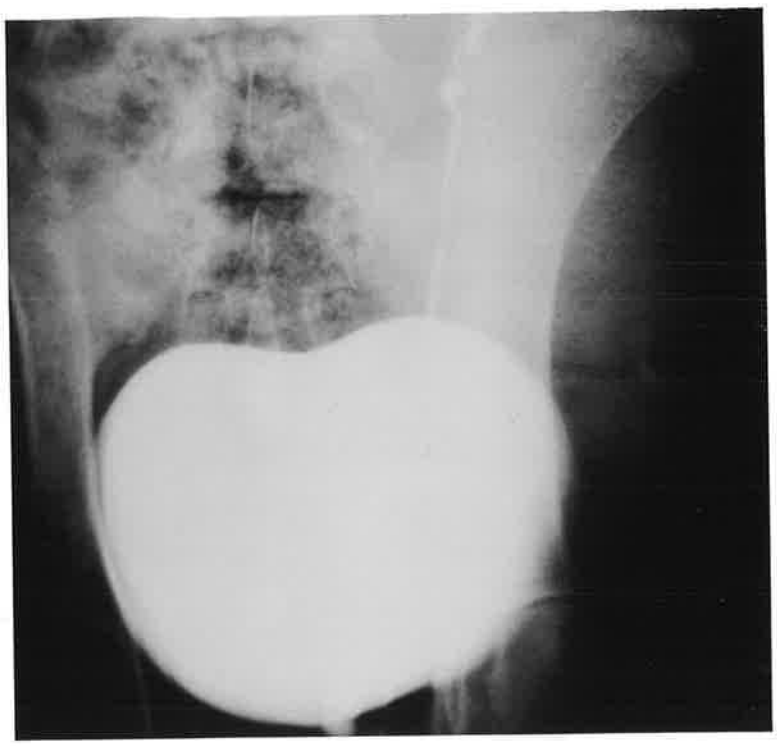


Figure 19B: A ***DMCC*** bladder (#8-46) with ***bad*** function shown on cystogram at 6 months (Volume = 221 ml: Compliance = 5.4 ml/cmH_2O @ 12 months).

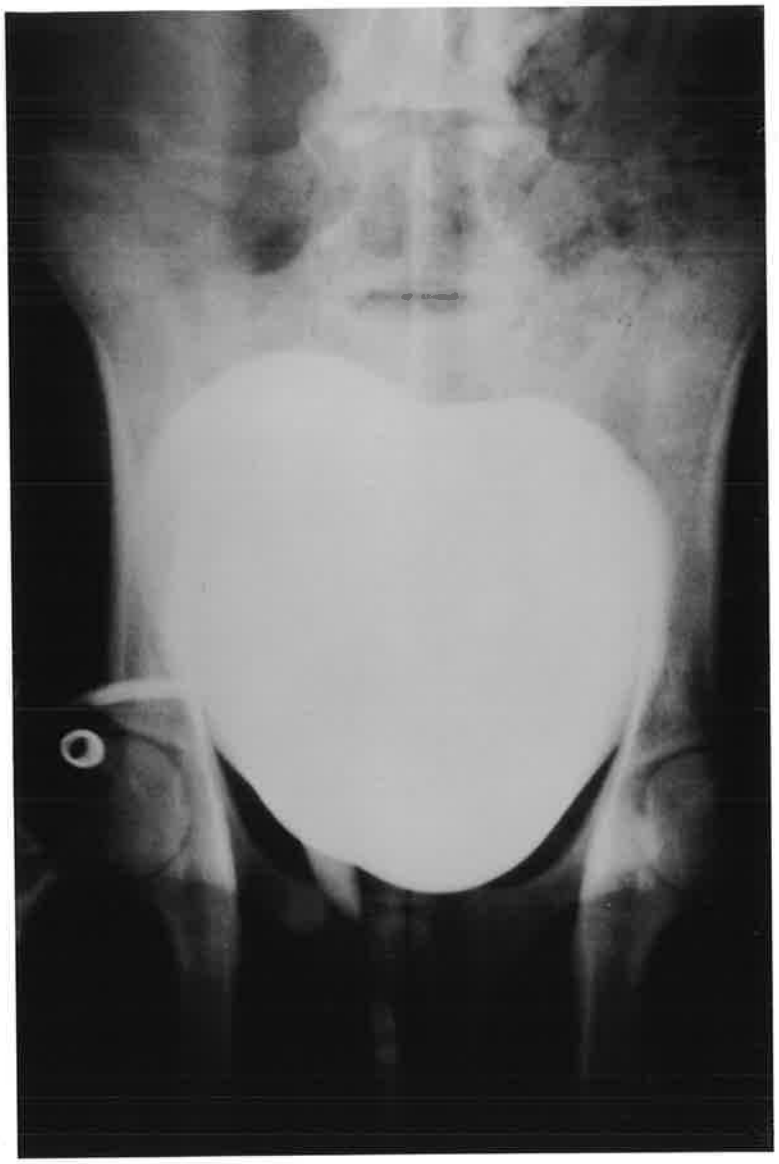


Figure 19C: A ***DMCC*** bladder (#8-46) with ***bad*** function shown on cystogram at 12 months (Volume = 221 ml: Compliance = 5.4 ml/cmH_2O @ 12 months).

Histology

The bladder histology has been grouped according to operation type and compared with the urodynamic outcome for each animal, the inter-relationships of which will be dealt with in the discussion. The total number of animals assessed is shown in Table 29 and the individual animal results are given in Tables 30-34.

The gastric mucosa was assessed on several occasions and found to be separated from the gastric muscle through the submucosal plane; in keeping with the ease of separation of the gastric mucosa in the sheep. The colon, on the other hand, was separated by different methods as the study progressed. Initially a very tedious dissection with diathermy was used, during which the muscle was significantly damaged, even-so, the separation was not as "histologically clean" as for the gastric mucosa. In the latter animals the separation was achieved by stripping with forceps, and the cleavage plane was seen histologically to be immediately below the lamina propria, which is reflected in the regrowth of the colonic mucosa in the DMGC animals (the last group to be included).

AAGC	24 of 27
DMGC	9 of 11
AAOC	8 of 10
AACC	9 of 9
DMCC	10 of 10
Total	56 of 67

Table 29: Summary of the histology studies compared to the total numbers of animals used in each study group.

Autoaugmentation Gastrocystoplasty

Table 30: Autoaugmentation Gastrocystoplasty - Urodynamics and Histology

No.	Name	Cull (d's)	Leak Point (last values) Vol.	Comp.	Histology
1.	-----	0	-	-	All components viable
2.	-----	0	-	-	-
3.	7-391	0	-	-	-
4.	7-88	0	-	-	All components viable
5.	-----	7	-	-	Viable mucosa
6.	6-378	13	-	-	Viable mucosa, + signif. inflammation
7.	7-38	13	-	-	Some mucosal loss + inflammation
8.	6-77	28	-	-	Inflammation - mild to moderate
9.	6-97	35	-	-	Inflammation - mild to moderate
10.	6-286	52	-	-	Inflammation - negligible
11.	6-82	63	-	-	Inflammation - mild
12.	5-428	70	-	-	Inflammation - negligible
13.	6-388	98	-	-	-
14.	7-36	147	170	3.4	Inflammation - negligible
15.	7-125	180	189	3.5	Ulcerative cystitis
16.	7-50	183	638	10.9	Cystitis/Infection
17.	0-151	194	130	7.7	Inflammation - negligible
18.	-----	196	-	-	Inflammation - negligible
19.	5-426	270	208	4.4	Inflammation + fibrosis
20.	4-330	280	279	9.8	No inflammation/fibrosis
21.	6-390	350	552	15.5	No inflammation/fibrosis
22.	5-284	378	725	34.7	No inflammation/fibrosis
23.	72-271	364	336	8.1	No inflammation/fibrosis
24.	72-277	364	219	8.5	No inflammation/fibrosis
25.	7-392	364	286	8.6	No Inflammation/fibrosis
26.	7-89	364	156	3.9	Inflammation - negligible
27.	7-37	364	472	12.8	No inflammation/fibrosis

Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20;

Gastric Mucosa

The gastric mucosa was easily removed by diathermy dissection of long vessels which passed between the muscle and mucosa. Histology showed an intact gastric mucosa with very little injury to the submucosa which was resected with the mucosa.

Urothelial Survival Studies: Immediate Sacrifice

In the four animals sacrificed after the procedure, all elements were seen to be macroscopically viable. In two of these the specimens were examined histologically. Sections from the gastric patch showed viable muscularis propria with an oedematous submucosa showing interstitial oedema, interstitial haemorrhage and lymphatic dilatation. There was no evidence of muscularis mucosae or gastric glands, with the surface layers coated by a thin layer of fibrin. Sections from the anastomosis site revealed viable bladder with portions of gastric muscularis propria and submucosa sutured to the bladder muscularis. Gastric epithelium was not identified in any level. The inner portion of the autoaugmentation segment of the bladder was composed of viable mucosa, oedematous subepithelial connective tissue and superficial portions of the inner longitudinal bladder muscle coat. Beneath this, there was a thin layer of adherent fibrin. The external portion, composed of the gastrocystoplasty, was of similar morphology to the previously described patch.

Urothelial Survival Studies: Up to Four Weeks

At one week, sections from the anastomosis site revealed mild chronic inflammation with proliferating fibroblasts and a multinucleated foreign body type giant cell reaction around suture material. The muscularis propria of the gastric patch was viable, although there was a chronic inflammatory serosal reaction present within the fused autoaugmentation and gastric muscle. The degree of inflammation was less prominent at sites more distant from the suture line. The surface mucosa of the autoaugmentation was normal in appearance, with a mild subepithelial chronic inflammatory cell infiltrate.

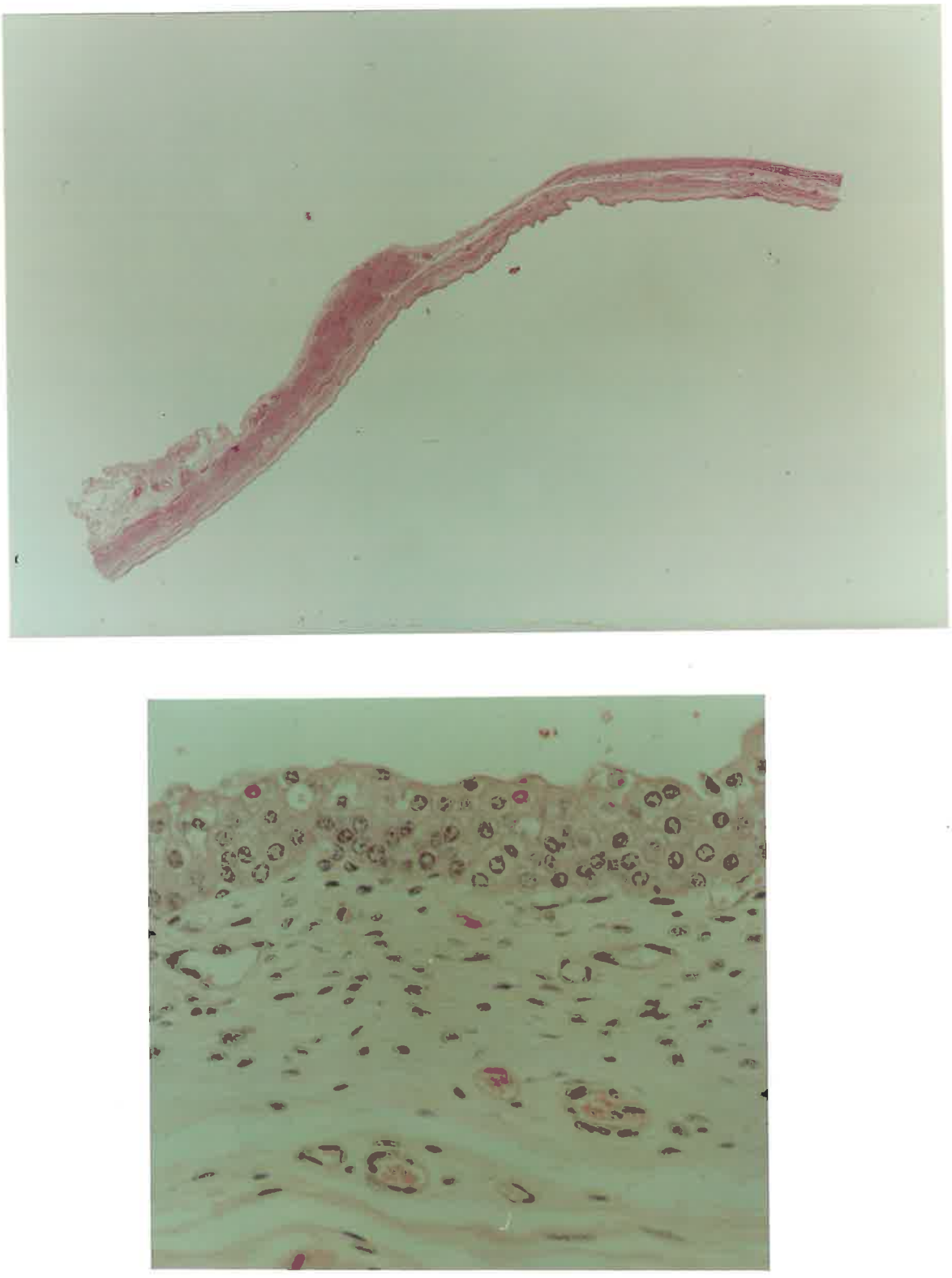


Figure 20: A. The macroscopic appearance of the adjacent portions of the new and old AAGC bladder wall at 4 weeks: B. A high power view of the gastric portion of the AAGC bladder showing the lack of inflammation at 4 weeks.

In one of the two sheep culled at two weeks the anastomotic site showed significant chronic granulomatous inflammation which extended into the subepithelial connective tissue of the autoaugmentation. The autoaugmentation transitional epithelium and subepithelial connective tissue were, however, present and viable, as was the muscularis propria of the gastric patch. In the second animal chronic inflammation with calcification at the anastomotic site was seen. Surface ulceration was also present involving the anastomotic site and adjacent areas, suggesting *minimal loss of the urothelium.* Away from areas of ulceration the mucosa was viable and all of the gastric and bladder muscle appeared viable.

At four weeks there was still inflammation around the polyglycolic acid sutures, however, further away from the anastomotic site the degree of subepithelial chronic inflammation was mild, the surface transitional epithelium appeared intact and relatively undisturbed. Similarly, the muscularis propria of the gastric patch was quite viable and normal in appearance. No gastric epithelium was seen under the gastric muscle.

Inflammation, Fibrosis, Gastric Mucosal Regrowth Studies - Five - Ten Weeks

Sections from the native bladder showed a normal architectural arrangement with a mild subepithelial inflammatory infiltrate beneath intact and viable epithelium, whereas the anastomosis revealed a less florid chronic inflammatory cell infiltrate than the earlier animals, with foreign body giant cell reaction and calcification around suture material only. There were also scattered haemosiderin-containing macrophages present. The gastric patch was viable and normal in appearance with a mild chronic granulomatous inflammatory infiltrate at the junction with the inner autoaugmentation. The transitional epithelium of the autoaugmentation was intact, with a chronic subepithelial inflammatory infiltrate which varied from mild to marked, depending on the section and the animal. Overall, the degree of inflammation appeared to have decreased with time. Sections from the gastrocystoplasty portion revealed no discernible difference between transitional epithelium, subepithelial connective tissue and superficial portions of the inner longitudinal layers compared to the native portion of the bladder. At the suture line, only very occasional foreign body giant cells were seen around suture material with minimal inflammatory infiltrate. The muscularis propria of the gastric patch was unremarkable, as were the kidneys. In animals #6-286 and #5-428 the histological appearances were particularly impressive; within the autoaugmentation gastrocystoplasty the gastric patch was completely normal in appearance with a normal submucosa in continuity with the residual muscle of the autoaugmentation. There was no inflammatory infiltrate between the two layers which appeared to be in continuity. The transitional epithelium of the autoaugmentation was normal, as was the subepithelial connective tissue as shown in Figure 21. No gastric epithelium was seen in any of the sections of the above four animals.

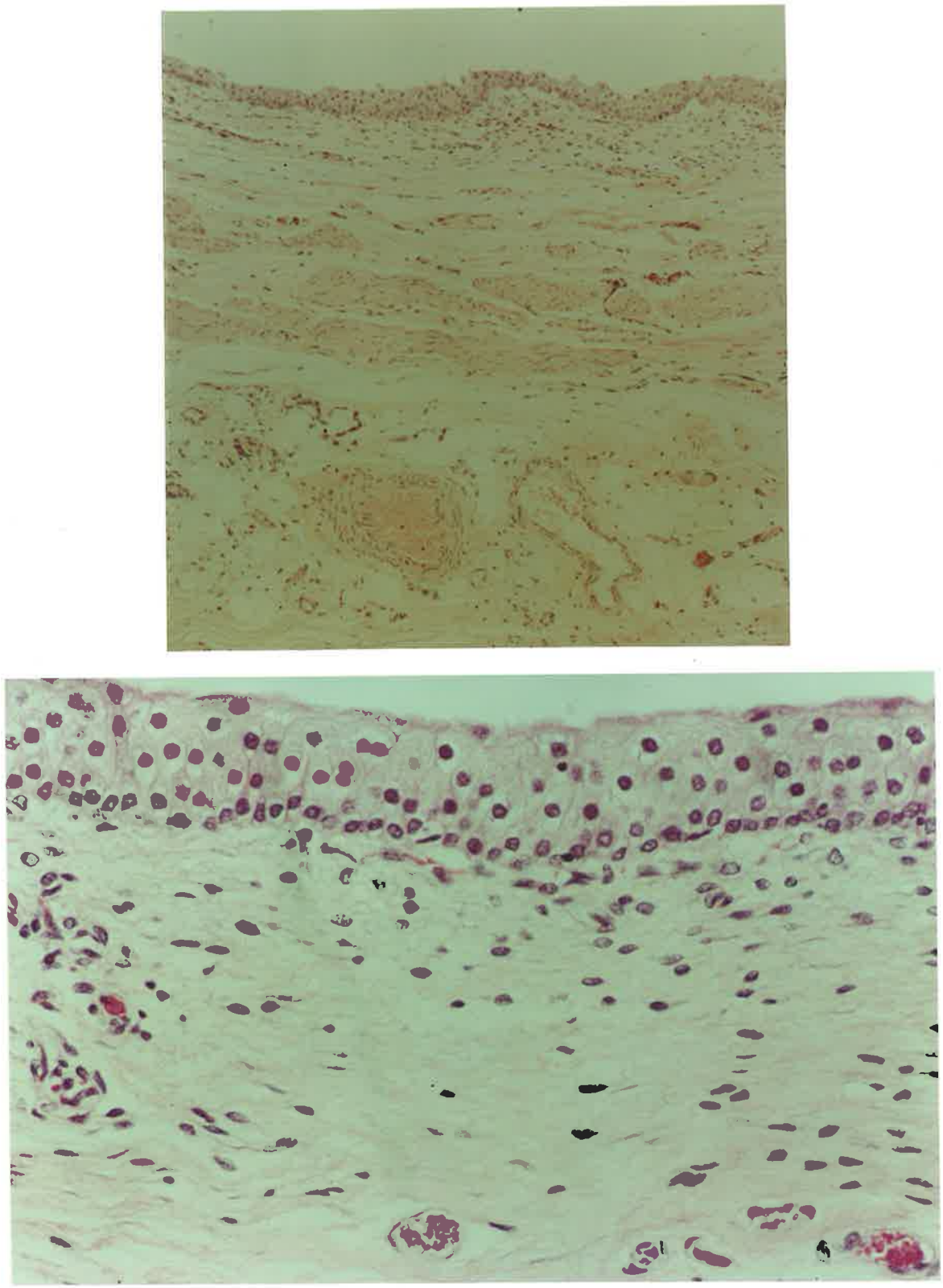


Figure 21: A. The low power appearance of a good AAGC bladder at 10 weeks (#5-428): B. A high power view of the gastric portion of the same bladder showing the lack of inflammation.

Inflammation and Fibrosis at Six and Twelve Months

Of the seven animals sacrificed at six months, four had a histologically satisfactory bladder with the inner surface of the bladder fully lined with urothelium. There was preservation of the gastric component of the bladder, with little or no inflammation of either the native, or gastric portions of the bladder. Where inflammation was present it was localised to the vicinity of the suture material. The remaining three had cystitis related to infection. One animal had ulcerative cystitis with marked inflammatory changes. No gastric mucosa was found in the area of inflammation and there was no mucous production evident on staining for mucin.

Seven sheep were sacrificed at one year, and a satisfactory histological appearance, with no inflammation or fibrosis, was seen in six of the bladders and only minimal inflammation in the gastric component of one.

Demucosalised Clam Gastrocystoplasty

Table 31: Demucosalised Clam Gastrocystoplasty - Urodynamics and Histology

No.	Name	Cull (d's)	Leak Point (last values) Vol.	Comp.	Histology
1.	-----	4	-	-	-
2.	72-251	7	-	-	Inflammation - acute +++
3.	72-282	7	-	-	-
4.	72-262	10	-	-	Inflammation - florid granulomatous
5.	72-258	14	-	-	Inflammation - florid; min ingrowth
6.	72-283	28	242	17.3	Hour-glass blad., mod inflam; urothel. lined
7.	72-293	153	219	9.1	Focal fibrosis
8.	72-292	154	152	6.7	Serosal abscesses
9.	72-288	364	146	5.5	Inflammation - chronic
10.	72-290	364	353	12.0	No inflammation/fibrosis
11.	7-391	364	359	16.3	Inflammation - chronic

Vol. = volume in millilitres; Comp. = compliance in ml/cmH_20;

Urothelial Ingrowth Studies

Sections from the animal sacrificed at seven days revealed unremarkable transitional epithelium on the bladder side of the augmentation. Marked chronic granulomatous inflammation was seen around suture material at the anastomosis site and over the surface of the gastric patch which was covered with adherent acute inflammatory and necrotic debris, with numerous neutrophils. The underlying submucosal tissue showed fresh granulation tissue formation, extending to the innermost portions of the muscularis propria. At the advancing edge of transitional epithelium there was pronounced pseudoepitheliomatous hyperplasia with minimal urothelial ingrowth over the granulation tissue covered stomach muscle. In the centre of the gastric patch there was quite marked fibrosis within the organising granulation tissue.

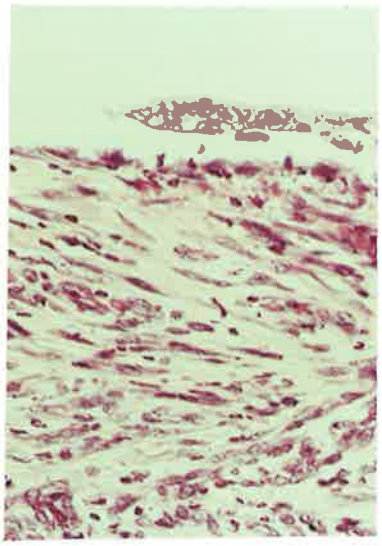
Again, at 10 days, the urothelium covering the detrusor muscle was unremarkable,

however, the gastric patch showed a significant chronic inflammatory infiltrate which included areas of dystrophic calcification, fibrosis and granulation tissue formation. At the dome of the gastric patch the smooth muscle showed eosinophilia and cytoplasmic vacuolation *highly suggestive of ischaemic damage*. The gastric muscularis propria appeared more viable closer to the anastomosis site. Again, there has been a minimal ingrowth of transitional epithelium over the markedly inflamed and necrotic tissue at the anastomosis site. Examination of cross-sections of the pedicle, which was submitted *in toto*, revealed an intact artery and vein with no evidence of thrombosis.

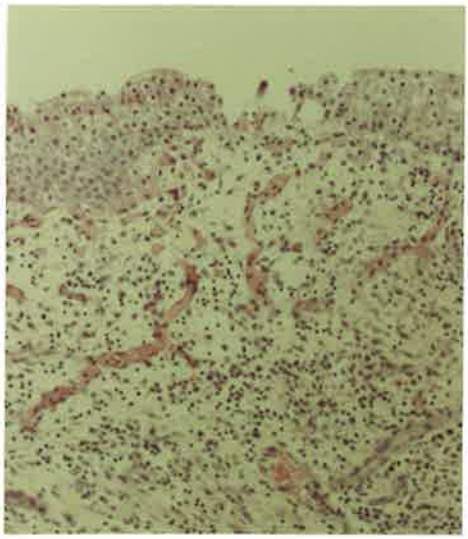
At 14 days, chronic inflammatory cell infiltrate was seen with aggregates of prominent calcification. The superficial portions of the gastrocystoplasty showed considerable fibrosis with aggregates of acute necrotic inflammatory debris attached to the superficial layers. At the junction with the transitional epithelium there was evidence of *incomplete ingrowth of epithelium* overlying the inflamed tissue.

At 28 days, the gastrocystoplasty was lined by relatively unremarkable transitional epithelium overlying loose subepithelial connective tissue which demonstrated a mild chronic inflammatory infiltrate. The sectioned bladder, however, had an *hour-glass appearance* with a stricture at the junction between the bladder and the gastrocystoplasty. This was associated with prominent chronic inflammation of the gastrocystoplasty.

Figure 22



A. Early ingrowth of the urothelium over the gastric muscle. The marked inflammation can be seen. The bladder had an hour-glass configuration.



B. The urothelium covered the gastric muscle at 4 weeks, but there was still significant inflammatory infiltrate.

Inflammation and Fibrosis at Six and Twelve Months

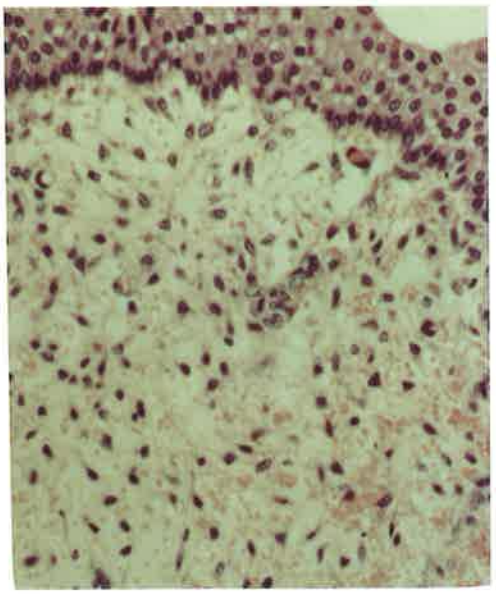
In the first of the two animals sacrificed at ***six months*** there was no evidence of significant inflammation in the subepithelial connective tissue over the gastrocystoplasty with successful completion of the re-epithelialisation. The serosal surface did, however, show adhesion formation with quite prominent focal fibrosis. In the second animal the changes were similar except that, within the serosal tissues there was marked inflammation and oedema with focal microabscess formation and aggregates of polymorphonuclear leukocytes and bacteria.

At ***12 months***, sections from animal #72-290 resembled very closely a standard gastrocystoplasty with autoaugmentation. Specifically, there was orderly surface transitional epithelium overlying a slightly fibrotic subepithelial connective tissue layer. Beneath this layer there was fat from the gastric patch and muscularis

propria. There was no significant inflammation.

The remaining two animals demonstrated surface ulceration of the transitional epithelium with an acute inflammatory infiltrate and extensive subepithelial fibrosis with focal granulation tissue formation. The superficial portions of the underlying gastric adipose tissue were also replaced by fibrous tissue in which there were aggregates of chronic inflammatory cells including occasional lymphoid follicles. There was scattered fibrosis within the muscularis propria of the gastric patch along with focal chronic inflammatory cells. In other areas the degree of inflammation was minimal and the mucosa was intact. The subepithelial inflammatory infiltrate extended from the anastomosis site to involve subepithelial connective tissue within the residual bladder.

Figure 23



A. A good DMGC at 12 months.

B. Continued inflammation in a DMGC bladder at 12 months.

Autoaugmentation Omentocystoplasty

Table 32: Autoaugmentation Omentocystoplasty - Urodynamics and Histology

No.	Name	Cull	Leak Point (last values) (d's)	Vol.	Histology Comp.	
1.	70-589		-	-	-	
2.	6-344		7	-	-	Dystrophic Ca^{++}
3.	72-260		56	55	4.0	Inflammation - mild
4.	7-387		56	-	-	-
5.	72-274		112	73	2.1	Inflammation + fibrosis
6.	70-580		180	201	5.2	Inflammation - moderate
7.	72-287		364	148	6.3	No inflammation/fibrosis
8.	72-289		364	207	8.2	Inflammation - chronic
9.	72-294		364	202	7.2	Inflammation - chronic
10.	7-389		364	122	3.2	Inflammation - chronic

Urothelial Survival Studies

After seven days sections revealed orderly bladder architecture, with a chronic granulomatous foreign body type inflammatory infiltrate. The bladder portion of the autoaugmentation was intact with orderly overlying transitional epithelium and negligible subepithelial connective tissue and inflammatory infiltrate. Scattered areas of the superficial portions of the inner longitudinal muscle layer of the bladder were present. The urothelium was seen to have survived throughout the created diverticulum (Fig.24A). The omentum beneath the autoaugmentation showed prominent septal fibrosis with fat necrosis and variable amounts of acute and chronic inflammation. Deep to the autoaugmentation in areas of prominent fibrosis there was dystrophic calcification with one focus of metaplastic bone formation (Fig.24B). In some sections the fibrosis formed a thick band beneath the autoaugmentation.

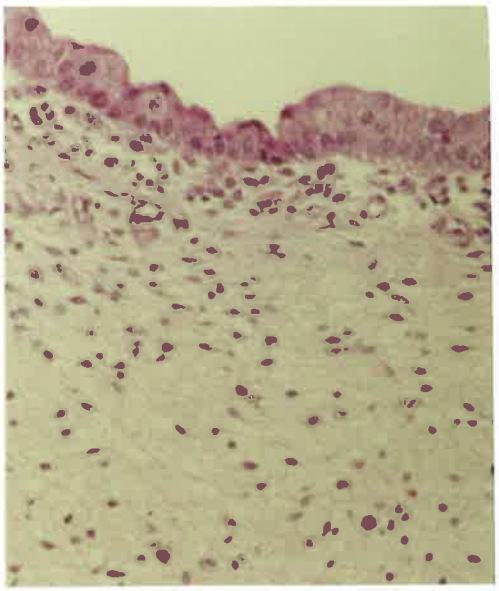
Inflammation and Fibrosis Up to Six Months

Sections from all bladder sites in animal #72-260, including the bladder and autoaugmentation, showed unremarkable transitional epithelium. In the portion of bladder covered by omentum, there was negligible inflammation. Whereas animal #72-274, sacrificed at 4 months, had marked chronic inflammatory cell infiltrate composed of plasma cells and eosinophils with increased vascularity and fibrosis of the subepithelial connective tissue (Fig.25A). There were also focal areas of lymphoid aggregates, an appearance similar to those of follicular cystitis. In this animal the mucosa, muscularis and attached omental flap were all viable and there was mild chronic granulomatous inflammation around suture material. The next animal was sacrificed at 180 days. It had preservation of transitional epithelium with a mild-moderate subepithelial chronic inflammatory cell infiltrate in the tissue lined by the omentoplasty. At the junction of the fat with the detrusor there was more moderate chronic inflammation with granulation tissue formation.

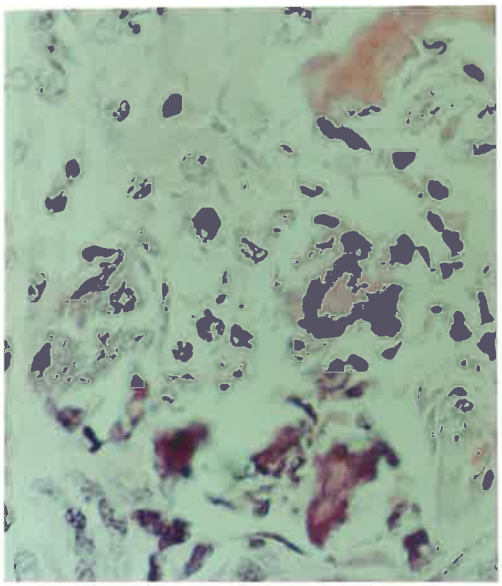
Inflammation and Fibrosis at One Year

In all four animals sacrificed at one year the sections demonstrated intact transitional epithelium overlying subepithelial connective tissue in which there was minimal fibrosis and no significant inflammation. The omental patches were intact. Animal #72-287 was particularly notable for its lack of inflammatory cells (Fig.25B).

Figure 24

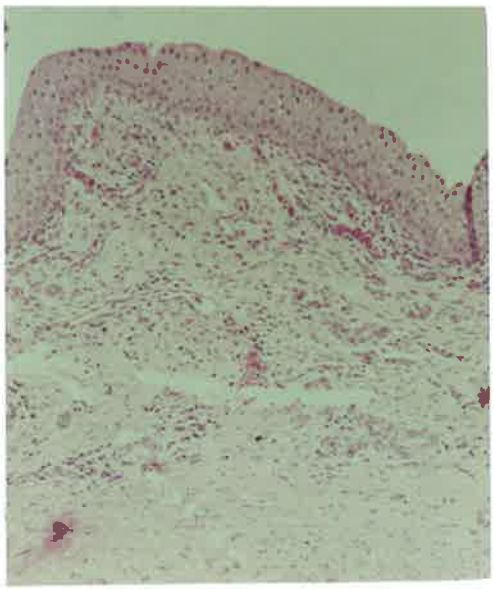


A. Urothelial survival under the omentum.

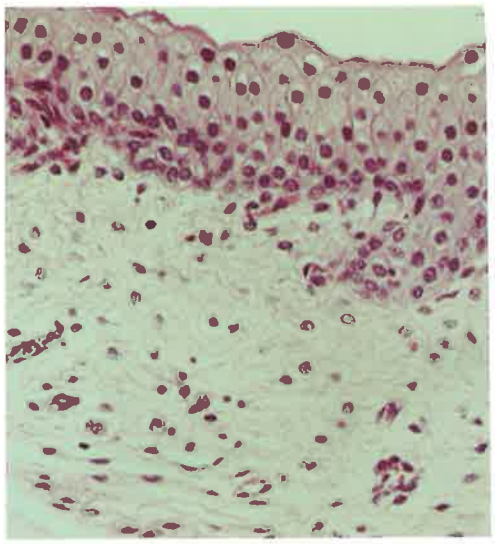


B. Dystrophic calcification at one week in an AAOC.

Figure 25



A. An inflamed and fibrosed AAOC bladder at 112 days.



B. A histologically satisfactory result for an AAOC bladder at one year.

Autoaugmentation Colocystoplasty

Histology of the Resected Colonic Mucosa

The earlier animals had the colonic mucosa removed by diathermy dissection. This resulted in the muscle macroscopically appearing oedematous and haemorrhagic at the end of the procedure. The colonic mucosa from these animals showed only occasional areas of full thickness submucosa, unlike the gastric mucosa which was cleaved more cleanly (consistent with the macroscopic impression). A colonic muscle specimen showed serosa, inner and outer layers of the muscularis propria, and occasional fragments of the outermost submucosa. There was no inner submucosa or mucosa present on the colonic muscle.

Because of the difficulty, and muscle damage of the diathermy denuding technique, the procedure was changed to peeling the mucosa with forceps. This produced much healthier muscle, but resulted in colonic mucosal regrowth. All animals with regrowth of colonic mucosal (five) had the gut lining removed by this latter technique. Histologically the muscle showed a greater proportion of submucosa preservation, although there was no evidence of mucosa on routine histology. Obviously, this was only a sample and not a study of all the denuded colonic muscle surfaces which must have had isolated areas of residual cells. Sections of the colonic mucosa removed by stripping, showed full thickness mucosa present in all layers but with variable amounts of muscularis mucosa. The line of separation generally went through the upper portion of the submucosa immediately beneath the muscularis mucosa, leaving a small strip of submucosa. Focally the muscularis mucosa was split and lamina propria was observed abutting the cleavage plane.

Table 33: Autoaugmentation Colocystoplasty - Urodynamics and Histology

No.	Name	Cull	Leak Point (last values) (d's)	Vol.	Histology Comp.	
1.	72-285		7	-	-	Inflammation - severe
2.	80-550		7	-	-	Inflammation - moderate
3.	7-448		28	-	-	Viable mucosa
4.	70-588		364	350	14.6	No inflammation/fibrosis
5.	80-538		364	351	11.3	Inflammation - negligible
6.	80-527		364	224	4.1	Inflammation - calculus
7.	80-537		364	197	9.0	No inflammation/fibrosis
8.	80-533		364	210	7.5	No inflammation/fibrosis
9.	8- 45		364	305	8.6	Inflammation - negligible

Urothelial Survival Studies

The two sheep sacrificed after one week had a moderate to severe degree of subepithelial oedema and interstitial haemorrhage in the colonic component of the autoaugmentation. There was also reactive fibrosis with dystrophic calcification noted at the junction of the colonic and detrusor muscle. Separation of the inner autoaugmentation from the outer colocystoplasty was also seen. The cavity thus formed was lined by reactive granulation tissue (Fig.26A). There was also prominent granulation tissue formation within the colonic serosal adipose tissue flap, which featured areas of dystrophic calcification. The mucosa was viable, although there was prominent subepithelial oedema which included large cystic spaces of oedema fluid overlying subepithelial tissue composed of prominent reactive granulation tissue. Sections also revealed loss of overlying mucosa which may have been artefactual, although the degree of submucosal oedema would certainly have contributed to urothelial loss. No colonic mucosa was seen in either of these animals.

Sections from the animal culled at one month showed the colocystoplasty to have

fused with the overlying bladder submucosal tissues (Fig.26B). The mucosa was quite viable and there was minimal chronic inflammatory cell infiltrate present between the muscle and the mucosa. Again there was no colonic mucosal regrowth.

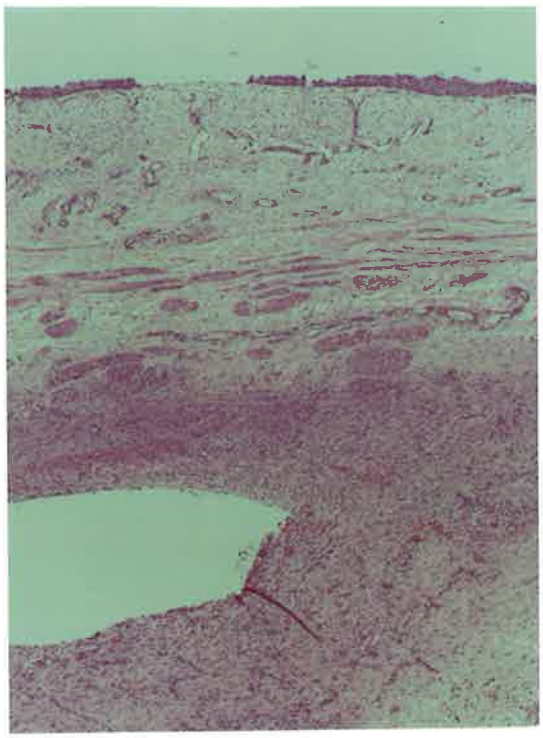


Figure 26A. An inflamed and fibrosed AACC bladder at 7 days.

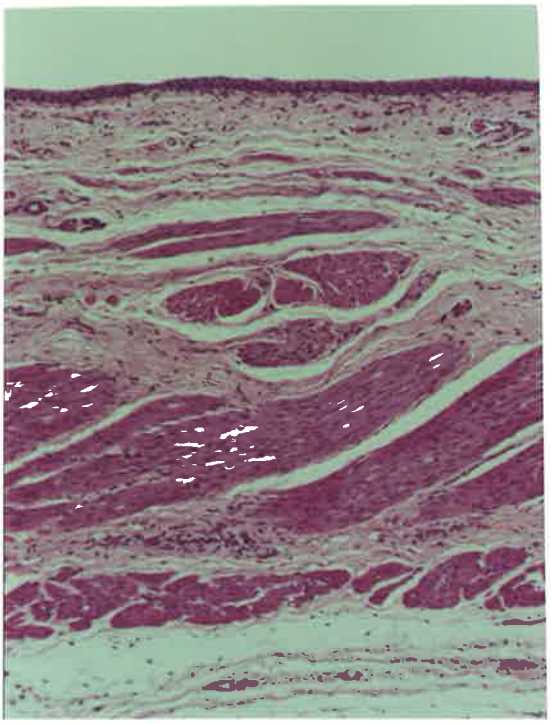


Figure 26B. A section of the AACC bladder at 28 days.

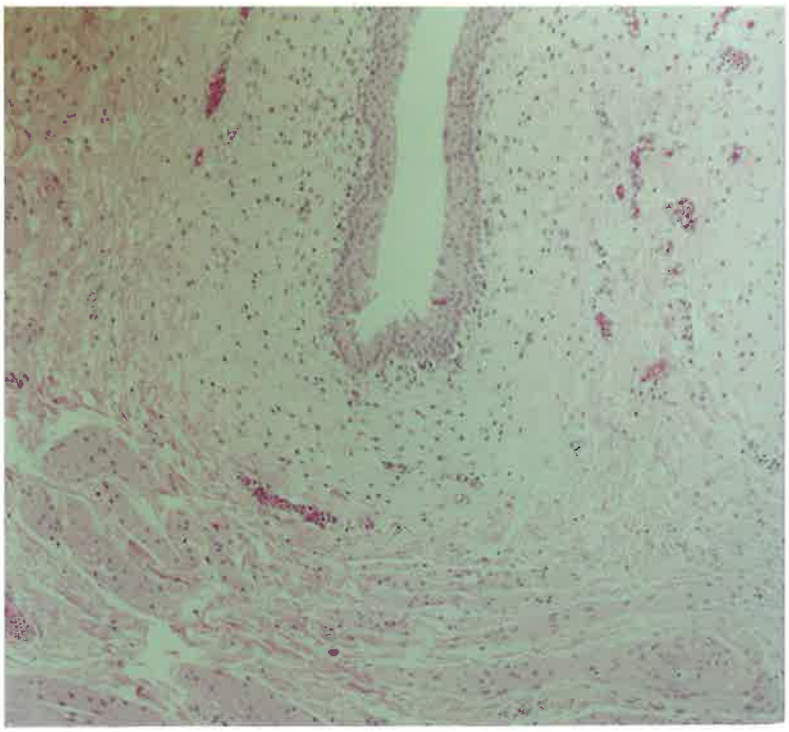


Figure 26C. A section of a histologically satisfactory, but urodynamically poor AACC bladder at one year.

Inflammation, Fibrosis and Colonic Mucosal Regrowth Studies at Twelve Months

No colonic mucosal regrowth was seen in this group (Fig.26C). It should be noted that these procedures were performed before the demucosalised colocystoplasty group were included in the study.

Four of the remaining five had very little inflammatory change with the colonic muscle lined with urothelium. In one animal (#80-527), sections from the autoaugmentation revealed unremarkable colonic musculature adherent to bladder which showed oedematous submucosa with a moderate acute and chronic inflammatory infiltrate including scattered lymphoid follicles, however the degree of inflammation was probably due to the associated bladder calculus.

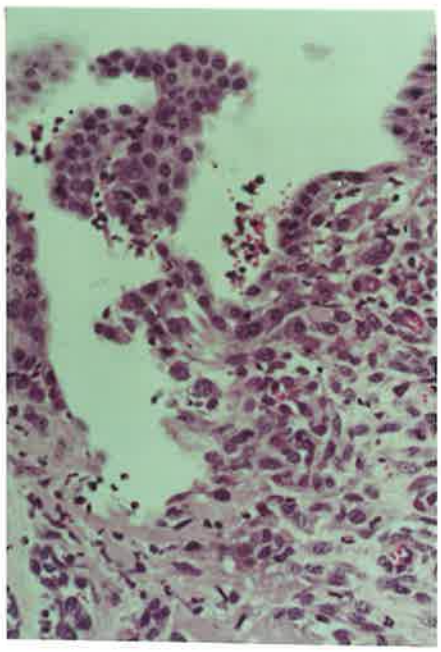
Demucosalised Clam Colocystoplasty

Table 34: Demucosalised Colocystoplasty - Urodynamics and Histology

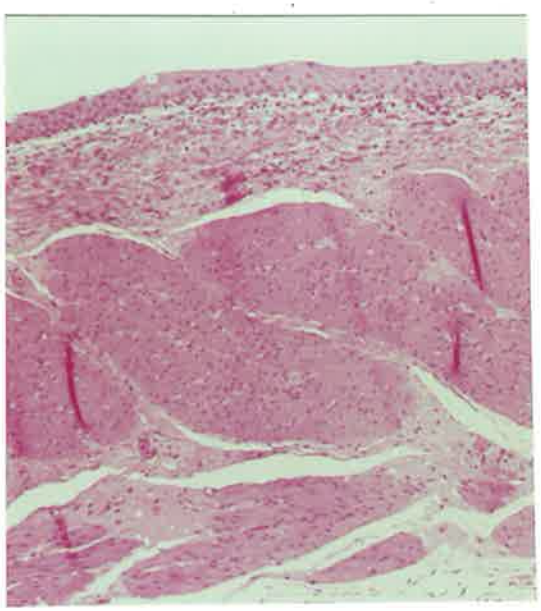
No.	Name	Cull	Leak Point (last values) (d's)	Vol.	Histology Comp.	
1.	7- 39		7	-	-	Inflammation - severe
2.	70-586		14	-	-	Inflammation - severe
3.	70-593		21	-	-	Partial urothelial covering
4.	7-247		28	-	-	Urothelial covering, inflamed
5.	8- 50		180	-	-	Colonic mucosa
6.	80-524		364	127	5.3	Fibrosis
7.	80-549		364	333	16.2	Colonic mucosa
8.	8- 43		364	452	32.9	Colonic mucosa
9.	8- 46		364	221	40.9	Colonic mucosa
10.	8- 44		364	327	7.3	Colonic mucosa

Urothelial Regrowth Studies

Figure 27



A. A DMCC prior to re-epithelialisation with marked inflammation.



B. Colonic muscle covered with urothelium at 4 weeks in a DMCC bladder.

In sections from the animal culled at one week, the native bladder was relatively normal. There was a chronic inflammatory infiltrate with giant cell formation at the anastomosis site. In the area of the colocystoplasty there was florid chronic inflammation with surface ulceration and granulation tissue formation, with no evidence of colonic mucosa, and no urothelial ingrowth over the colonic muscle.

At 14 days the mucosa, and the residual bladder, were generally unremarkable except for a mild chronic subepithelial inflammatory infiltrate. Under the colonic muscle there was still generalised absence of mucosa with a profound acute inflammatory infiltrate with micro abscess formation. In areas where there was less inflammation, the submucosa had undergone fibrosis with evidence of fragmented coverage with urothelium.

One week later animal #70-593 had similar inflammatory changes, although the degree of inflammation was less. There was, however, quite prominent subepithelial fibrosis, but re-epithelisation over the colocystoplasty was reasonably extensive, although some areas still showed prominent ulceration. The epithelial ingrowth was applied directly to the fibrotic submucosal tissue.

After four weeks the features were much the same as they had been a week earlier, and similar to the DM*G*C at the same stage. There was a mild to moderate chronic inflammatory subepithelial infiltrate with a subepithelial layer of variable thickness. The epithelium was almost directly applied to the muscularis propria of the colocystoplasty in some areas. The re-epithelisation appeared virtually complete.

Inflammation, Fibrosis and Colonic Mucosal Regrowth Studies at Six and Twelve Months

At six months, there was negligible inflammation of the bladder components. Significantly, there were ***islands and aggregates of colonic epithelium*** not overgrown by transitional epithelium.

Animal #80-524 was the only animal sacrificed in this group that did not have colonic mucosa in the bladder at 12 months, but it did have histological changes consistent with its poor urodynamic results; there was minimal residual inflammation, but the subepithelial connective tissue was abnormal, being composed of a loosely arranged oedematous fibrous tissue of variable thickness.

In the remaining four animals colonic mucosa was found on the colonic muscle. In some areas the appearances were no different to those of the DMGC at the same stage, with transitional epithelium closely applied to muscularis propria of the underlying muscle, in this case, colon. There was only a very narrow layer of subepithelial connective tissue present in places. Of greater significance, however, were ***islands of viable colonic epithelial mucosa*** (Fig.28A) both along the surface of the specimen and *deeper within the muscularis*. There were also occasional islands of transitional epithelium surrounding small cystic dilated spaces. In parts colonic epithelium had been overgrown by transitional epithelium. Also seen were large dilated cysts full of mucous which had erupted, giving the appearance often seen in resected ileal conduit specimens (Fig.28B).

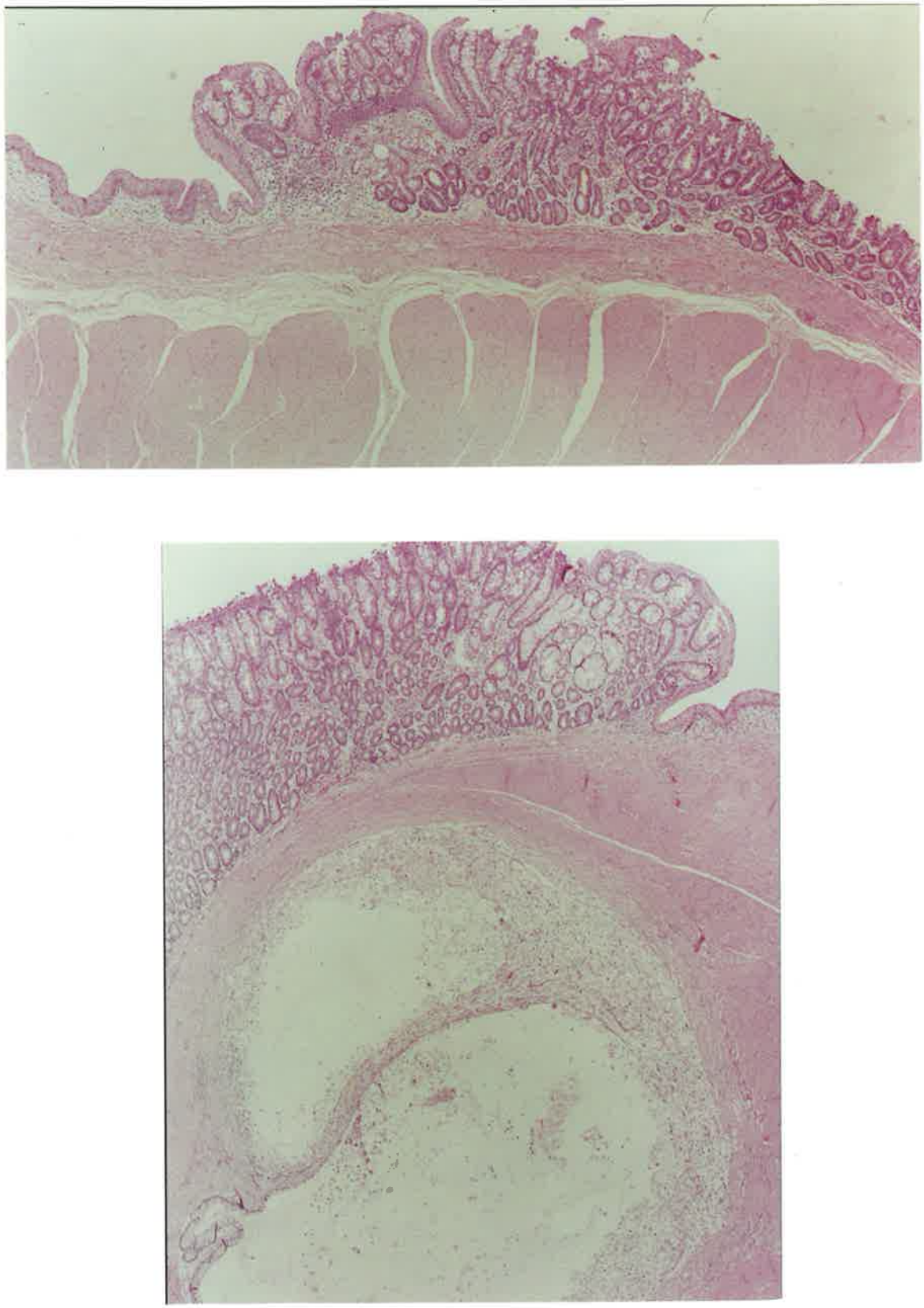


Figure 28: A. ***Colonic*** mucosa regrowth at 12 months: B. Mucous cyst formation in the colonic portion of a DMCC at 12 months.

Clinical Application of Urothelial Bladder Augmentation

MATERIALS AND METHODS

A total of 15 children have had a bladder augmentation using the urothelial bladder augmentation principle. The five who had an AAGC and the four who underwent an AACC had a procedure which evolved directly from the animal laboratory studies. The development of the ureterocystoplasty and diverticulocystoplasty resulted from the recognition of the value of urothelial lining for augmented bladders, therefore, these six children have been included in this study. These latter cases are important contributions as both the uretero-pyeloplasty and diverticula procedures have not been described in association with bladder augmentation surgery before.

Autoaugmentation Gastrocystoplasty

Five children had an AAGC. Four as a primary bladder augmentation, and the last boy had his procedure as part of an undiversion. They each had multiple nutritional parameters measured, including vitamin B_{12}, folate, serum iron, total iron binding capacity, white cell count and haemoglobin. The serum gastrin was measured initially at three monthly intervals.

All five children were given intravenous H_2 antagonists at operation and for five days after. They were fasted for 12 hours prior to the surgery, and were given intravenous Ampicillin (25mg/kg), Gentamicin (2mg/kg) and Metranidazole (10mg/kg) at the time of anaesthetic induction, and for thirty-six hours.

Urodynamic studies were carried out in the first four children preoperatively and up

to two years after the operation (Table 34). The bladder was filled on each occasion with 19% urografin at a filling rate of 20 ml per minute. The pressure profile was computer recorded and the bladder visualised with screening. The fifth child did not have a urodynamic study prior to the augmentation as his bladder was a closed cavity containing prostatic secretions and debris. A biopsy was taken of the removed gastric mucosa in all patients to ensure complete removal of the submucosa with the gastric lining.

Case 1: DB, a 16 year old young man with spina bifida had incontinence while on clean intermittent catheterisation (CIC) and anticholinergic medication. A nuclear medicine scan showed renal scarring and a cystogram showed a severely trabeculated bladder with bilateral grade V vesicoureteric reflux (VUR). He was wet both day and night, which required the wearing of a pad and frequent changes of clothes.

Case 2: JW, a 10 year old spina bifida boy who was incontinent on four hourly intermittent catheterisation and was intolerant of anticholinergics due to frequent side effects. His upper tracts were normal on ultrasound. His bladder was small volume and high pressure as shown in Table 34.

Case 3: KF, a 12 year old girl, with a neuropathic bladder due to a cerebrovascular accident, who was incontinent on Oxybutinin and three hourly catheterisation.

Case 4: DP, an eight year old girl who was born with a thoraco-lumbar myelomeningocoele and hydrocephalus. She had a small, trabeculated bladder and renal impairment despite anticholinergics, CIC and bilateral ureteric reimplantation for VUR.

Case 5: CD, a 16 year old young man born with spina bifida, who presented for

undiversion. He had an ileo cutaneous ureterostomy and appendectomy at 17 months of age. A cystogram and cystoscopy prior to his AAGC revealed an impassable urethral stricture, therefore, a two stage procedure was planned. The first step was an AAGC, and four months later an undiversion into the autoaugmented bladder was performed. Between the two operations he had intermittent bladder filling via a suprapubic catheter to encourage bladder enlargement. At the second operation the ileal conduit was incorporated into the augmented bladder and an intubatable stoma was fashioned from the combination of a tube of sigmoid colon and a mobilised skin tube.

Autoaugmentation Colocystoplasty

The four children in this group had their bowel prepared with 1.5-2 litres of Go-litely, until their bowel motion was clear. They were also given fluid diet for two days pre-operatively. The peri-operative antibiotic management was the same as for the AAGC group of patients.

Case 1: SG was a 9 year old girl who was born with a lumbo-sacral myelomeningocoele. She was noted to have VUR, renal dysplasia and an elevated creatinine in the first three years. Intermittent catheterisation, and anticholinergic medication failed to prevent a deterioration of the upper tract, therefore a ureteric reimplant was performed in 1990. This settled her urinary infections, but she continued to have incontinence both day and night. A urodynamic study was performed in November 1992, which showed a small volume, unstable high pressure bladder with gross unstable contractions of up to 67 cm of water. The end fill volume was 27 ml and the compliance less than 1 ml/cm of water. The Probanthine was changed to Oxybutinin and a second urodynamic study, performed

three months later, showed improved stability but with a capacity of only 40 ml.

Because the child was underweight it was felt the use of her stomach as a source of enteric muscle was unwise, so a routine sigmoid colocystoplasty was planned, with the proviso that, if the colon could be demucosalised without significant damage to the muscle, an AACC would be performed.

Case 2: AJ was a girl born with a lumbosacral myelomeningocele and bilateral talipes equinovarus. She had her back closed on the 5th day of life. Her horseshoe kidney remained stable, but she had poor bladder emptying, therefore she was commenced on CIC in 1988 at the age of one year. In 1991 her wetting was improved with anticholinergics, but not resolved, and she developed hydronephrosis by early 1993. A urodynamic study showed a high pressure bladder and a follow-up nuclear medicine study indicated that there had been deterioration in her renal parenchyma, despite the commencement of Oxybutinin. A further urodynamic study did not show any improvement in the pressure profile with Oxybutinin (Table 35).

Case 3: DH had her small sacral meningomyelocele closed soon after birth in 1981. A left ureteric reimplant was performed in 1986 for recurrent urinary tract infections whilst on intermittent catheterisation. Her urinary incontinence was not controlled on the combination of anticholinergic medication and CIC. A urodynamic study, without the antispasmodic, identified a bladder with unstable contractions and compliance of 1.0 ml/cmH_20 at a volume of 100 ml. As her kidneys had remained stable, and her incontinence was initially managed satisfactorily by conservative means, no intervention was planned. A pre-operative study showed a pressure of 30 cm H_20, with a volume of only 150ml, while on Oxybutinin. Bladder augmentation was planned because her wetting had worsened, and an AACC was performed on 17.11.93, with the addition of a bladder neck

wrap using a strip of rectus sheath.

Case 4: EG had an AACC at the age of 11 years on 23.2.94. She was born with a thoracolumbar spina bifida deformity, and required back closure and ventriculoperitoneal shunting in the first month of life. Her progress was marked by a spinal fusion at 10 years of age. Her kidneys were normal on ultrasound and a nuclear medicine scan, but her cystogram showed a large paraureteric diverticulum. A pre-operative urodynamic study indicated the bladder to be low volume and poor compliance (Table 35) and she was constantly wet on CIC and Oxybutinin.

For both forms of autoaugmentation enterocystoplasty the post operative management was similar. In theatre, the bladder was distended with saline instilled through a urethral catheter. For the first 12 hours after the operation the bladder was drained dependently. Thereafter the catheter bag was placed 15 cm above the bladder to encourage the urothelial and muscular layers to adhere. After 10 days, hourly catheter clamping was commenced and progressed to three hourly CIC over the following few days. For the remainder of the next month the bladder was drained continuously overnight, and via CIC during the day. After a cystogram at one month all were converted to daytime catheterisation only. In the fifth AAGC case the bladder was filled for 30 minutes three times each day with increasing volumes of fluid for four months, prior to incorporation of the ileal conduit as part of his undiversion and continent stoma formation.

Ureterocystoplasty

Case 1: CW was irritable for two weeks before he presented as a sick, four month old infant. He had normal kidneys on ultrasound at 18 weeks gestation and was thought to have a normal urinary stream postnatally. On investigation he was found to have an Enterococcal urinary infection and bilateral hydroureteronephrosis. An antegrade cystogram, through a suprapubic catheter, showed a typical congenital obstructing posterior urethral membrane. When biochemically stable, his urethra was examined endoscopically, and the obstructing membrane was seen to have a small posterior defect, to prolapse as suprapubic bladder compression was applied and to split on passage of the cystoscope. He had recurrent urinary tract infections with grade five VUR into his left kidney. His bladder volume was small and his pressure lowered only by the reflux into his upper tract. An extraperitoneal, two incision nephrectomy and ureterocystoplasty was advised and performed at nine months of age.

Case 2: SC presented at 12 days of age with urinary tract infection, renal failure and metabolic acidosis. A cystogram revealed a very trabeculated bladder with multiple pseudo diverticula and gross left VUR. The prostatic urethra was dilated and a convoluted urethral diverticulum was demonstrated to cause obstruction of the membranous urethra. An isotope renal scan showed bilateral poorly functioning, scarred, small kidneys. A vesicostomy was established and closed 2 months after urethral surgery. His renal function showed progressive deterioration, so that at the age of nine years he underwent a living related donor renal transplantation. Pre-transplant urodynamic studies showed that he had a low pressure, good volume bladder. Subsequently he was able to void spontaneously with satisfactory bladder emptying and only intermittent wetting which persisted despite Oxybutynin. A video-urodynamic study performed two years later revealed a high pressure unstable bladder, with native ureter VUR which had become bilateral. The storage capacity

was 184 mls, a significant proportion of which was in the left kidney and ureter, and the degree of trabeculation had increased. A ureterocystoplasty and Teflon injection of the right ureteric orifice was therefore carried out.

Case 3: AB was found to have bilateral hydronephrosis and a thick walled bladder at 24 weeks gestation. Right renal aspiration at 28 weeks recorded normal fetal renal biochemistry. As the amniotic fluid remained stable the pregnancy was continued to 37 weeks without further intervention. Postnatal investigation confirmed gross right uretero-hydronephrosis and echogenic parenchyma and minimal renal tissue on the left. He was further investigated with an antegrade cystogram and cystoscopy. An obstruction at the level of the bulbar urethra, seen on the cystogram, was noted to consist of a membrane sweeping down from the level of the verumontanum with a 3mm defect present in its posterior aspect. Much of the membrane was disrupted by passage of the endoscope, and the remainder was resected with diathermy. This boy continued to undergo further renal functional assessment after initial stabilisation of his creatinine at 70 mmol/l. His bladder was demonstrated to be small volume and high pressure (Table 36), his left kidney was non-functioning, and his urethra was able to be catheterised, indicating that his redundant ureter would not be needed as a catheterisation stoma. He was considered a candidate for ureterocystoplasty.

Case 4: MP was born with an anorectal anomaly and apparent normal bladder function prior to his posterior sagittal anorectoplasty. He was however noted to have grade five VUR. After the repair of his anorectal anomaly he developed retention, and was commenced on CIC. A urodynamic study indicated that his bladder pressures were kept low by progressive marked distension of his left upper tract. As his bladder emptying had not improved and he had recurrent urinary tract infections it was decided that surgical management of his reflux was indicated, and as he still required CIC, a ureterocystoplasty was deemed appropriate. Pre-

operative studies showed a partial right pelviureteric junction obstruction, so the dilated left ureter was anastomosed to the longitudinally incised upper ureter, pelviureteric junction and pelvis of the right side, preserving the left kidney which was providing 30% of overall renal function. This is the first description of transuretero-pyeloplasty. His operation was performed through a midline transperitoneal incision.

Case 5: DC was noted to have spina bifida prenatally. Following his back closure, soon after birth, he developed hydrocephalus and urinary retention, and bilateral inguinal herniae. His cystogram showed only mild bladder trabeculation, but gross dilatation of his left ureter and pelvicalyceal system. A urodynamic study indicated the bladder was small volume and high pressure, with a significant proportion of his 37 ml urine storage capacity (Table 36) in his left ureter and kidney. Despite CIC and prophylactic antibiotics he developed urinary tract infections and a reduction in the differential function of the left kidney. An intravenous pyelogram was performed pre-operatively to study his ureteric anatomy; it showed a normal right ureter and pelvicalyceal system, and left hydroureteronephrosis. A transperitoneal, transureteroureterostomy and ureterocystoplasty were planned.

Diverticulocystoplasty

Case 1:

G.F. was born with a lumbar myelomeningocele, which was closed on the first day of life. His neurological deficit consisted of an asymmetric paraplegia and neurosensory loss from L3. He developed hydrocephalus, which required the insertion of a ventriculo-peritoneal shunt in the third week of life.

At four months of age a video-cystometrogram showed a non-compliant high pressure bladder, without unstable contractions. There was no VUR and the kidneys were normal on ultrasound. The infant was started on CIC but had frequent urinary tract infections with fever, offensive urine, behaviour changes, and abdominal pain, and he was not kept dry by the catheterisation.

A repeat cystogram showed a trabeculated bladder and urodynamics again recorded bladder pressures over 100 cm of water, with a functional capacity and leak point of 65 ml (Table 37). The CIC was increased to 2.5 hrly and prophylactic antibiotics were commenced. A circumcision was performed and anticholinergic medication was given. These measures failed to prevent wetting or recurrent symptomatic urinary infections.

The patient was first investigated by myself at 32 months of age. The kidneys were normal on an ultrasound and nuclear medicine scan, but the bladder was thick walled and showed two large postero-lateral diverticula. A cystogram showed multiple small diverticula over the bladder dome, and the two large diverticula postero-laterally.

In view of the paraureteric diverticula, the poorly compliant, high pressure bladder,

wetting and recurrent urinary tract infections, a decision was taken to remove the infective foci and concurrently improve the bladder volume by incorporating the diverticula into the bladder wall rather than discard them. The operation was performed at the age of 33 months.

OPERATIONS

Autoaugmentation Gastrocystoplasty

In all patients the stomach was identified through a long midline incision and the position and size of the appropriate portion of stomach needed for the augmentation was identified. Adequacy of the length of the right gastroepiploic arcade was checked and branches of the right gastroepiploic to the greater curve and duodenum were divided up to the distal limit of the gastric patch. After preparing the vessels, the wedge segment was clamped, incised, and separated from the remainder of the stomach, which was closed with a continuous polyglycolic acid suture. The gastric mucosa of the isolated segment was removed from the muscle using diathermy dissection, with care to injure the mucosa rather than the muscle, while avoiding leaving islands of gastric mucosa. The gastric mucosa was sent for histological assessment to determine the adequacy of the submucous dissection.

Next, the bladder muscle was incised in the midline, from the anterior to the posterior bladder neck region. The muscle was separated from the urothelium through the submucous plane for approximately one third of the bladder muscle to mucosa contact, resulting in herniation of the bladder mucosa. The urachal remnant was sutured to the mid-point of the gastric muscle flap which was then sutured edge to edge with the bladder muscle, thus covering the exposed bladder mucosa with the raw surface of the gastric muscle. The bladder mucosa was, therefore, left intact, with both bladder and stomach muscle covering it.

All the patients in this group had previously had a ventriculo-peritoneal shunt inserted and therefore had a number of intra-abdominal adhesions which lengthened

the time of the procedure, and made dissection of the vascular pedicle to the stomach segment difficult.

Case 4 had also had ureteric reimplants prior to the AAGC. This resulted in it being necessary to leave a thin strip of bladder muscle on the anterior aspect of the urothelium to prevent tearing of the bladder lining.

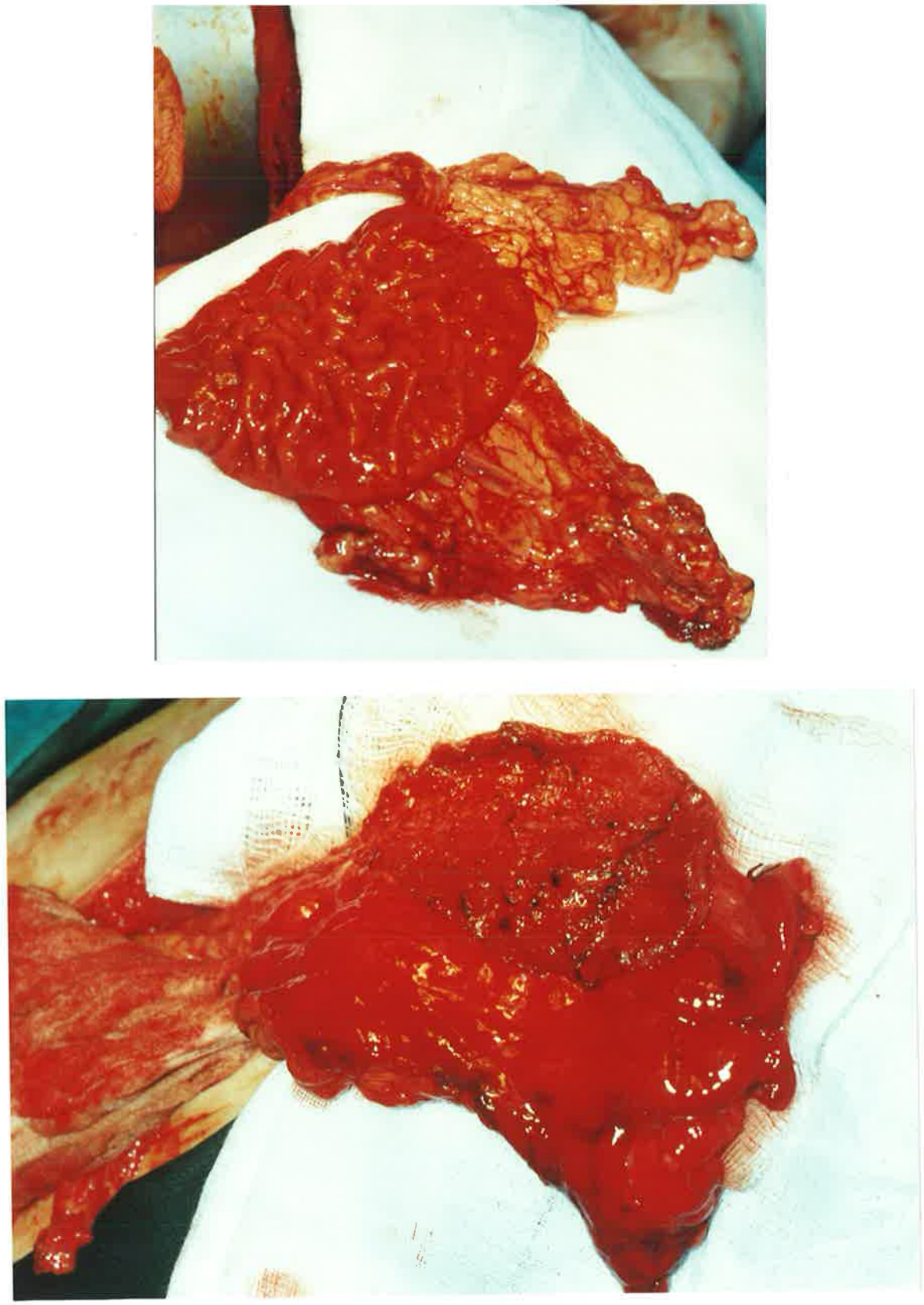


Figure 29: A. The stomach segment prior to partial resection for the AAGC: B. The denuded stomach prior to inclusion into the bladder.

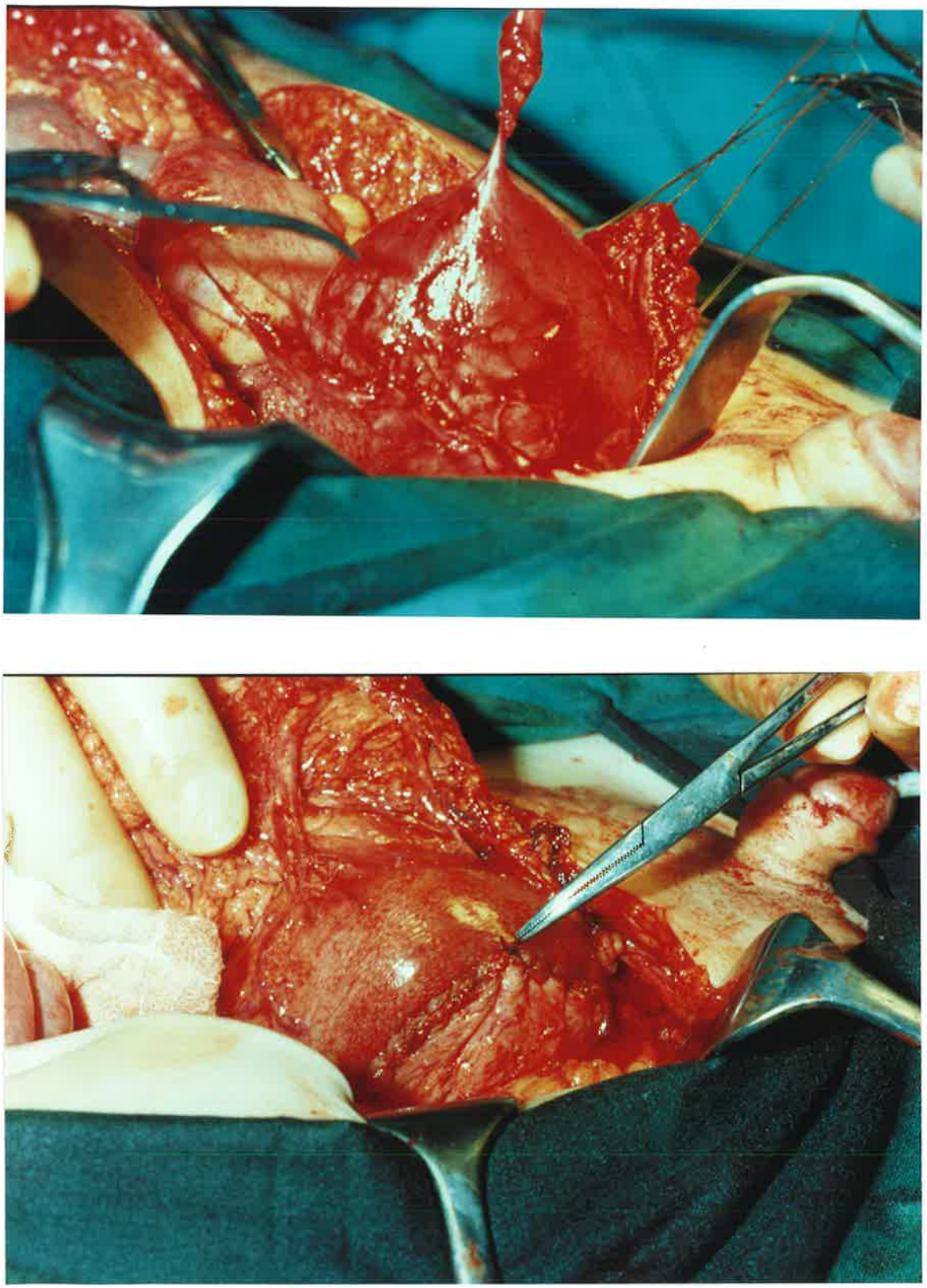


Figure 29: C. The urothelium bulging between the edges of the detrusor muscle after the autoaugmentation: D. the muscle of the stomach and bladder are in place at the end of the AAGC procedure.

Autoaugmentation Colocystoplasty

Most of the sigmoid colon was mobilised on the inferior mesenteric vascular pedicle, separated from the faecal stream, then opened along its antimesenteric border with diathermy, and cleaned with betadine. Colonic continuity was restored with a single layer, 2/0 polyglycolic acid suture anastomosis. Dissection of the mucosa from the underlying muscle was then commenced using diathermy dissection. Care was taken to remove the submucosa to prevent epithelial regrowth. To check the quality of this dissection the mucosa was examined histologically. This part of the procedure took up to two hours. Bladder autoaugmentation was performed in the same manner as for the AAGC. The demucosalised muscle was sutured to the bladder in the clam fashion, over the intact bladder mucosa, with the bladder mucosa sutured to the mid-point of the colonic patch via the attached urachal stump. The bladder muscle was hitched to the psoas muscle in the standard manner in this group.

The bladder was drained for 24 hours via a catheter placed in the dependent position, and subsequently with the catheter bag elevated to 15cm above the bladder for 10 days.

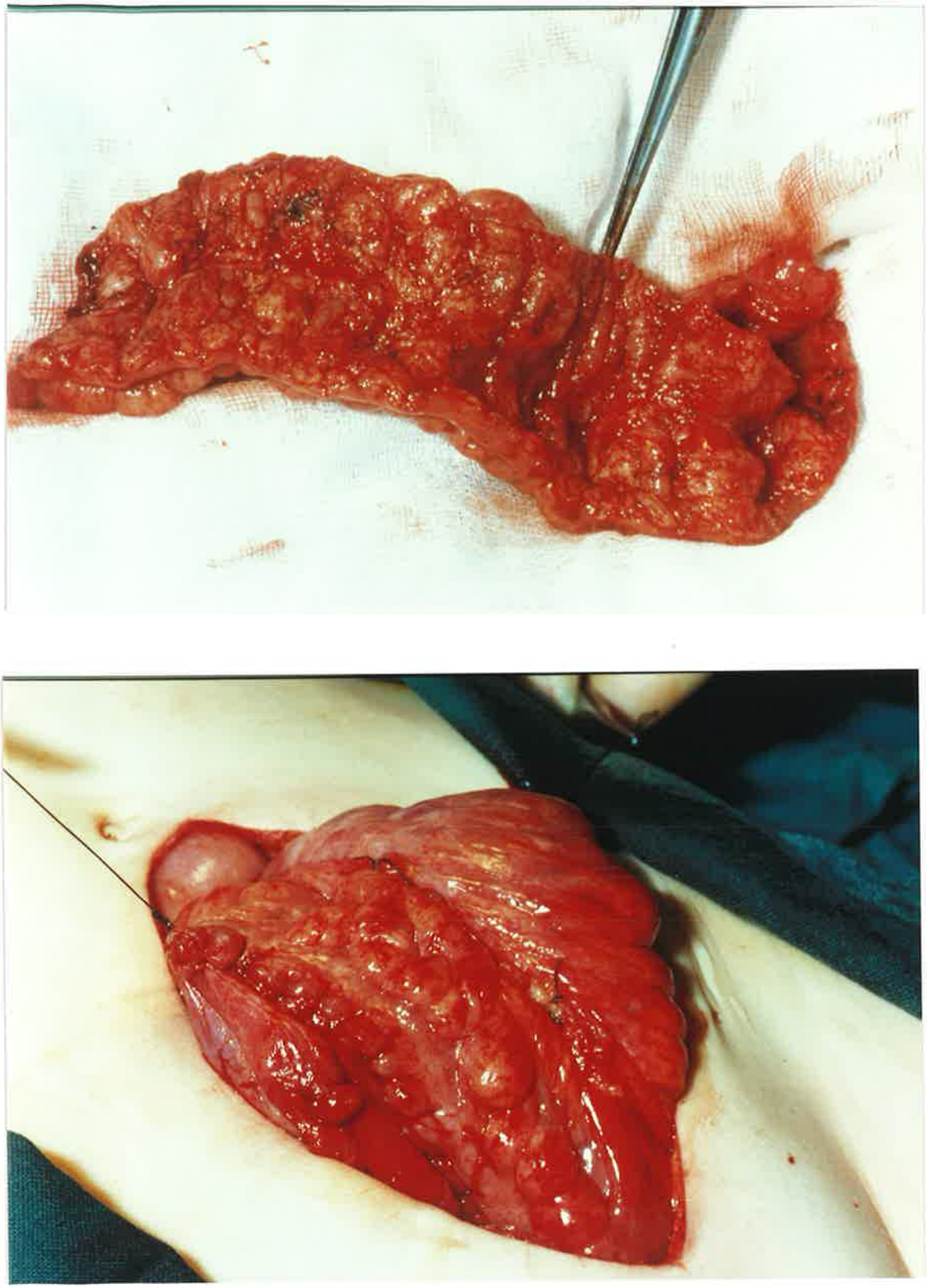
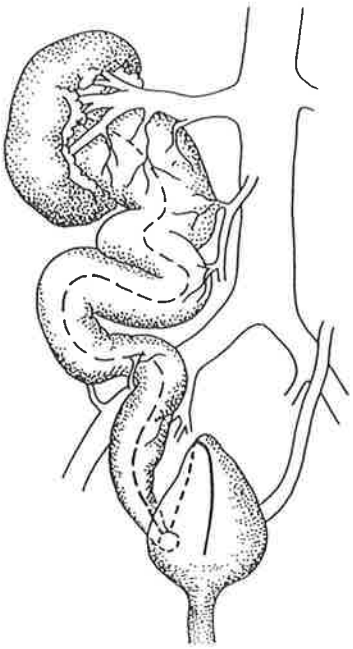


Figure 30: Autoaugmentation Colocystoplasty - A. The denuded segment of colon prior to inclusion into the bladder: B. The completed Autoaugmentation Colocystoplasty.

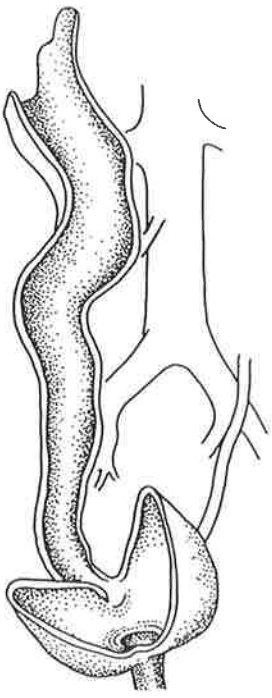
Ureterocystoplasty

Extraperitoneal procedure with nephrectomy: Fig.31 & 32: the three boys who had this procedure were placed in the semi-lateral position, the kidney was mobilised through a lateral, subcostal, muscle cutting incision. The blood supply of the ureter was preserved during mobilisation down to the pelvic brim, with the peritoneum left intact. The kidney was removed, the upper end of the ureter tied and the ureter placed in the pelvis and the flank wound closed. The bladder and mobilised ureter were exposed via a transverse suprapubic skin incision and the ureter further dissected, taking care to preserve its lower lateral blood supply and avoid entering the peritoneum. When the ureter was freed sufficiently, the bladder was opened from the anterior bladder neck, over the dome, to the orifice of the ureter from which the kidney had been removed. A 12FG catheter was inserted into the ureter, which was opened along its antero-medial border. The lateral aspect of the vesicoureteric junction was not dissected, to avoid compromise of the ureteric vasculature. The free edges of the inferiorly based ureteric flap were then sutured to the edges of the incised bladder with a continuous 3/0 Vicryl suture. In the third patient the right sided VUR was managed by the injection of 0.5ml of Polytef paste under the ureteric orifice, in anticipation of the possible need of a ureter as an intubatable stoma. A suprapubic bladder catheter was left in situ and the abdominal wound was closed.

Figure 31: Extraperitoneal Ureterocystoplasty



A. The bladder and ureter incision line used after a flank incision nephrectomy.



B. The bladder and ureter incised.

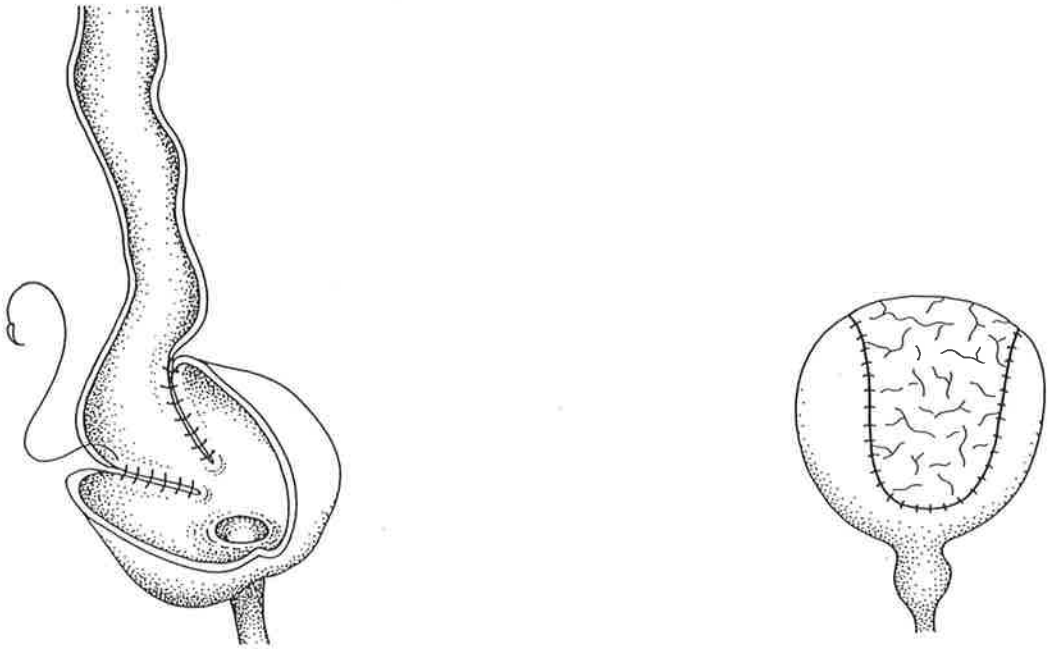


Figure 31: C. Parallel suture lines anastomose the ureter and bladder: D. The completed ureterocystoplasty.

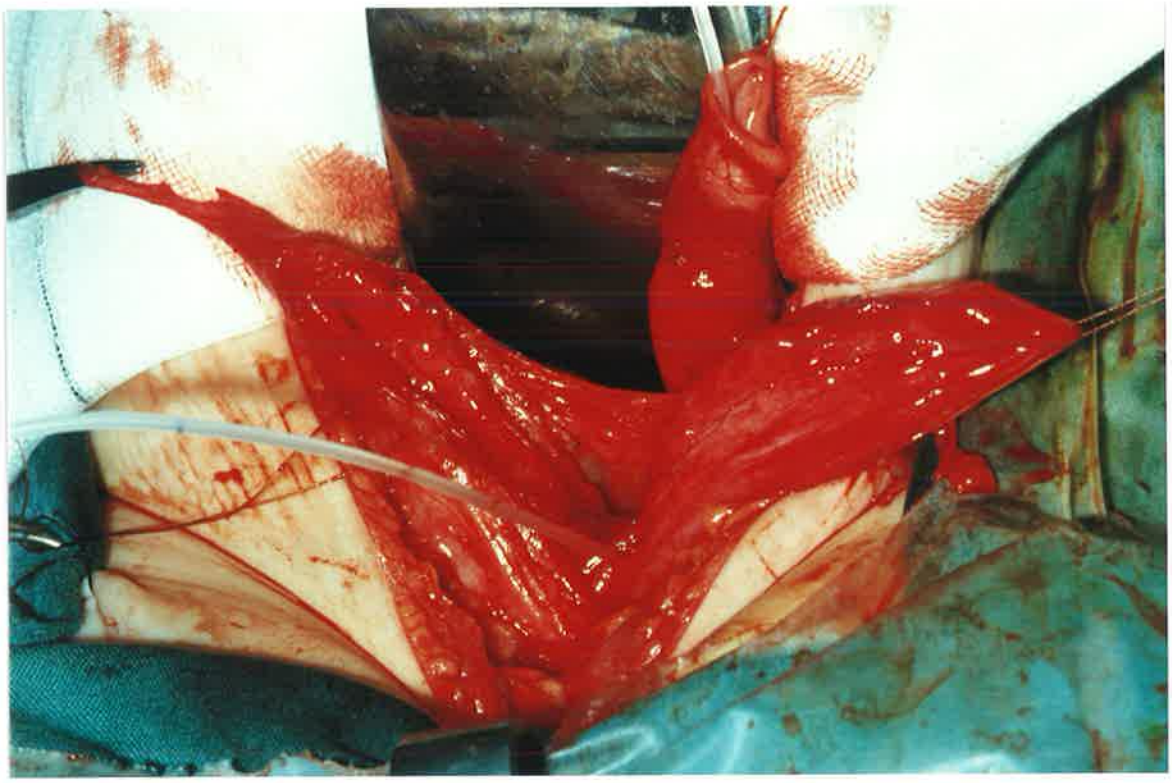


Figure 32A: The dilated ureter to be used for the ureterocystoplasty is mobilised and catheterised.

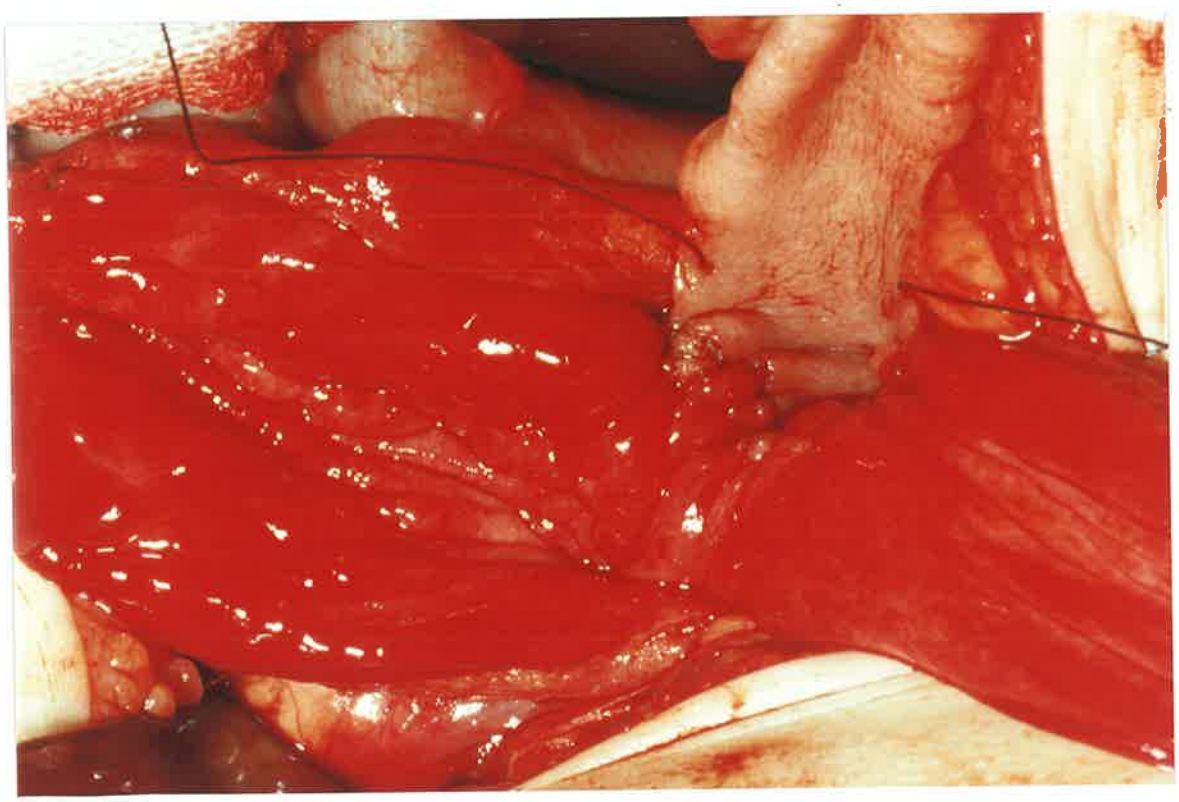


Figure 32B: A longitudinal incision has been made in the ureter.

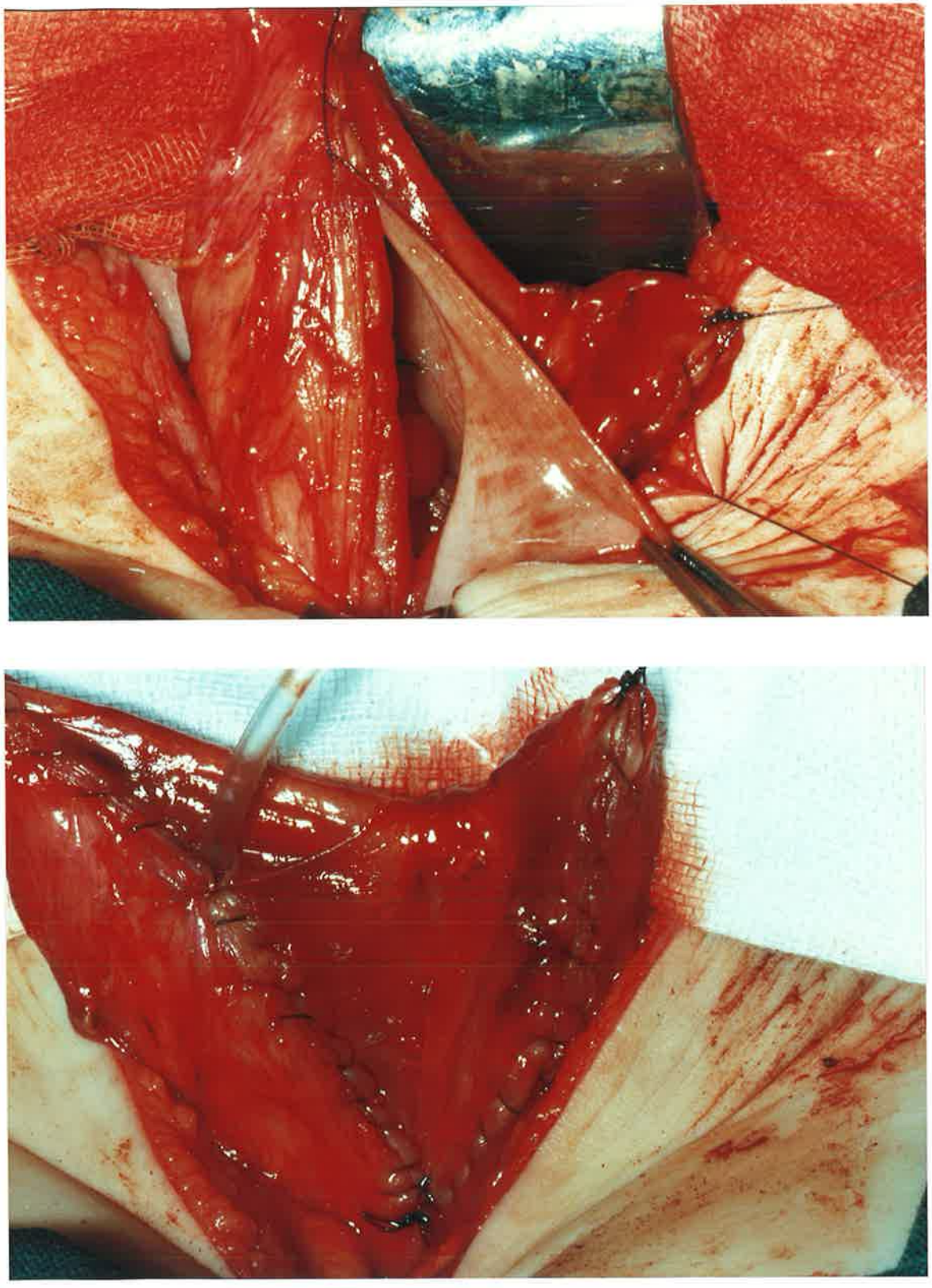


Figure 32: C. Parallel sutures incorporate the ureter into the bladder wall with the neo-bladder virtually completed: D. An anterior view of the completed ureterocystoplasty.

Transperitoneal procedure without nephrectomy: *Fig.33 & 34*: In two boys the renal function of the refluxing side was sufficient to demand preservation of the kidney.

Case 4: this boy also had a moderate degree of pelviureteric hold-up, which was also evident macroscopically at the time of operation.

Through a midline incision the small bowel mesentry and the right colon were mobilised to give access to the retroperitoneal space up to the level of the renal pelvis on each side. The left ureter was divided 3cm below the pelvis and positioned against the right pelviureteric junction which it reached by passing anterior to the inferior mesenteric artery. The upper right ureter and lower pelvis were then mobilised and opened longitudinally. The extreme narrowness of the junction made this step difficult (Fig.33A). With a probe down the ureter, an end-to-side anastomosis was performed (Fig.33), leaving the distal end of the upper left ureter bridging the narrow portion of the upper right ureter. A ureterocystoplasty was then performed with the lower end of the left ureter in the same manner as described for the previous boys. A redivac drain was placed in both renal beds and a nephrostomy tube was inserted into the left kidney.

Case 5: through a midline incision the small bowel mesentry was mobilised sufficiently to allow the tortuous left ureter to be anastomosed to the normal (small) right ureter as an end-to-side transureteroureterostomy, just above the pelvic brim (Fig.34). The right ureter was only minimally disturbed. A ureterocystoplasty was performed with the lower left ureter, and the wound was closed with the only drain being the suprapubic catheter.

Figure 33: Transperitoneal Ureterocystoplasty without nephrectomy - transuretero-pyeloplasty

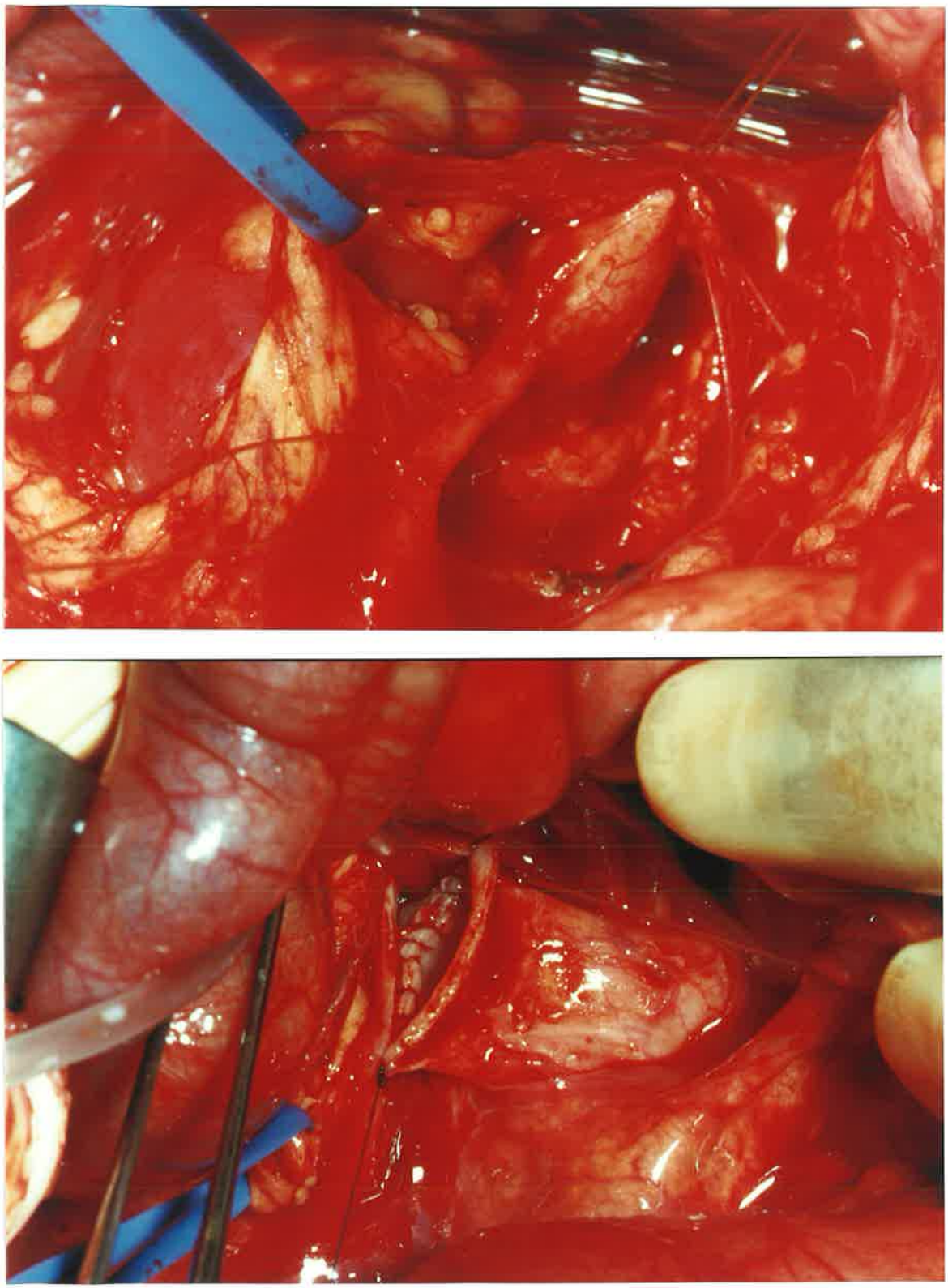


Figure 33: A. The partially obstructed right pelviureteric junction before incision: B. Large left ureter joined to the right pelvis, upper ureter and pelviureteric junction.

Figure 34: Illustrations of the Transperitoneal Ureterocystoplasty.

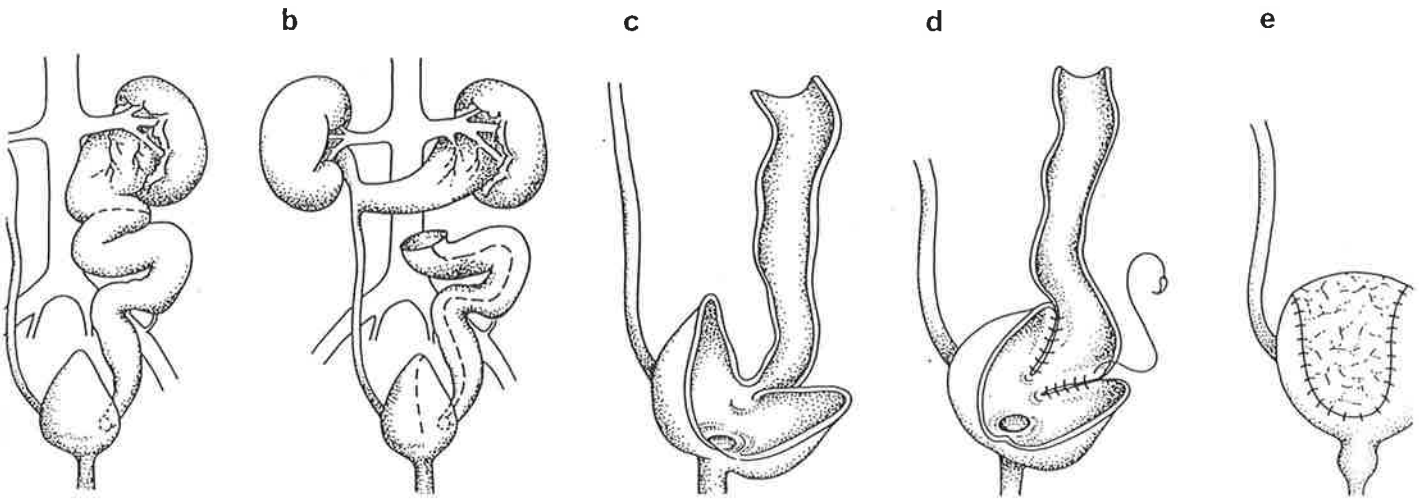


Figure 34: The dilated ureter (A) is divided just below the kidney and the upper ureter is anastomosed to the contralateral ureter (in this case upper ureter). The subsequent bladder and ureter incisions are indicated (B). The ureter is incised longitudinally (C) and sutured into the open bladder (D), giving a clam cystoplasty appearance at the end of the procedure (E).

Diverticulocystoplasty

The thick walled and trabeculated bladder was opened through a Pfannenstiel incision and an extraperitoneal approach (Fig.35). A midline anterior incision, beginning at the dome of the bladder, was extended half way down the anterior wall. From here the incision extended toward the orifice of each diverticulum, which had been identified from within the bladder. The ureteric orifices were splinted separately. The diverticula were partly mobilised from their outer surface, particularly the portion resting against the bladder. The junction of the two diverticula and the bladder could then be appreciated and the incision was extended partly around the origin of each diverticulum. Subsequently, parallel incisions in the diverticula were extended from their bladder attachment to their apex. This produced bilateral vascularised flaps, based on the lateral bladder attachment of the former diverticula, with an undisturbed lateral blood supply. Care was taken not to interfere with the blood supply of the lower ureter. The diverticula flaps were integrated into the bladder with Polyglycolic acid sutures and the ureters were buried in the bladder muscle using the Lich-Gregoir technique. The flaps covered a large area on the anterior wall extending to the dome of the bladder; a suprapubic, as well as ureteric catheters were placed, and the bladder closed.

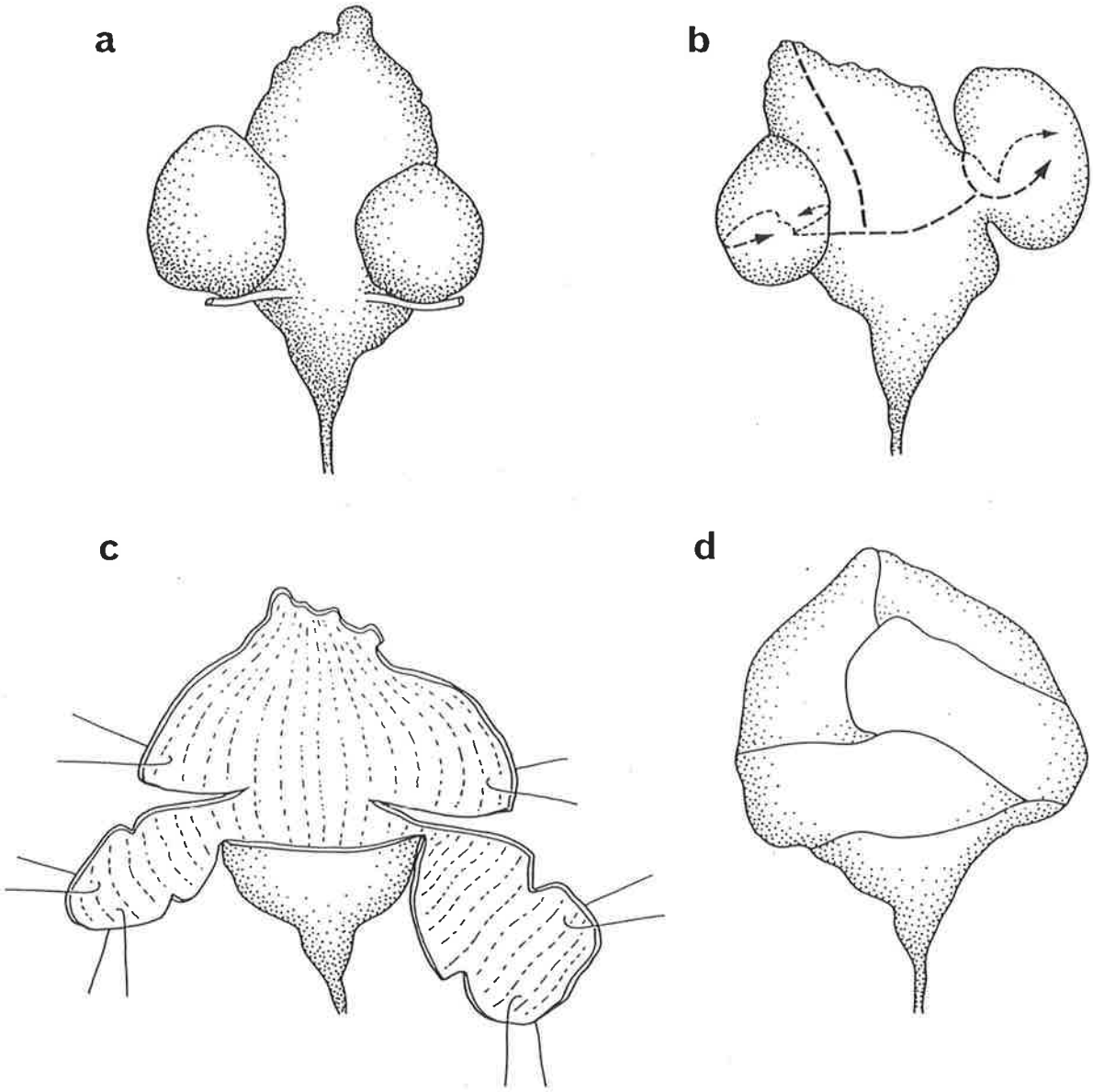


Figure 35: The two diverticula were mobilised on a vascular pedicle based laterally and sutured into the anterior wall of the bladder: A. Bladder and diverticula (posterior view): B. Incisions (oblique anterior view): C. Flaps formed (anterior view): D. Reconstructed bladder (anterior view).

RESULTS - PATIENTS

Autoaugmentation Gastrocystoplasty

The urodynamic results are shown in Table 34. The *clinical* and *radiological* results are as follows:

The gastric mucosa for all patients showed full thickness mucosa with the complete submucosa in most of the sections. In areas where the submucosa was not completely intact it appeared to have been damaged by the diathermy. In all patients, urine contained debris in the early post-operative period which, when examined histologically, showed urothelial cells. This loss of urothelium may have influenced the augmentation outcome, but was seen in *Case*s 2 and 3, one of whom had an excellent result and the other much improved by the procedure.

Case 1: DB had improvement in his incontinence which was reduced to minimal wetting overnight, his grade five VUR was reduced in severity, and his progressive renal deterioration was stabilised. His bladder dynamics continued to improve, after only a moderately good result at three months. He was tolerating up to 800 ml, with a bladder volume of 500ml on his latest urodynamic study at 24 months (Fig.36). A minor deterioration in his left renal function prompted bilateral ureteric reimplants at that stage. His bladder was smooth walled and the two components of the bladder could not be readily differentiated from within. Importantly, there was no evidence of any gastric mucosa within the bladder.

Case 2: JW's wetting has improved, but he continues to be incontinent, related to continued unstable contractions, which have not been able to be controlled by anticholinergics due to intolerance of the medication. His bladder volumes on

catheterisation are in excess of 600ml.

Case 3: KF had an excellent response to the AAGC, with complete resolution of her incontinence and an improved bladder configuration on cystogram (Fig.37). She has been dry on a single daily dose of Oxybutinin, with catheterisation volumes of 400ml (Table 34).

Case 4: DP developed cloudy urine ten days after her AAGC and significant numbers of epithelial cells were seen on cytology, suggesting sloughing of part of the autoaugmentation. An ultrasound three months later showed a double component bladder which was also seen on a cystogram (Fig.38). The two components of the bladder were united at a second operation; one component was formed by the stomach and the other by the original bladder with both lined by urothelium and separated by a bridge of urothelium. The cystogram appearance and urodynamic values have subsequently improved, with bladder volumes at two years of up to 400ml on CIC, and a compliance of 15.5 ml/cmH_2O on the urodynamic study.

Case 5: CD had his bladder volume increased to 1000ml over a four month period after his second operation, and his upper tract remained stable. A urodynamic study was performed 12 months after his second operation which showed a good volume, low pressure bladder, from which he continues to reflux. Reimplantation of his ureters was not possible at the time of the augmentation because of their short length. He remains well on six hourly CIC, with very little bladder mucous and no urinary tract infections.

Cases 2 and *3* have normal renal function; cases 2, 3 and 4 had transient intolerance of large meals, which resolved over a 6-12 month period, and no significant

gastrin abnormality was seen in any patient, although a transient rise occurred in *Case 4* prior to her second operation.

Table 34: Compliance and bladder volumes preoperatively, and at 3, 12 and 24 months after the AAGC.

Case	1	2	3	4	5
Compliance (ml/cmH_2O)					
Pre-operative	1.0	1.0	1.0	1.0	-
3 mths	6.9	3.5	11.3	1.0	-
12 mths	12.0	10.2	11.4	6.0	34.0
24 mths	75.0	41.8	40.0	15.5	-
Volumes (ml)					
Pre-operative	50	50	80	90	-
3 mths	277	282	170	50	-
12 mths	348	409	410	160	480
24 mths	500	418	321	208	-

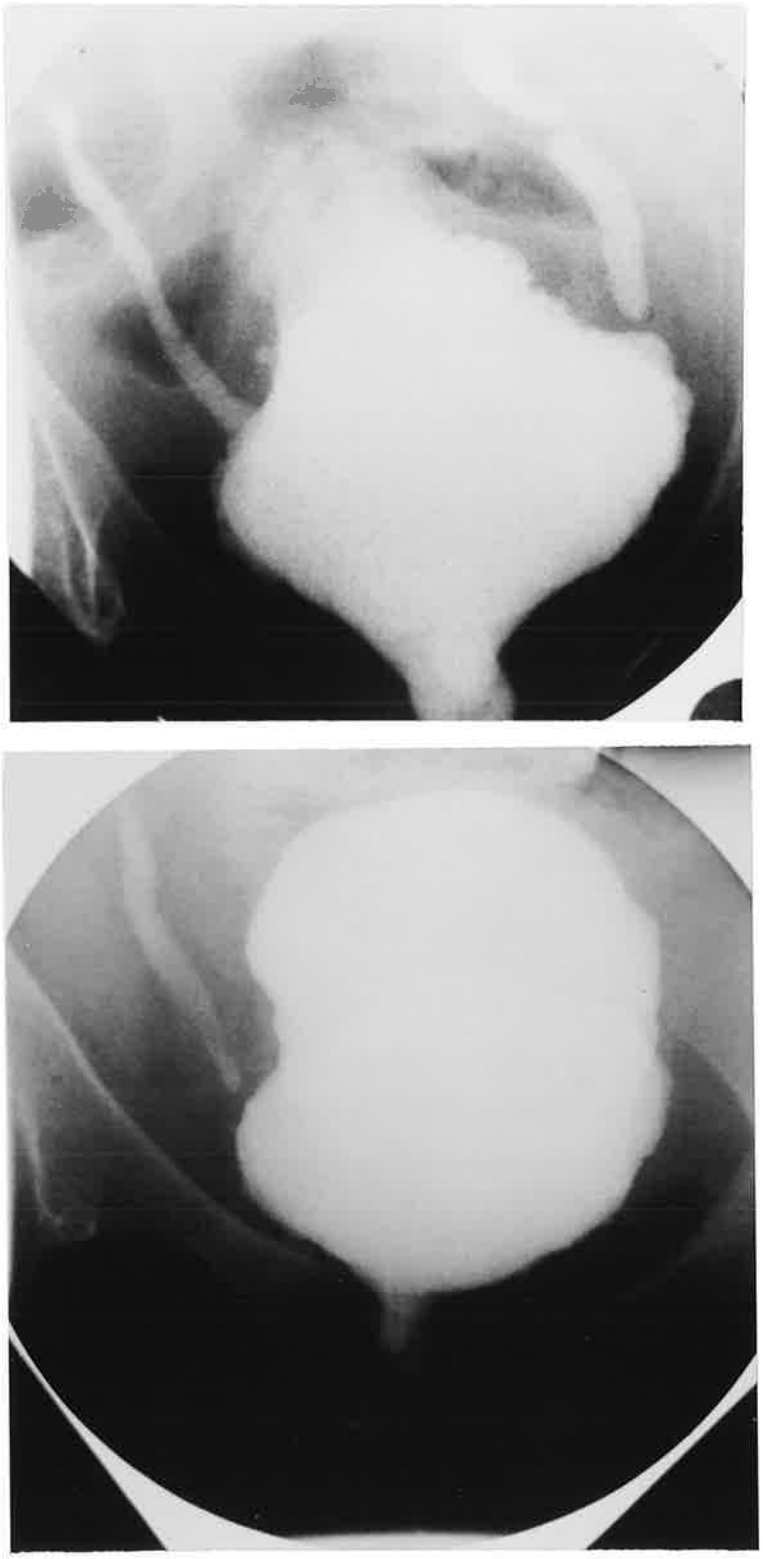


Figure 36 - *Case 1*: This boy's highly trabeculated bladder had high grade vesicoureteric reflux pre-operatively (A). The gastric component can be seen in the follow-up study at 24 months (B).

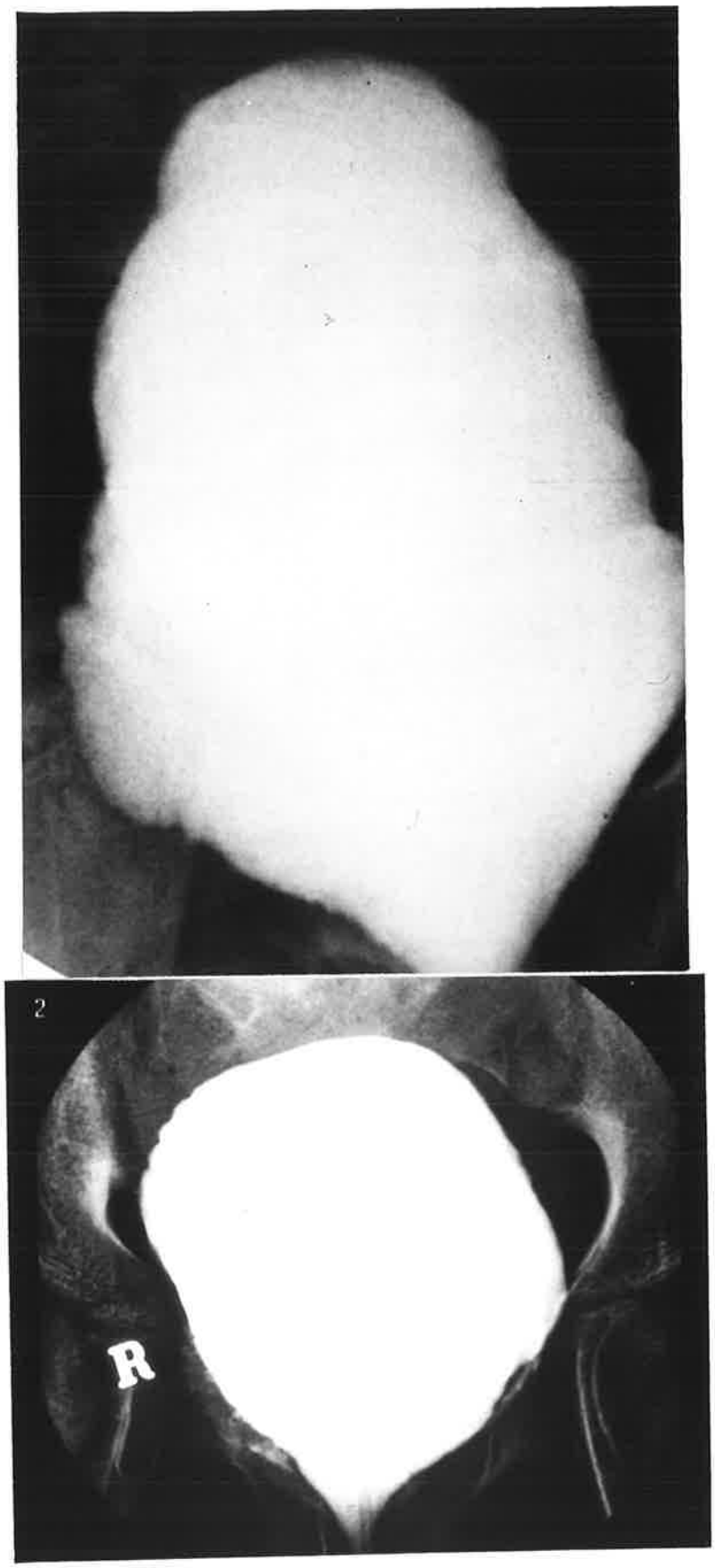


Figure 37 - *Case 3:* A good bladder shape following an AAGC. The pre-operative (A) and post-operative cystograms are both given (B).

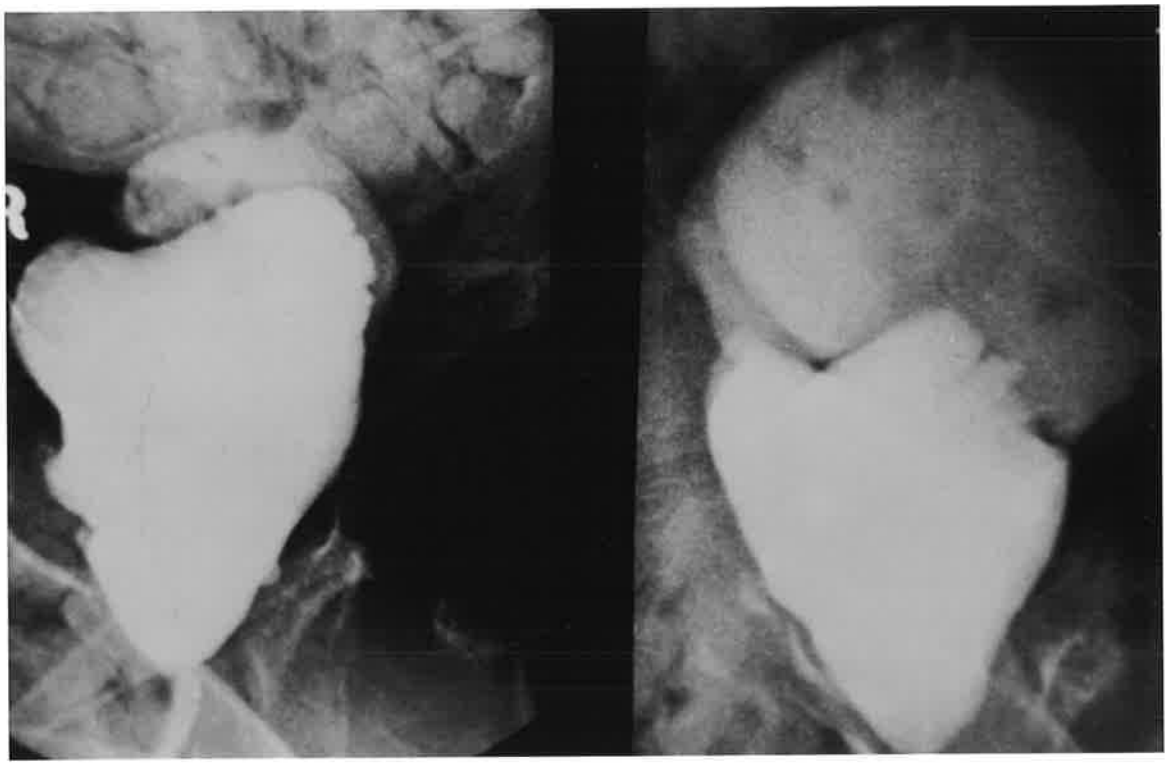


Figure 38 - *Case 4*: A double bladder was initially seen at 6 weeks with a small rim of contrast over the dome of the bladder (A). At five months the formation of the double bladder was more definite, with contrast having leaked into the gastric component of the bladder from the native bladder below (B).

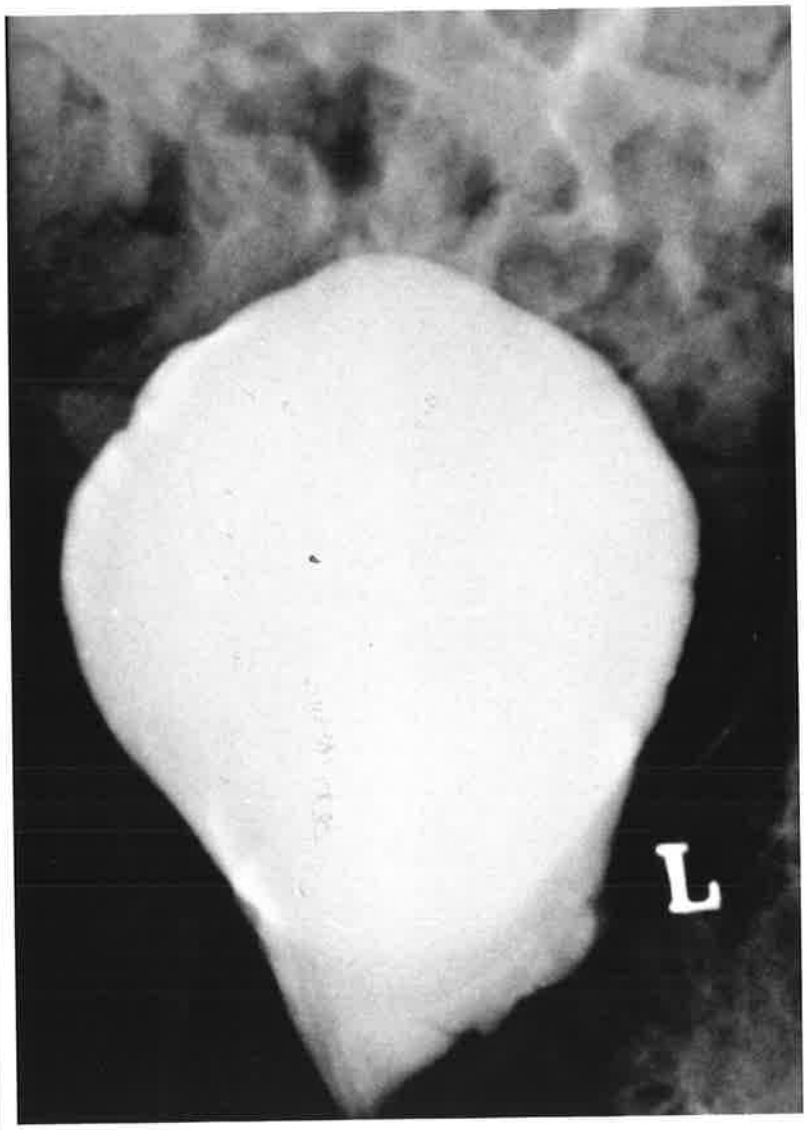


Figure 38C - *Case 4*: after the gastric and original bladder components have been united at a second operation.

Autoaugmentation Colocystoplasty

The mucosa of the colon was histologically assessed in three of the four patients to ensure complete removal of the submucosa. In each, the submucosa was included in the resected specimen. In one, the mucosa was presented *in toto*, in the other two a portion was submitted. The resection margin was in the deeper layers, with evidence of diathermy damage of the adjacent submucosa in all cases.

Case 1: SC has made an excellent post-operative recovery, and had CIC volumes of 100 ml at three weeks, and was dry between catheterisation. Her bowel function was unchanged by the operation. A urodynamic study was performed four months after the AACC which demonstrated a fill volume of 213 ml with a leak pressure of 15 cmH_2O and a compliance of 14 ml/cm H_2O (Fig.39). The contour of her bladder was also satisfactory when compared to the preoperative appearance and was similar to *Case 3* (Fig.40). At 12 months her CIC volumes were up to 300 ml and she was dry both day and night apart from the occasional accident. Her urodynamic study at 12 months showed an insignificant decrease in volume soon after an infection.

Case 2: AJ continued to have wetting, but with improved catheterisation volumes which appeared to be improving with time. She also initially had a significant problem with diarrhoea and faecal incontinence which settled with codeine phosphate. Her initial urodynamic study, however, showed a less satisfactory bladder volume, which improved at 12 months to a volume of 300ml. She is now dry, with stable kidneys and bladder volumes of up to 400ml on CIC.

Case 3: DH had a urodynamic study three months after surgery which showed a peak volume of 579ml with a compliance of 30ml/cm of water. Her CIC volumes

were up to 700ml and she is now usually dry both day and night. Her bowel function has been normal.

Case 4: EG in the early post operative period there was a small amount of cellular debris followed by two days of blood stained urine, this was confirmed to be associated with a resistant strain coliform urine infection. Her bladder on cystogram appeared unsatisfactory at 10 days, but had improved significantly at one month; at two months her wetting had significantly improved and her catheterisation volumes had increased to 450 ml, despite having a urinary tract infection. Her urodynamics study at three months were not satisfactory, however a further study at 12 months showed a good bladder (Table 35).

Table 35 shows the urodynamic results at three months for the FOUR AACC patients.

Case		1	2	3	4
Compliance (ml/cmH_2O)					
Pre-operative		1.0	3.7	7.5	1.6
3 mths		15.0	4.5	29.5	2.5
12 mths		13.9	12.3	26.9	22.5
Volumes (ml)					
Pre-operative		40	225	150	156
3 mths		213	137	579	130
12 mths	(UTI)	195	307	484	450

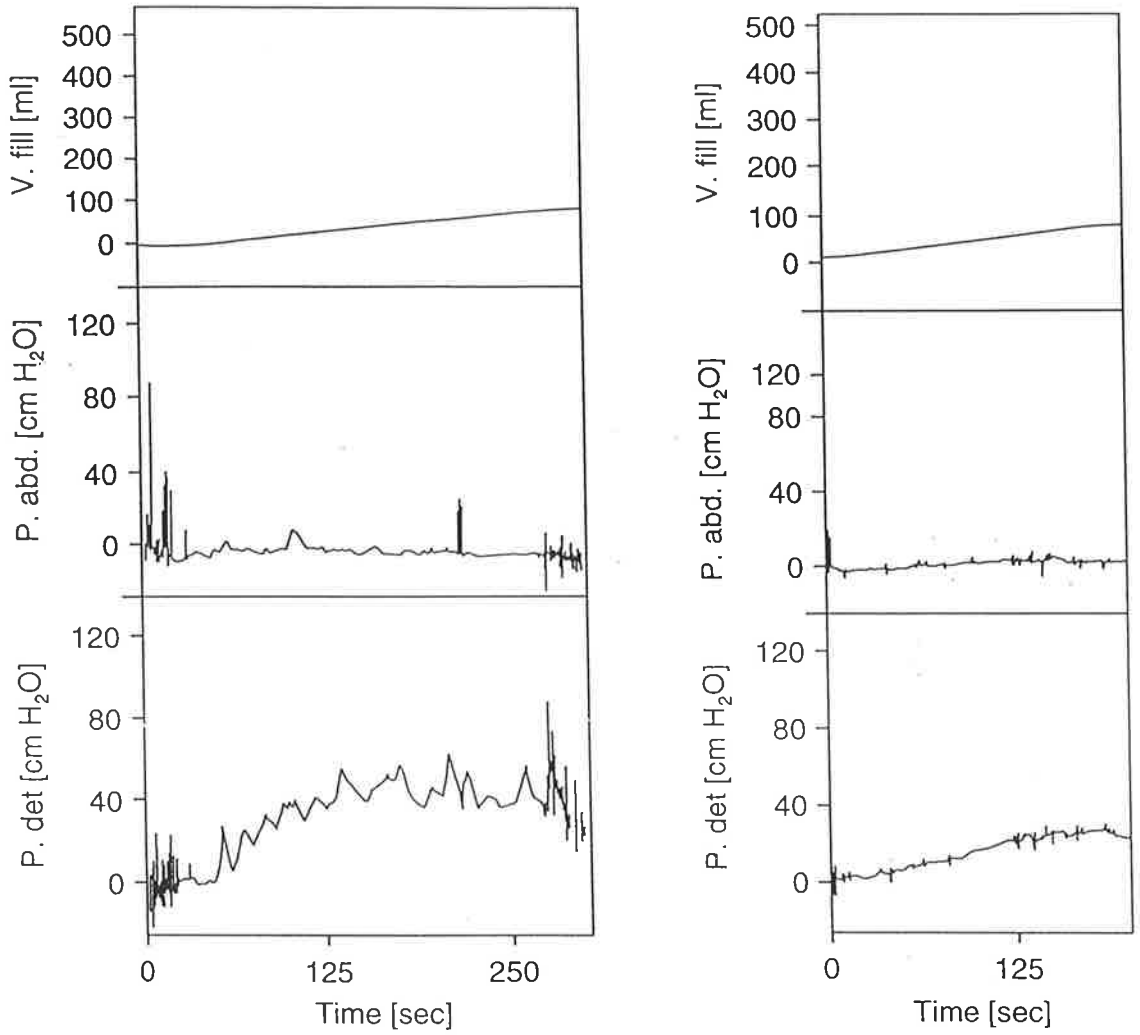


Figure 39A+B - *Case 1*: The urodynamic chart prior to anticholinergic medication (A) and while on anticholinergic medication (B) before augmentation.

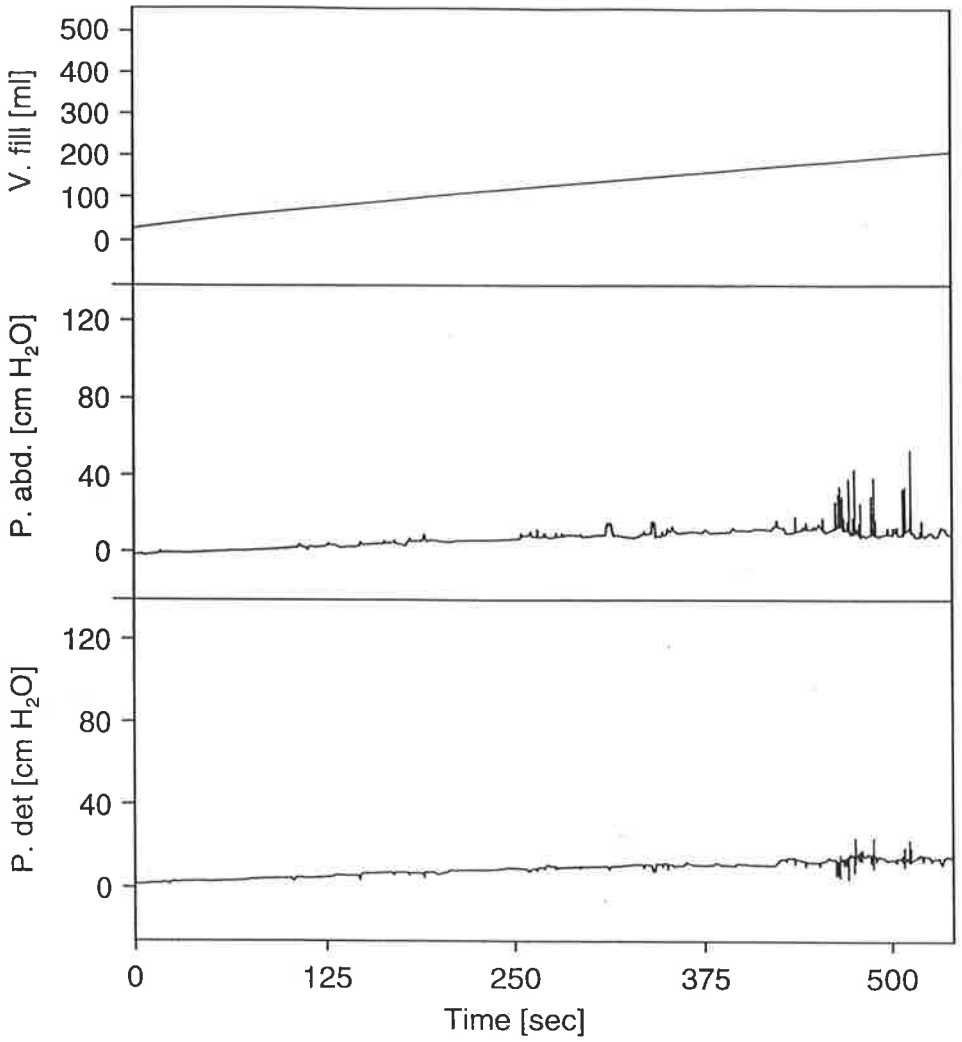


Figure 39C - *Case 1*: shows the tracing after the AACC.

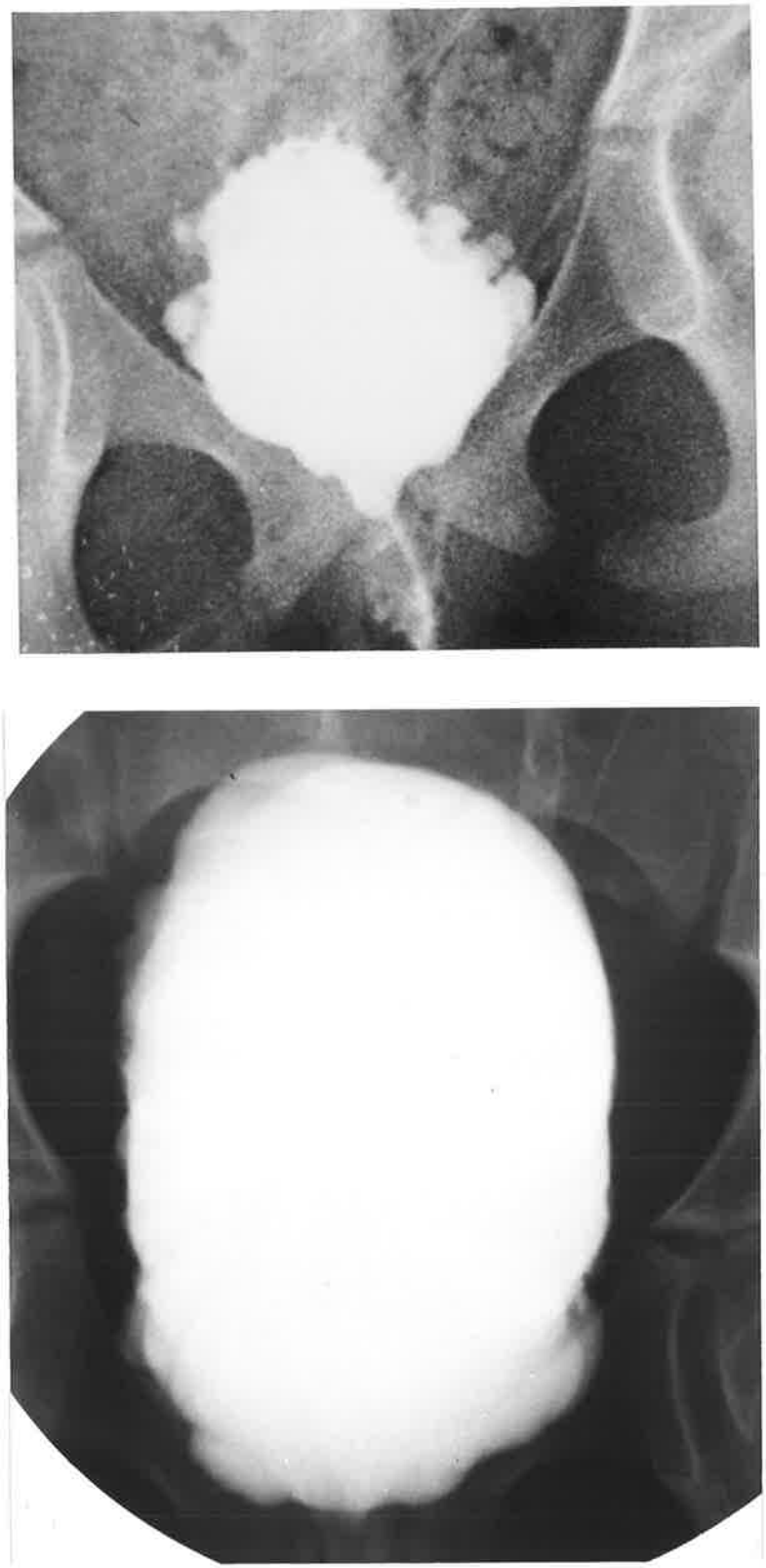
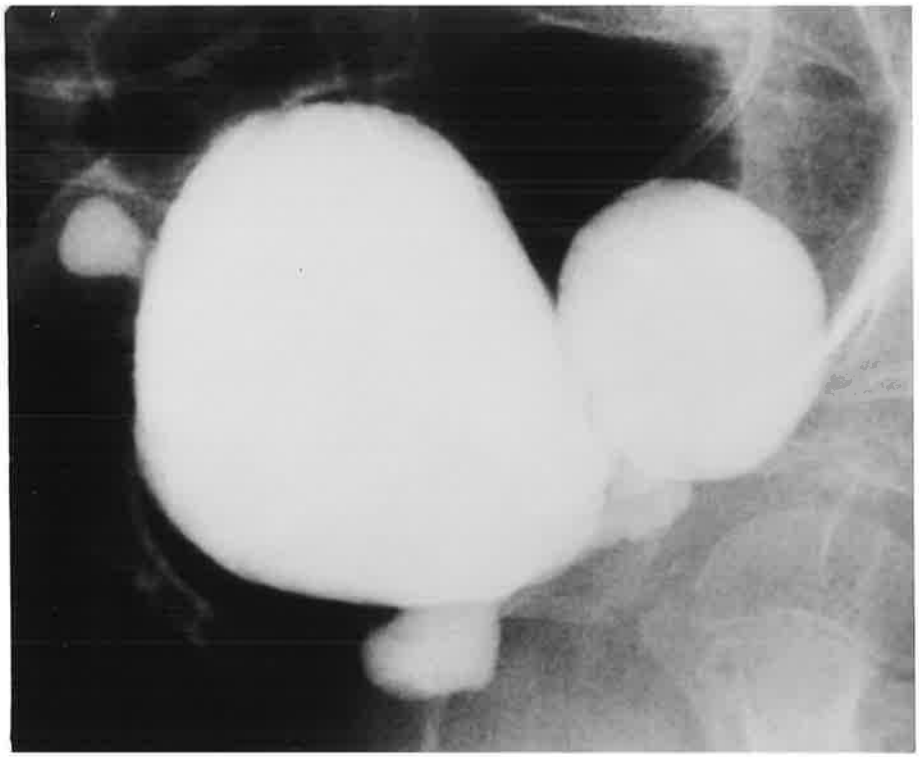


Figure 40 - *Case 1*: The pre (A) and post (B) operative cystograms of the first AACC patient.



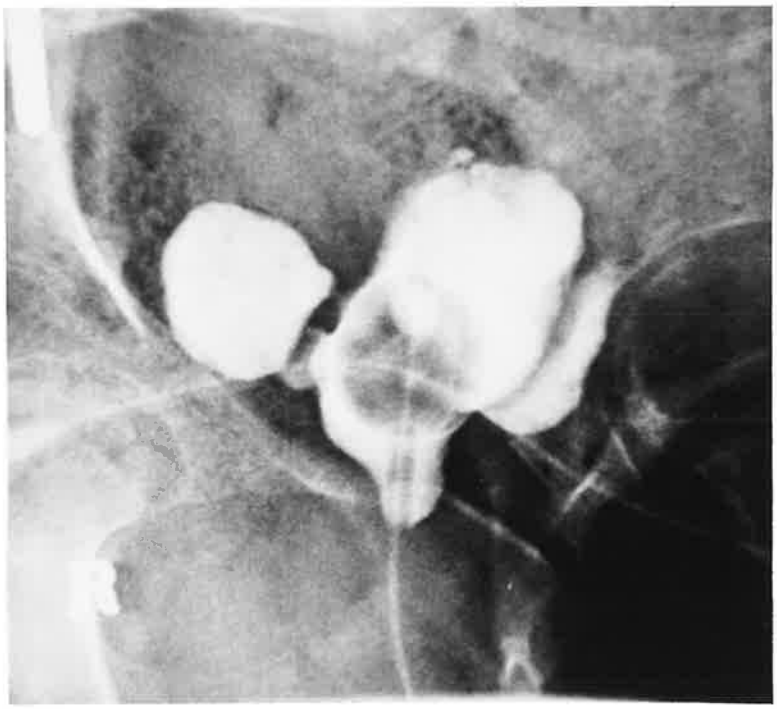


Figure 41A+B - *Case 4*: A preoperative cystogram and one 10 days after an AACC. The initial post-operative appearance was poor.

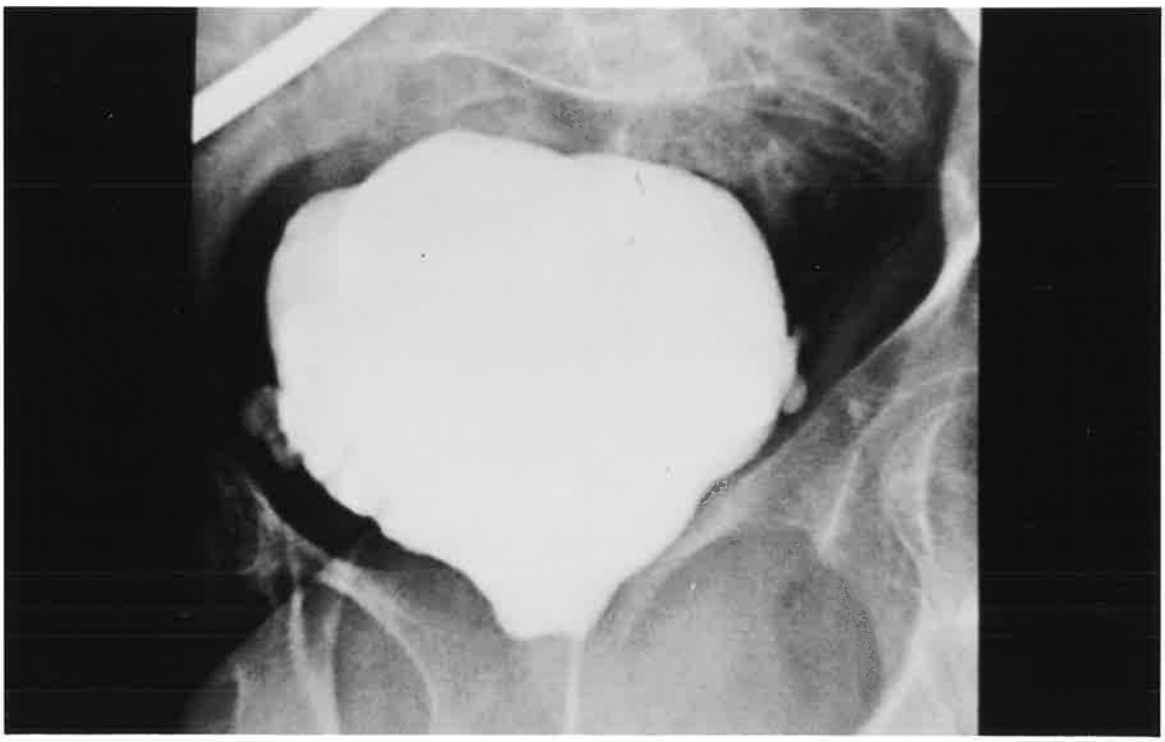


Figure 41C - *Case 4*: A post-operative cystogram at 6 weeks, showing significant improvement form the bladder configuration seen at 10 days.

Ureterocystoplasty

All these boys made a satisfactory recovery from their operation and none required blood transfusion. Two of the three boys, not on CIC prior to the procedure, continue to void spontaneously, the third had a continent stoma formed subsequently. The urodynamic results are given in Table 36. It must be remembered that the volumes and pressures recorded in patients with high grade VUR do not completely reflect the state of the bladder, and that modest improvement in the urodynamic result may be associated with significant improvement in the vesical component of urine storage. Also, a reduced infection risk has been concurrently achieved by the elimination of VUR.

Case 1: The remaining kidney continued to grow and he was free of urinary tract infection. He did appear to have some difficulty voiding, and significant residual volumes, which have improved with time.

Case 2: (Fig. 42 & 43) In the initial post-operative period the serum creatinine rose, which was attributed to vesicoureteric junction obstruction of the transplant ureter, secondary to the bladder being constantly empty while on drainage. The problem was solved by the re-introduction of anticholinergic and elevation of the catheter bag to allow the bladder to expand. The boy was continent on twice daily Oxybutinin thereafter, but developed some dilatation of the transplant pelvicalyceal system which was resolved by two hourly voiding and increasing the Oxybutinin. He has remained free of urinary tract infections and no longer has reflux into either his transplant or the remaining native kidney. He had moderate residual bladder volumes and persistent elevation of his serum creatinine, therefore the right ureter was used to form an intubatable stoma for CIC, after which up to 600ml was stored in his bladder with half being voided urethrally.

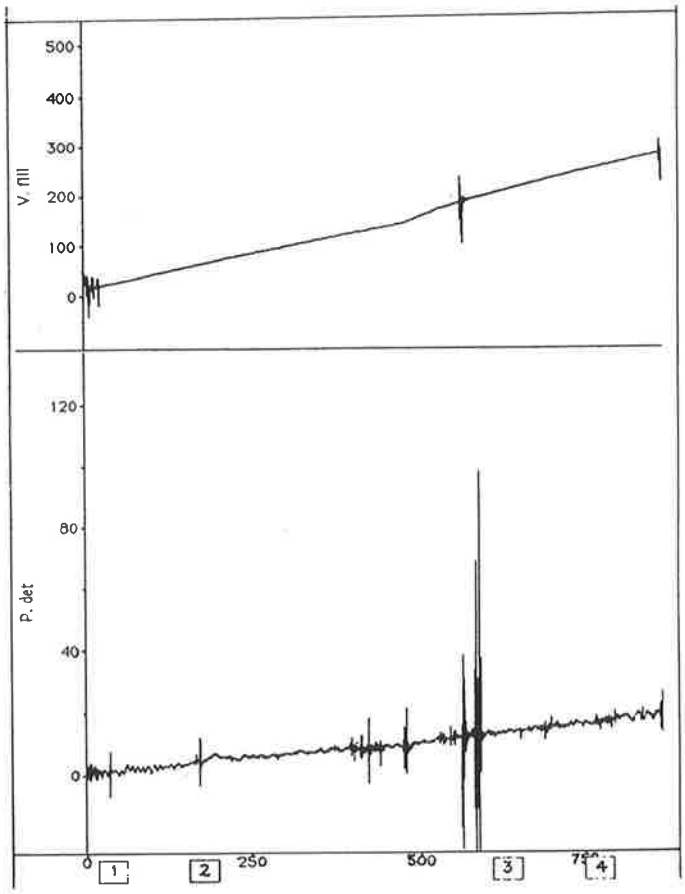


Figure 42A: The urodynamic study of *Case 2* before ureterocystoplasty.

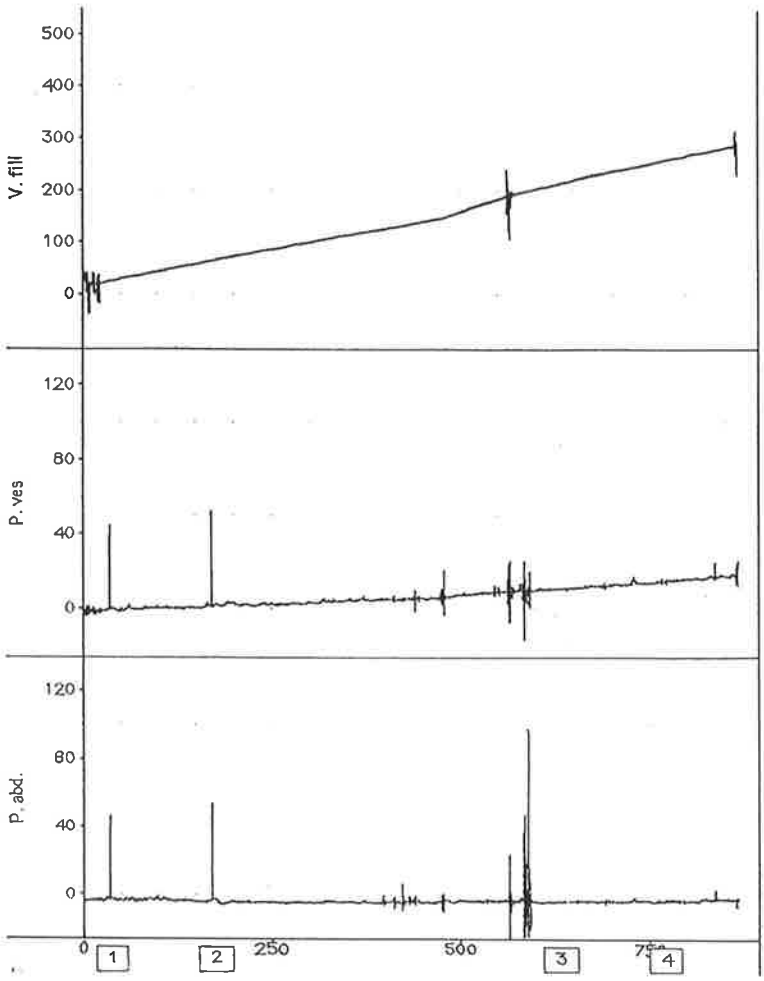


Figure 42: The urodynamic study of *Case 2*, six months after ureterocystoplasty.

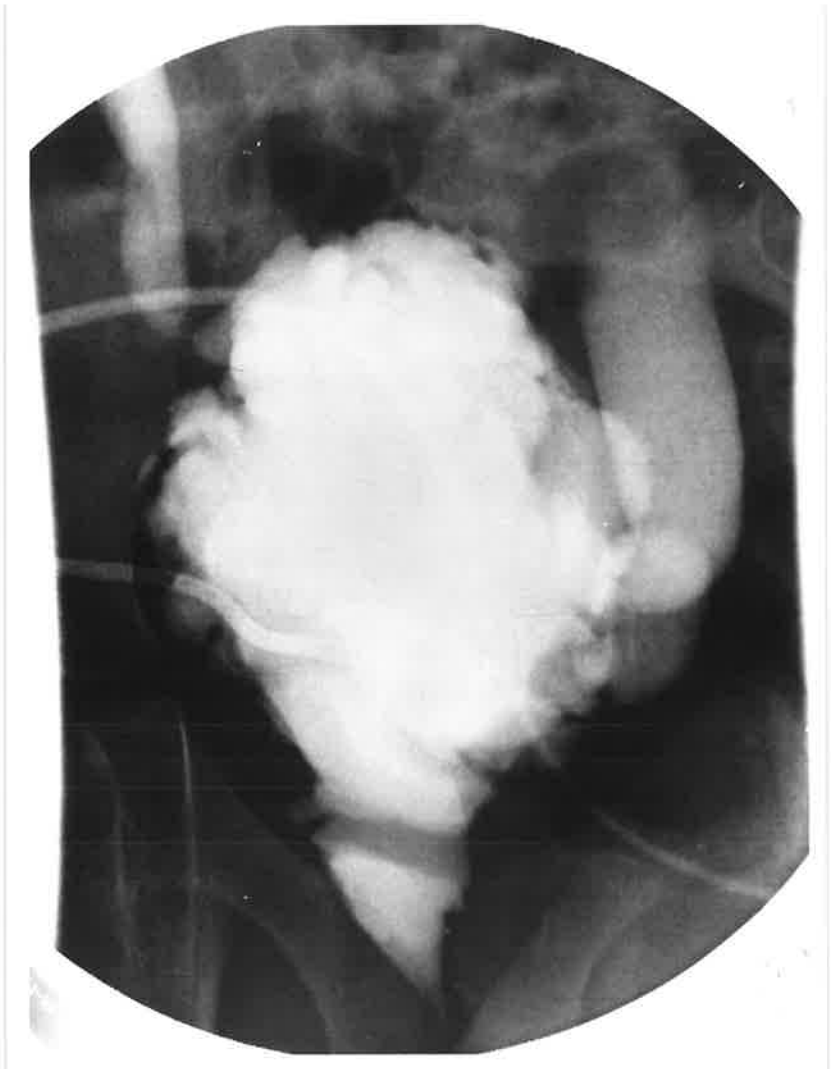


Figure 43A: The **preoperative** cystogram of *Case 2.* Reflux into a wide left ureter and marked trabeculation of the bladder can be seen.

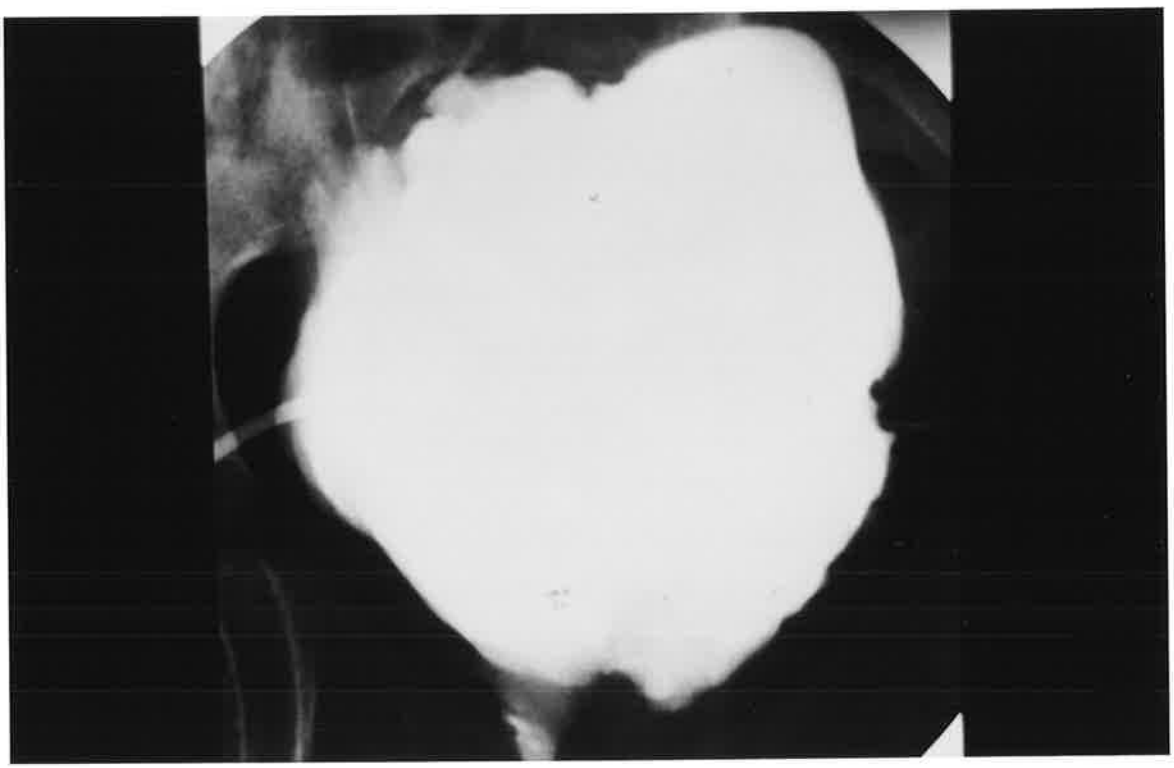


Figure 43B: The **post-operative** cystogram of *Case 2.* The bulging ureteric portion of the bladder is evident as a wide mouthed diverticulum. The reflux into the right native ureter was treated by Teflon injection intra-operatively.

Case 3: AB made a good recovery from his procedure and has had stable function of his poor right kidney. His bladder emptying has been incomplete, but he has been free of symptomatic infection and has a very large bladder with low pressures (Table 36).

Case 4: Intermittent catheterisation volumes decreased to 50 ml in the first three months, as the boy appeared to be voiding between catheters. His upper tract dilatation increased initially, after the ureterocystoplasty and transuretero-pyeloplasty procedure. He had two episodes of milky urine with positive urine culture which settled with increased oral fluids, more frequent catheters and antibiotics. An ultrasound at three months showed a large bladder with a smooth contour and minimal hydronephrosis. A urodynamic study soon after showed a much improved bladder, although the bladder volume appeared to decrease, the volume instilled in the preoperative study resulted in marked dilatation of the left renal pelvis and ureter; the post operative study reflected only the bladder storage, which was obviously improved with a volume of 108 ml at a pressure of 20 cmH_20 (Fig.44). The nuclear medicine study showed good function and drainage of the upper tracts, with preservation of the differential function (Fig.45A).

Case 5: DC had one urinary tract infection in the first few months after his ureterocystoplasty, but remained well without any evidence of pyelonephritis. His upper tracts remained stable without any evidence of obstruction at the ureteroureterostomy (Fig.45B). He continued to have unstable contractions on follow-up urodynamic studies, tolerating 48 ml at three months and 57 ml at eight months before leaking. However, he held up to 120 ml on catheterisation and all of the 57 ml was in his bladder, rather than the small proportion of the 37ml capacity in the pre-operative study. The ureteric segment was seen on the urodynamic study to bulge as a wide mouthed diverticulum during the initial stages of bladder contraction, thus improving the bladder compliance (Fig.46).

Case	1	2	3	4	5
Compliance (ml/cmH_2O)					
Pre-operative	6.7	9.0	1.7	21.6	0.4
3 mths	-	15.7	-	4.9	0.8
12 mths	30.0	84.5	13.5	6.8	6.0
Volumes (ml)					
Pre-operative	100	184	40	154	37
3 mths	-	260	-	131	48
12 mths	300	338	303	170	73

Table 36: The urodynamic results for the five Ureterocystoplasty patients.

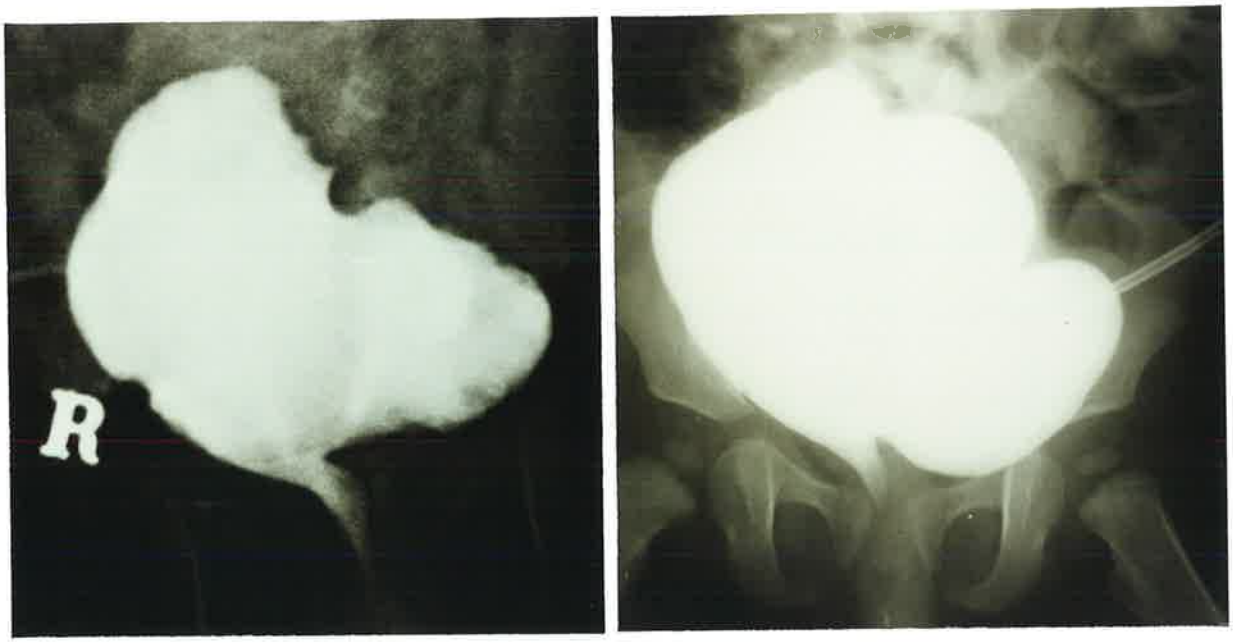
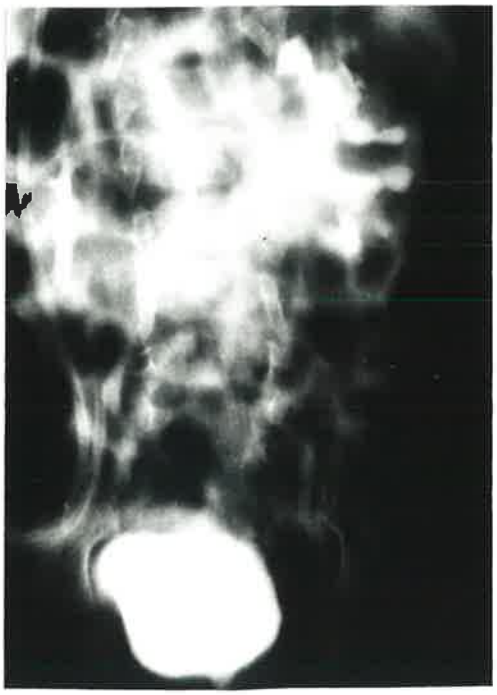


Figure 44: The early (A) and late (B) post-operative cystogram of *Case 4.* The bladder shape was initially less satisfactory than for the other boys, but improved with time.

Figure 45

A: The post operative MAG 3 scan of *Case 4* who had a transureteropyeloplasty.



B: An IVP post transureteroureterostomy and ureterocystoplasty in *Case 5*, showing good drainage and minimal hydronephrosis.

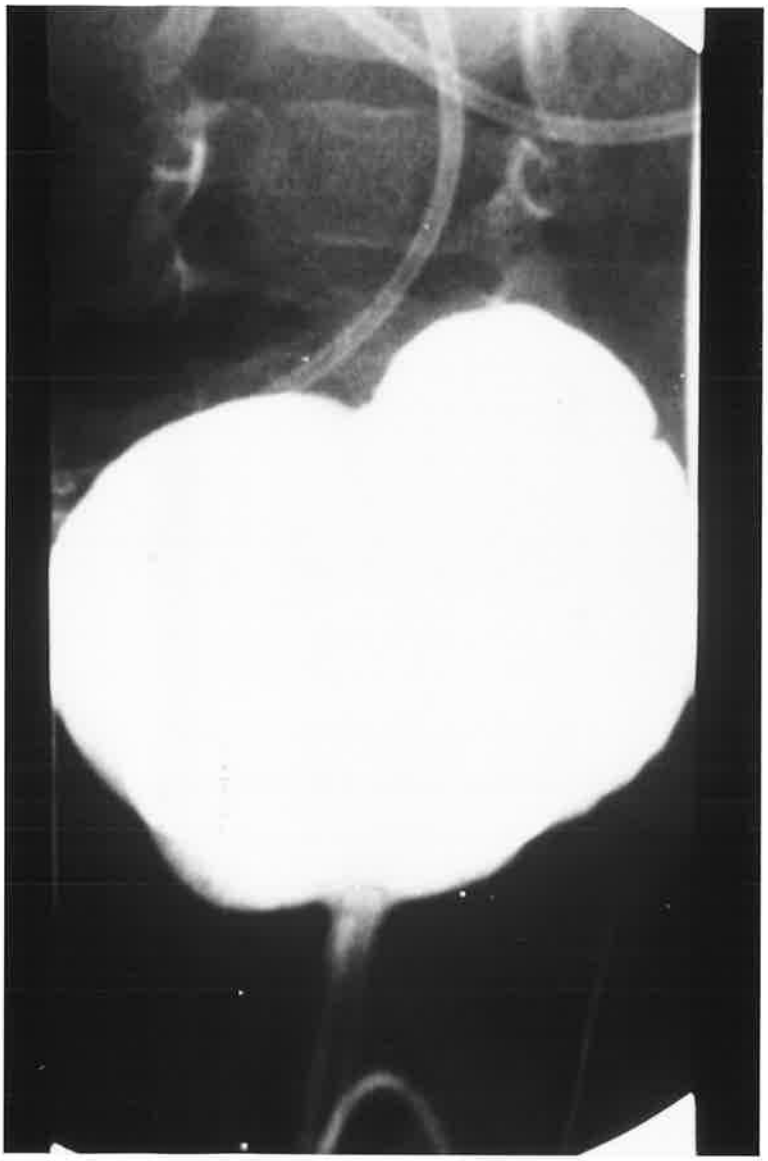


Figure 46A: *Case 5:* The ureteric portion of the bladder can be seen to bulge only slightly, early in a video-urodynamic study.

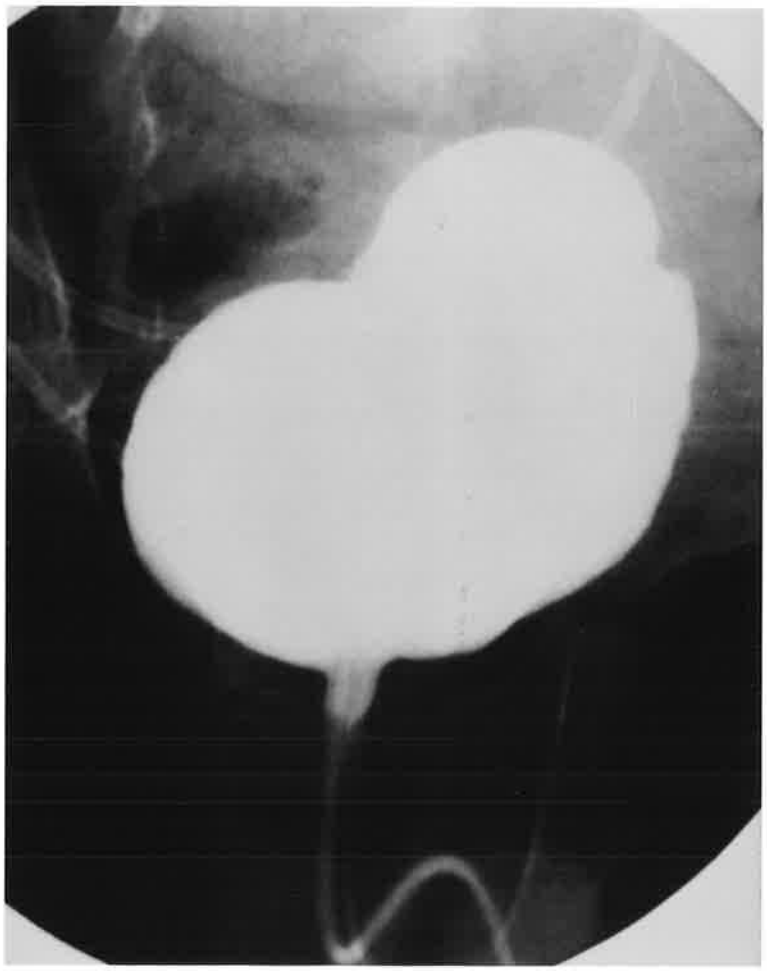


Figure 46B: *Case 5:* As the study progresses, with further filling of the bladder the ureteric portion of the bladder becomes more obvious.

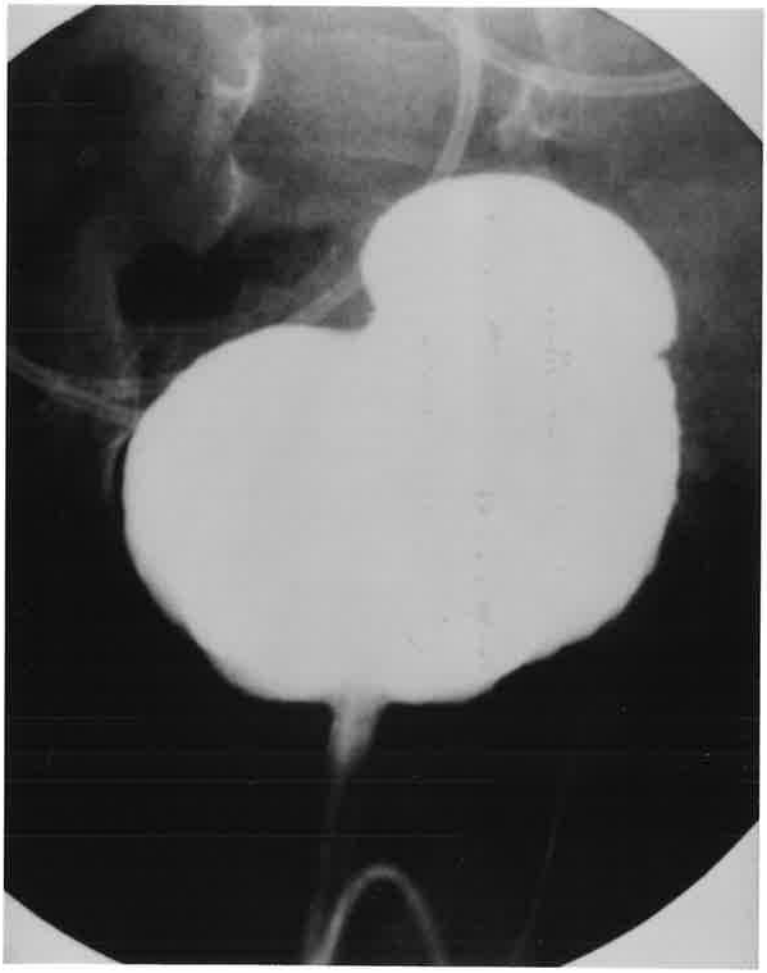


Figure 46C: *Case 5:* Toward the end of filling, a bladder contraction was seen, but no pressure rise was recorded initially, probably due to the increased compliance provided by the prominent bulging of the ureteric portion of the bladder.

Diverticulocystoplasty

GF has been well since his operation and his kidneys have continued to grow, as shown on ultrasound. Four months after the operation a cystogram demonstrated a much better bladder configuration which tolerated 150 ml during the cystogram (Fig.47). A urodynamic study, performed 15 months after the operation confirmed the increased functional bladder volume and a decreased end fill pressure compared with earlier investigations (Table 37: Fig.47), and notably, the pressure only rose above 20 cm H_2O beyond 70 ml filling (the child's usual volume obtained by CIC). All urodynamic studies were performed without anticholinergic medication. He is dry on 4 hourly catheterization during the day, being only minimally wet at night. His final urodynamic study was at 72 months of age and, although his urodynamic values had not continued to improve, his bladder was regularly drained of 200 ml following the commencement of anticholinergics.

Table 37: Compared results of two pre-operative and the post-operative cystometrograms.

Age (mths)	Wt.	Vol.	Pres.	Compl.
Pre-operative				
7	6.5	60	95	0.6
24	10.5	65	90	0.7
Post-operative				
48	12.2	70	***20***	3.5
48	12.2	110	65	1.7

Wt. in Kilograms; Vol. = volume in millilitres;
Comp. = compliance in ml/cmH_20; Pres. = pressure in cmH_20;

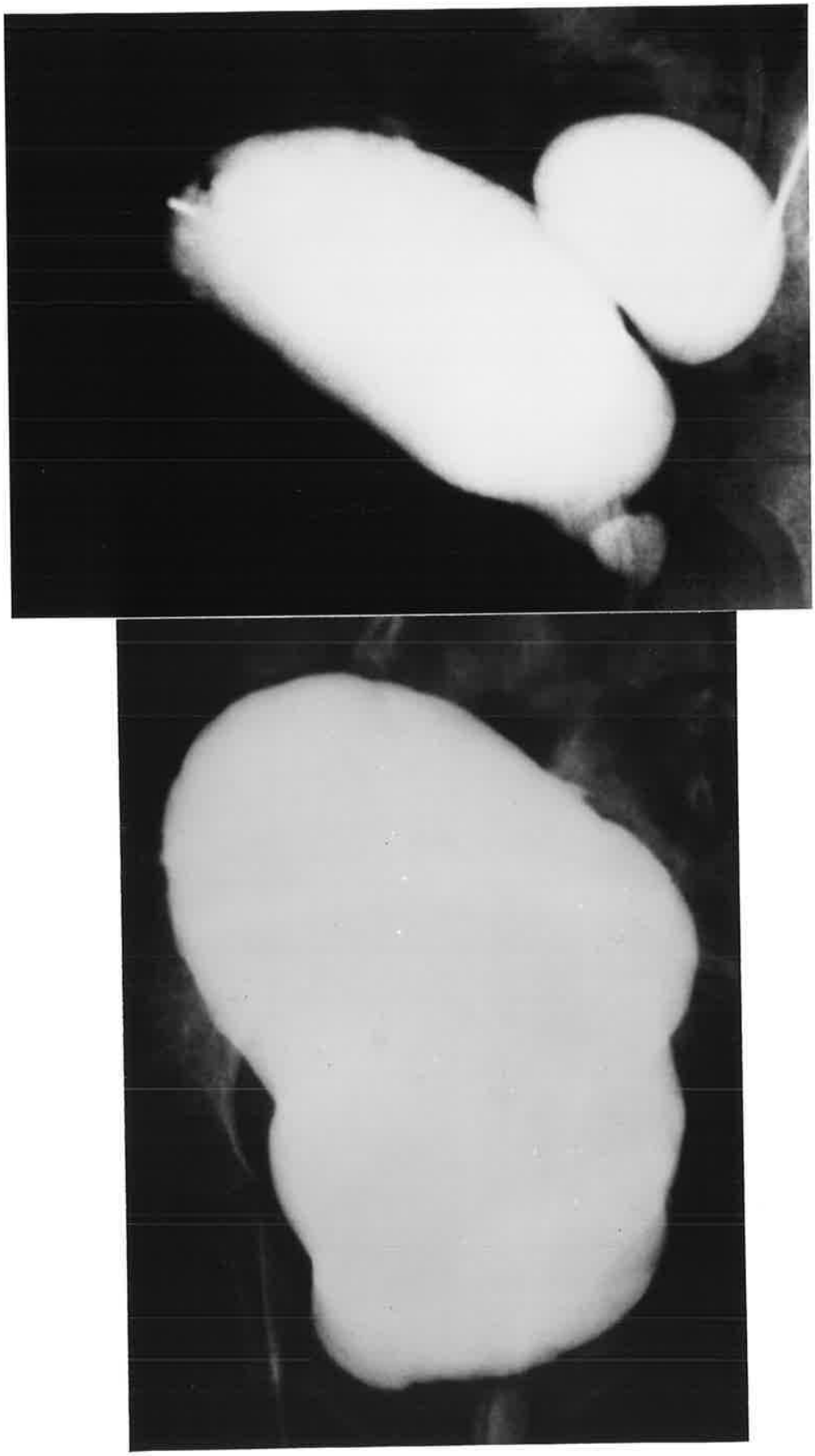


Figure 47: The pre-operative cystogram (A) shows the two large paraureteric diverticula to be approximately equal to the volume of the body of the bladder. The post-operative study shows a much improved bladder (B).

DISCUSSION

This work has developed alternative bladder augmentation techniques to those in which gut mucosa is incorporated into the urinary tract. It has explored a number of methods of providing both muscle and mucosa for bladder enlargement, without incorporating gut lining. The clinical results are preliminary, but sufficiently encouraging to be a stimulus to others to explore the techniques (as has already occurred [104-106]), and perhaps expand on them. The rationale for change has already been presented in the introduction.

SHEEP STUDIES

Suitability of the Sheep Model

In interpreting the results of the animal experiments it is important to establish whether the model is adequate for comparison with other animal studies and the human bladder. The sheep bladder is similar to the dog and the pig, in that the bladder is almost entirely intraperitoneal, with a more extensive serosal covering than humans. Both the dog and the pig have been extensively used for bladder augmentation experiments and are thought to be adequate models [24,30,64,90,102,107]. A neuropathic bladder has not been used, incontrast to the work by Mau [102]. As all of these animals has a thinner walled bladder than man, each would conceivably be more difficult to autoaugment than the human neuropathic bladder, therefore, if the results are reasonably satisfactory in sheep they may well be applicable to humans. The pig and the dog have also been used for the autoaugmentation cystoplasty procedure by others, where operative success has been demonstrated, and preservation of the mucosal blood supply appears to be similar to sheep [30].

The sheep is an inexpensive animal that is easier to handle than the calf [71], and is notionally a superior model for bladder augmentation than the rat [6,7,45,93], ferret [14] and rabbit [12,108]. In the smaller animal, epithelial loss on the undersurface of the added muscle would be repaired relatively more quickly, thus making it inappropriate to extrapolate the findings to larger animals and man.

The main draw-back of comparing sheep to humans was the inability to intervene when there may have been inadequate emptying of the bladder or the presence of urinary tract infections. Intervention was not possible with such a large group over the twelve month study period, remembering that the clinical cases were all expected to be on CIC. Intermittent catheterisation cannot be performed in sheep because the male urethra is long and narrow and ewes have a hypospadiac urethra. The addition of bladder drainage may have improved the animal results.

Comparison of Operative Techniques

It was difficult to prepare the animals for the use of either the fourth stomach or the colon because of the inordinately long period required to ensure the appropriate fourth stomach was empty, and the inability to perform enemas prior to the colonic operation; intra-operative contamination was, therefore, more common than would normally be expected during operations on humans.

The gastric procedures required a longer incision than either the colonic or omental operations, because of the need to mobilise the stomach. The animals recovered more quickly from the omentocystoplasty than the colocystoplasty, and much quicker than the gastrocystoplasty sheep. The prolonged convalescence for animals with a gastrocystoplasty was due to a not surprising reluctance to feed. However, overall, the surgery was well tolerated.

The autoaugmentation procedure was identical for the gastric, omental and colonic procedures. The mobilisation of the omentum was an easy undertaking, accomplished quickly, and resulted in the shortest operative time for all the autoaugmentation procedures. The stomach wedge was mobilised on the right gastroepiploic vessels, the isolation of which was time consuming, but relatively easy. An adequate pedicle length was readily obtained, and there was never any doubt about the blood supply to the gastric patch at the end of the procedure. The pedicle was not at risk, as it sat comfortably in the right paracolic gutter.

In comparison, the colonic muscle was extremely difficult to demucosalise, with either colonic mucosal regrowth or poor outcome for the muscle. It would appear that others have had the same difficulty judging from the heart-shaped appearance seen in the published cystograms in other demucosalised enterocystoplasty experiments [14]. I believe this configuration is due to a contracted augmentation segment which is associated with a urodynamically unsatisfactory bladder [14], as shown in the cystograms of the animals with poor bladders (Figure 13). This heart shape to the bladder was not seen when autoaugmentation was added to seromuscular gastrocystoplasty. However, the colonic augmentations had poor urodynamic results with or without augmentation, results which appeared due to the poor tolerance of the sheep colon to demucosalisation.

Mucosal Regrowth

The separation of the gastric mucosa from the muscle was easily achieved with diathermy dissection without risk of leaving residual gastric mucosa or damage to the gastric muscle. The plane between the two layers was easily identified, with long vessels coursing between the submucosa and the gastric muscle. Consequently, no gastric mucosal regrowth was noted in any of the late follow-up

animals, consistent with Blandy's contention that removal of the submucosa prevents gastrointestinal epithelial regrowth [10]. Blandy provided a low power magnification of the different cleavage planes, indicating that the submucosa should be removed to prevent bowel mucosa regrowth [67]. Gonzalez seems to have erred in his recent publication on the AACC; he demucosalised the bowel by stripping the mucosa, leaving a "shiny surface". He recorded that three of his sixteen cases had mucosal regrowth, after having success with a dog model in which there was no recorded mucosal regrowth [106,109]. The results obtained by Gonzalez indicate that Blandy's contention is correct.

This thesis is the first recorded work using a demucosalised gastric flap for bladder augmentation, a technique which has been adopted in three other centres [104,105,110], following presentation of this work.

The removal of sheep colonic mucosa was initially thought to be impossible, as judged by preliminary dissections of the colon in cadaver sheep. The procedure was persisted with, because of the number of workers who had been successful in using both large and small bowel as a demucosalised enterocystoplasty [5-7,9,10,64,68,71]. It is not surprising that most animal model studies have shown bowel mucosal regrowth and that the clinical use has been minimal [9,66], with no recent reports; the degree of difficulty of the procedure would be prohibitive. Early in this study, the colonic mucosa was removed with diathermy dissection, in the same manner as the gastric mucosa had been denuded. The length of operation differed markedly to that of the stomach - removal of the colonic mucosa took over two hours using this technique; the increased handling of the colon appeared to damage the thin muscular layer significantly, and therefore an alternative technique was developed. The mucosa was stripped with forceps, which has been described by others [71,72,106]; using this method the colonic muscle was denuded in 20-30 minutes and looked much healthier. Unfortunately, the AACC animals were

operated on before the DMCC group, resulting in a different approach between to the two groups. In all, there were five animals who had regrowth of colonic mucosa, all of which had the mucosa removed by stripping only, and all were in the DMCC group.

From these observations, the gastric muscle seemed to be the appropriate choice of gut muscle for autoaugmentation enterocystoplasty in children, provided the demucosalisation characteristics of the human stomach are the same as the sheep.

Urothelial Ingrowth

The rate of urothelial ingrowth has been recorded to range from two to four weeks [10,65,68] over both the serosal surface and the inner surface of segments of demucosalised gut. A total of nine animals (five DMGC; four DMCC) were studied to investigate the rate of regrowth under colon and stomach muscle. Full coverage of the incorporated segment was not seen before four weeks, and this was associated with a marked degree of inflammation; as expected from the finding of heterotopic calcification by Blandy [69]. The gastric and colonic muscle in the DMCC and DMGC groups was covered by urothelium at six and 12 months, but the intervening period of inflammation and fibrosis resulted in bladders which were often less satisfactory than the control group. The AAGC results were better than for the DMGC bladders, indicating that the autoaugmentation protects the gut muscle from fibrosis. This was not the case for the sheep augmented colonic muscle, probably because the muscle damage in the AACC group resulted in poor urothelial survival and, therefore, inflammation similar to that seen in the DMGC and DMCC procedures. This was highlighted by the development of a bladder calculus in one of the AACC animals.

Urothelial Survival

Autoaugmentation has been carried-out in a number of guises, and has only become popular recently. Initial studies used small portions of a viscus, covering the denuded lining with either fascia or muscle [16,17]. The more recent application has involved a variable degree of resection of the detrusor muscle [29,30,32,74]. The survival of the urothelium has been shown to be on the basis of the submucous vascular plexus, demonstrated on fluoroscein angiographic studies [30], and seen in the operative photo of Fig.5A. The aim of this part of the study was to confirm the survival of the urothelium under gastric and colonic muscle and the omentum. In all, seven sheep were culled to study the survival of the urothelium. The four AAGC animals had virtually complete urothelial survival, with minor epithelial loss in only one animal. For the AACC bladders the urothelial survival was less satisfactory, and in the AAOC animal, heterotopic calcification was seen. This calcification suggests there had been a leak of urine, which would fit with the finding of an early urine leak in a significant number of autoaugmentation patients [30,35], including the one reported case of laparoscopic autoaugmentation [34]. Incomplete survival of the autoaugmented bladder would account for the poor results for the AAOC sheep, and the variability in the results for the AAGC and AACC animals. In those with an inadequate bladder, the non survival of the bladder lining may have allowed for urine contact with the muscle and subsequent fibrosis. It is of interest that three of the four AAOC animals, followed for 12 months, had smaller bladder volumes than in those studied at six months. This may explain why this has been the first animal study to suggest that autoaugmentation is not a satisfactory bladder augmentation technique, a finding consistent with the poor late follow-up results in patients [39]; the early outcome may be more favourable because of the lack of time for the maturation of the collagen and the development of fibrose contracture.

Further investigation, with attempts to develop a way of improving the adherence of the urothelium to the muscle, possibly by laser welding, should be undertaken. In the present technique, it is possible that a loss of urothelium could come from a combination of separation of the mucosal and muscle layer by serous fluid, and the dubious submucosal blood supply of the urothelium, which may be over-come by better adhesion of the mucosa to the muscle.

Urodynamic Results

The most notable feature of the urodynamic results is the variability within each of the groups and the improvement in some animals from six to 12 months. The numbers at 12 months are too small for meaningful comparison between groups, but interesting changes were seen in the leak volumes for individual animals.

The AAOC group generally had poor results, with only two bladders having a volume greater than 250 ml, or a compliance above 10 ml/cmH_20. The remaining nine urodynamic study results were poor, with no improvement with time.

In the AAGC animals, seven of the 13 bladders at six months, and four of six at 12 months had a volume of greater than 250ml; the bladders were significantly greater in size than the control group at six months ($p<0.01$); the only bladder procedure which was recorded to be so. All the AAGC bladders increased in volume with time, some nearly doubling their capacity. This would seem to indicate that the gradual decrease in the inflammation allows the muscle covered with urothelium to increase in size and ability to hold urine at low pressure. In comparison, the DMGC was less satisfactory at six months with only one of five tolerating a volume of 250 ml. Unfortunately there were only three bladders for urodynamic assessment at 12 months. The inflammation and fibrosis resulted in one becoming smaller

between the six and 12 month study, while the initially good bladder improved further, and one moderately bad bladder became satisfactory. At no stage were the best results for this group as good as the best AAGC bladder. It would have been preferable to have had more in the DMGC group, but the six month results are no better than the control group, whereas the AAGC volumes are.

Both the AACC and the DMCC groups showed the ability of the muscle-backed, urothelial-lined bladder to improve with time, with each group having animals with a larger bladder volume at 12 months than at six months. However, the numbers are not sufficiently large to achieve statistical significance. Never-the-less, none of the 11 bladders in these groups were 250ml at six months, but three of six AACC bladders and three of five DMCC bladders had developed a capacity in excess of 300ml at 12 months. The lack of difference between the AACC and DMCC is most likely due to the poor survival of the autoaugmentation under the colonic mucosa, because of the delicate nature of the sheep colonic muscle, and the degree of injury caused by diathermy dissection of the colonic mucosa.

Histology Versus Urodynamic Results

A review of the matched urodynamic and histology results seems to further support the use of the combination of the autoaugmentation plus enterocystoplasty. Seven of the thirteen AAGC animals with both histology and urodynamics had a good result for each investigation. Three of the remaining six had acceptable routine histology, but poorly functioning bladders. Detailed analysis of the collagen types in these bladders may have indicated why there was a disparity between the histology and function.

The DMGC bladders on the other hand showed marked inflammation in all except

one of the two with acceptable urodynamics. The other DMGC animal with a good urodynamic result had a bladder which showed chronic inflammation, the only gastric augmented bladder with mismatched histology and function.

The AAOC bladders also generally reflected their histology in the urodynamic results, with all but one with poor bladder volume having a good correlation between the two parameters. In the colonic augmentation groups, one further animal had a poor bladder volume, but no significant inflammation or fibrosis on routine histology. The most striking finding was the presence of the colonic mucosa in five of the DMCC animals, a feature which could not be proven to interfere with the urodynamic function of the bladder.

Overall, the correlation between histology and urodynamics was good, and did not differ significantly between the groups.

In summary, the sheep studies appeared to provide an adequate model for bladder augmentation, although the results were quite variable, probably related to the limited post operative management possible with long-term follow-up in sheep. However, the difficulty of demucosalising the colon did not concur with reports from other animals and from the subsequent results in humans.

Aspects not Studied

Firstly, having lined a piece of gut with urothelium, what are the electrolyte absorption characteristics? No attempt was made to look at the absorptive and secretory features of the augmented bladder, as sufficient work has been published to suggest that urothelium is superior to gut mucosa in the urinary tract. A number of studies have shown the almost universal metabolic acidosis when small and large

bowel are incorporated into the bladder [2]. The absorption of chloride and ammonium from the colon and potassium from the ileum have been investigated in both animals and man [90,111,112], all of which differs from normal urothelium which has concentration gradient fluxes only [113,114]. In contrast, the stomach has a secretary function, which causes secondary perforation and the haematuria-dysuria syndrome in a routine gastrocystoplasty [40,43,63].

The nature of the absorptive characteristics of regenerated urothelium has only been tested in animals at this stage. It would appear that, in those animals studied, gut or peritoneum lined by urothelium has the same physiology as normal bladder urothelium [10,14,65]. One can assume that the lining of the colon and stomach, covered by either autoaugmentation or urothelial ingrowth, is relatively non-absorptive, but, to be certain, this should be specifically investigated.

Secondly, the make-up of the bladder collagen indicates its ability to act as a low pressure reservoir; the degree of fibrosis has been judged on light microscopy, and no attempt was made to do a detailed collagen analysis, which should be included in future work.

The third area of interest not investigated includes the seven types of bladder augmentation which *could* have been added to the study. These include;

1. Small bowel enterocystoplasty
2. Large bowel enterocystoplasty
3. Gastrocystoplasty
4. Bladder incision and suture
5. Autoaugmentation without omentocystoplasty
6. Demucosalised small bowel cystoplasty
7. Neuropathic bladder model

The small bowel, large bowel and gastric routine enterocystoplasty groups were not used because the first step in the experiment was to show whether the operation of AAGC was possible. This was achieved and histologically very good bladders were obtained. Therefore, it was felt appropriate to show whether the neo-bladder was significantly better than a control bladder rather than compare it with a group of animals that may have had a different set of complications, particularly as the most appropriate comparison would have been with gastric mucosa lined gastrocystoplasty. Given the high rate of acid secreting complications in humans, it seemed unethical to subject the sheep to routine gastrocystoplasty, particularly as they were not able to have CIC; intermittent catheterisation reduces the gastric distension which seems to be significant in producing an increased acid output and haematuria. The mucous production [115], bladder perforation [80,116-121] and the haematuria-dysuria syndrome [43,95,121-126] were potential problems for the sheep, if any of the routine enterocystoplasties had been used.

The sham operation was not used because the AAOC animals had a bladder worse than the control group, strongly suggesting that merely splitting the bladder had little to do with the bladder enlargement outcome. Autoaugmentation was not performed without addition of the omentum because of concerns about bladder rupture and the knowledge that when dogs have an autoaugmentation the urothelium becomes covered with the omentum [Cartwright and Snow - personal communication] (not surprisingly). The omental migration occurs in the dog because the bladder is intraperitoneal, as it is in the sheep.

Small bowel demucosalisation enterocystoplasty was not feasible in the sheep; attempts were made to demucosalise the small bowel in cadaver sheep, but while demucosalisation of the colon is very difficult, small bowel is virtually impossible to denude (the desire to avoid the nutritional complications of using the small bowel in children also discouraged me from persisting).

Of the seven groups suggested as possible additions, one is now being studied; a neuropathic model created by a supratrigonal, full thickness circumferential incision [127-129] will hopefully provide further evidence to justify widespread use of autoaugmentation enterocystoplasty.

An important point of omission in the animal studies was not including a psoas hitch, which may have allowed the animal results to be more impressive. This step was not included as it was considered that it may interfere with bladder emptying and thus adversely affect the well-being of the animals.

CLINICAL APPLICATION

Autoaugmentation Gastrocystoplasty

The five patients who had an AAGC are now well, all with an improved bladder, and all are free of gastrointestinal symptoms, although the second boy continues to have some daytime wetting because of bladder spasms. The other four patients have a good bladder and have had a marked improvement in their wetting, with improving results with time. Three had trouble with intolerance of large meals for up to 12 months after their operation, which has not been a widely recorded problem [130]. The Seattle group have used stomach for routine gastrocystoplasty in a large number of children, without documenting a similar difficulty [44]. The segment, position and size did not appear to differ from their experience when this work was presented to Mitchell's group. I would postulate that the problem may be more frequent than they have documented, but note the spontaneous resolution of the problem in the three cases.

The bladder of the first patient improved significantly from the three month study to the 24 month study, at which time ureteric reimplants were performed. It was interesting to note that on opening the bladder it was not possible to differentiate the two components from within the bladder cavity, in keeping with the findings in sheep. Also, there was no evidence of gastric mucosa regrowth. It would seem that a moderately good result subsequently improves, as often seen with routine enterocystoplasty, and as occurred in the sheep. The need for late follow-up in any animal model is highlighted by this finding.

A contrast between the sheep and children was the degree of difficulty in the separation of the gastric mucosa from the underlying muscle. The sheep has a very loose

submucosal plane which allows diathermy removal of the mucosa and submucosa without any damage to the underlying muscle, in less than 30 minutes. On-the-other-hand, it is difficult to remove the mucosa from the human stomach, usually taking 90 minutes to denude an appropriately sized patch; In spite of the technical difficulty it was possible to completely remove the gastric mucosa and submucosa.

The important difference between the AAGC and routine gastrocystoplasty is the avoidance of the complications of the presence of the acid producing mucosa. Perforation, haematuria-dysuria syndrome and metabolic alkalosis have been recorded, all of which are avoided by removing the gastric mucosa. No such symptoms were seen in any of this small group, and the serum gastrin levels are all within normal limits, which differs with the hypergastrinaemia seem with the use of the routine gastrocystoplasty [43,123,124,126].

The initial reports of this procedure have prompted the use of the autoaugmentation gastrocystoplasty in Seattle [105] and New Zealand [104], and reports on the use of non-secretory gastrocystoplasty and sigmoid enterocystoplasty at the April, 1994 European Paediatric Urology Conference [110,131]. Robinson *et al.* reported five patients from New Zealand, with moderate improvement in their urodynamic results and significant improvement in their clinical status [104], as did Mitchell in six patients [105]. Ricardo Gonzalez has conducted parallel work with the colon, having operated on 16 patients [106], starting his clinical work seven months after the initial Adelaide procedure. Despite this initial enthusiasm, further information and results from the clinical and laboratory use of this technique are awaited. Laboratories in Germany, Switzerland, Italy, and North and South America have already commenced work on further testing the autoaugmentation enterocystoplasty.

Autoaugmentation Colocystoplasty

Having initially considered it impossible to separate the colonic muscle and mucosa in the sheep, and finding the early results for the AACC/DMCC group were poor, it was only after due consideration and consultation that the first patient in this group was scheduled for operation. This under-weight girl was considered inappropriate for bladder augmentation using stomach, particularly as three of the five AAGC patients had difficulty eating adequate meals initially. The previous good results for demucosalised enterocystoplasty in animals [64,68] favoured the use of the AACC clinically, particularly with the suggested (but not proven) good results in humans [9,66]. The ability to prevent mucosal regrowth in demucosalised gut, when the full-thickness of the submucosa is removed, also helped to justify the use of colon. A routine colocystoplasty was therefore planned, unless the colon could be adequately demucosalised, in which case an AACC was to be performed. The initial denuding was very similar to that of the human stomach, more difficult than the sheep stomach, but far easier than the sheep colon. The relative ratio of available colon to stomach was larger than in the sheep, in which the sigmoid colon is very small and the fourth stomach larger than the human stomach.

Of the four patients in this group, only one has had a complication from the use of the bowel. She initially had diarrhoea which was able to be controlled by Codiene and subsequently settled completely. In a patient with poor bowel control, the reduction of the absorptive surface is a significant change, and may be an indication for using the stomach in such a child.

Three of the AACC bladders are now excellent, two of which had very good early results; better than the early AAGC results. The colon is now my preferred option for

autoaugmentation enterocystoplasty, though long-term follow-up results and larger numbers of patients need to be carefully followed to ensure the suitability of these new techniques.

Ureterocystoplasty

Ureterocystoplasty has been developed concurrently in a number of centres. The first patient in this series had his operation prior to recent publication of the technique, based on previous experience of deterioration of the contralateral kidney after nephroureterectomy in boys with obstructive uropathy. The first two recent Journal of Urology publications by Bellinger [47] and Churchill *et al.* [46] addressed the problem of avoiding gut mucosa in the urinary tract, and overcame the presence of a functioning kidney by adding a transureteroureterostomy, however they failed to appreciate the option of performing the procedure extraperitoneally when nephrectomy is indicated. The original description was not quoted by these authors; a case was reported by Eckstein and Martin in 1973 [132]. The fourth publication by Wolf [48] reported the use of the extraperitoneal approach, but used a ureterocystoplasty technique which effectively leaves a diverticulum on the back of the bladder. I would recommend the extraperitoneal, two incision approach, where the high grade refluxing kidney is not functioning. An additional technique in this series, which has not been previously published, was the use of the upper ureter to ameliorate a contralateral pelviureteric junction abnormality *(Case 4)*.

Ureterocystoplasty has the advantage that it deals with high grade vesicoureteric reflux while giving some prospect of bladder improvement, thus avoiding the predisposition to infection, without adversely affecting the contralateral kidney. A relatively modest

improvement in the apparent bladder dynamics (as in *Case 5*) should be viewed in this context, particularly as the procedure can be used early in life, and the assessment of the bladder in isolation is impossible preoperatively, due to the immediate reflux into a wide open ureter in these cases. Many Paediatric Urologists now consider this procedure to be the ideal bladder augmentation, in the appropriate patient. This view is supported by four of the boys in this study who had an average three-fold increase in their bladder volume.

The procedure should never be undertaken without anticipating the need for intermittent catheterisation; therefore a boy with a *non-intubatable urethra* should not have his ureter used for a cystoplasty as it is better kept as an intubatable stoma, and the bladder augmented in some other way. In *Case* 2 it was possible to use his ureter because of the presence of a renal transplant, even though his *urethra* was known to be non-intubatable; one further boy was not considered suitable for a ureterocystoplasty because of his irregular urethra.

The possible need for catheterisation is highlighted in this group of boys; two had CIC pre-operatively, one has had a continent stoma formed, and one has significant residual urine volumes, but is voiding satisfactorily; only one has a normal voiding pattern.

Diverticulocystoplasty

Large paraureteric diverticula are seen with chronic high intravesical pressures, and once developed, result in an increased incidence of urinary tract infections because of their incomplete emptying. In general, surgical or endoscopic diverticulectomy is recommended because of obstructive complications, stone formation or risk of

malignant transformation [133]. In children, only the infective, and ureteric or urethral obstruction complications are relevant. When the diverticula are preserved, but incorporated into the wall of the bladder, the source of chronic infection and stone formation is eliminated, thus removing the malignancy risk of the diverticula lining, which is due to the chronic inflammation associated with infection.

This boy is unique as he is the only recorded case of diverticulocystoplasty, and not surprisingly so; the desire to have a urothelial lined bladder augmentation is relatively recent, and the increased recognition of the complications of bladder augmentation is even more recent. Also, there are very few cases that are likely to be suitable for such a procedure. As for the ureterocystoplasty, the aim of the operation is to remove the potential for infection without interfering with the urodynamic characteristics of the bladder, and hoping to improve them. The incorporation merely creates a wide-mouthed diverticulum, and should not be embarked upon unless it is accepted that the child will require intermittent catheterisation. This boy's bladder dynamic improvement has been only modest, but his infections have been virtually eliminated.

This technique has the benefits of being extraperitoneal and does not preclude the use of other bladder augmentation techniques in the future.

Comparison with Routine Enterocystoplasty

It is obviously important to look, not only at the patients treated by these new procedures, but also at the clinical and urodynamic results for routine enterocystoplasty. Also, it should be remembered that many long-term complications are avoided by providing a urothelial lining and the infection risk is reduced when

either ureterocystoplasty or diverticulocystoplasty are performed.

Most reports indicate good results for enterocystoplasty [4,42,134-136], with better results when detubularised gut is used [52]. Not all authors have been so successful. For example, Cher and Allen [137] reported seven children between six and 14 years of age with a routine enterocystoplasty who had an average post-augmentation volume of only 100ml, and an average compliance of 2.9ml/cmH_2O; volumes as low as 50ml and compliance values of as low as 1.0ml/cmH_2O were seen; such results are unacceptable, and would have been considered a failure in this study. Smith *et al.*, in a series of 74 adults over a 20 year period had only a 58% success rate, with 10% having a capacity of less than 200 ml [138], Kockelberger *et al.* found "no statistically significant effect on any urodynamic parameter" for enterocystoplasty in a group of 45 patients [139], Cheng *et al.* had poor results in 24% [140], and Sethia *et al.* had a decrease bladder volume in 2/11 [141]. Others have shown the need for on-going anticholinergic medication [142] and the need for subsequent urinary diversion [139]. Woodhouse found poor results in nine of 16 spina bifida females who underwent clam cystoplasty [143]. In a study of 48 patients with various forms of gut mucosa lined enterocystoplasties, Pagani *et al.* found a number of complications, including an hour-glass deformity in eight, anastomotic diverticula in seven, two with acute retention due to mucous plugging and a urinary fistula in one [144]. Gastrocystoplasty urodynamic results have been few in number, but have generally shown satisfactory bladder dynamics [44,145]. However, Atala *et al.*, in a more detailed report of 20 patients with post-operative urodynamics, achieved a bladder volume increase of as little as 20%, with an average augmentation volume of 350 ml and as low as 200 ml [146]; Gonzalez re-operate on patients who have had an AACC, which has not been required in this study group. The nine autoaugmentation enterocystoplasty patients have had a 50-900% increased bladder capacity with a median increase of 228 ml; results which

compare favourably with those for routine enterocystoplasty and these results, added to the fact that a number of complications have been avoided, suggest that autoaugmentation enterocystoplasty is a viable option.

CONCLUSION

The sheep experiments have demonstrated the feasibility of demucosalisation of the sheep fourth stomach, the usual survival of the urothelium under the gastric patch and the ability to produce an augmented bladder. It appears that the urothelium of an autoaugmentation does not always survive, and when urine is in contact with the denuded muscle, through a defect in the autoaugmentation, poor urodynamic results are seen. This latter point is yet to be confirmed, but is supported by finding sheep bladders covered by urothelial *ingrowth* to be often worse than the control group and the same as the poor AAGC bladders. The autoaugmentation survived less well under the colon of sheep because of the inadvertent injury to the colon while trying to ensure permanent demucosalisation. In the animal model, areas which would be worth expanding on are; absorptive physiology, ways to adhere the mucosa to the muscle patch, and the application to a neuropathic bladder model. However, it does seem certain that the combination of autoaugmentation and demucosalised enterocystoplasty is needed for the best chance of a favourable urothelial bladder augmentation outcome.

The new techniques used in the patients have all had the benefit of producing a urothelial lined reservoir, and ureterocystoplasty and diverticulocystoplasty are successful in removing the predisposition to urinary tract infection and pyelonephritis. They are also successful in improving the urine storage capacity of the bladder and are able to be used in the first year of life, thus preventing the need for urine diversion. As for all bladder augmentation methods, they should not be applied without anticipating the likely need for CIC.

The operations take longer than a routine enterocystoplasty, and are more difficult to

perform. In particular, both the bladder and bowel dissections are tedious and time consuming, however, but the effort seems worth the investment, given the long-term complications that are avoided. Obviously, on-going surveillance is needed to ensure that a new set of complications is not generated by these procedures. With careful attention to operative detail and post-operative care, the "urothelial lined" approach to cystoplasty will hopefully provide those who need a bladder augmentation with a better future. On-going extensive animal studies, and careful clinical follow-up is required to ensure appropriate use of this new concept.

REFERENCES

1 Filmer RB, Spencer JR. Malignancies in bladder augmentations and intestinal conduits. *J. Urol.*, 1990 143:671-678.

2 Nurse DE, Mundy AR. Metabolic complications of cystoplasty. *Br. J. Urol.*, 1989 63:165-170.

3 Nurse DE, Mundy AR. Assessment of the malignant potential of cystoplasty. *Br. J. Urol.*, 1989 64:489-492.

4 Mayo ME, Chapman WH. Ileocecal bladder augmentation in myelodysplasia. *J. Urol.*, 1988 139:786-789.

5 Martin LSJ. Uroepithelial lined ileal segment as a bladder replacement: experimental observations and brief review of literature. *J. Urol.*, 1959 82:633-649.

6 Oesch I. Neourothelium in bladder augmentation. *Eur. Urol.*, 1988 14:328-329.

7 Badiola de F, Manivel JC, Gonzalez R. Seromuscular enterocystoplasty in rats. *J. Urol.*, 1991 146:559-562.

8 Salle JL, Fraga JCS, Lucid A, Lampertz M, Jobim G, Putten A. Seromuscular enterocystoplasty in dogs. *J. Urol.*, 1990 144:454-456.

References - Cont'd

9 Campbell EW. Reconstruction of the bladder with a seromuscular graft. *J. Urol.*, 1957 78:236-241.

10 Blandy JP. The feasibility of preparing an ideal substitute for the urinary bladder. *Ann. Royal Coll. Surg.*, 1964 35:287-311.

11 Kropp BP, Eppley B, Prevel R, Harruff R, Badylak S, Adams MC, Keating MA, Rink R. Experimental assessment of small intestine submucosa as a bladder substitute. *J. Urol.*, 1994 151 (Suppl):501A. Abstract.

12 Goldstein MB, Dearden LC. Histology of omentoplasty of the urinary bladder in the rabbit. *Invest. Urol.*, 1966 3:460-469.

13 Jelly O. Segmental cystectomy with peritoneoplasty. *Urol. Int.*, 1970 25:236-244.

14 Weingarten JL, Cromie WJ, Paty RJ. Augmentation myoperitoneocystoplasty. *J. Urol.*, 1990 144:156-158.

15 Büyükünal SNC, Kaner G, Celayir S. An alternative treatment modality in closing bladder exstrophy: use of rectus abdominis flap - preliminary results in a rat model. *J. Pediatr. Surg.*, 1989 24:586-589.

16 Huggins CB. The formation of bone under the influence of epithelium of the urinary tract. *Arch. Surg.*, 1930 22:377-408.

References - Cont'd

17 Neuhof H. Fascia transplantation into visceral defects. *Surg. Gynecol. & Obstet.*, 1917 24:383-427.

18 Gücer T, Özkardes H. Vesica fellea - a new substitute for the bladder? An experimental study. *Br. J. Urol.*, 1992 70:269-270.

19 Fishman IJ, Flores FN, Scott FB, Spjut HJ, Morrow B. Use of fresh placental membranes for bladder reconstruction. *J. Urol.*, 1987 138:1291-1294.

20 Lima SVC, Noroes JAA, Carvalheira F, de Mendonca PP. Bladder exstrophy. Primary reconstruction with human dura mater. *Br. J. Urol.*, 1981 53:119-124.

21 Kelâmi A. Duraplasty of the urinary bladder - results after two to six years. *Eur. Urol.*, 1975 1:178-181.

22 Novick AC, Straffon RA, Koshino I, Banowsky LH, Levin H, Kambic H, Nose' Y. Experimental bladder substitution using a biodegradable graft of natural tissue. *J. Biomed. Mat. Res.*, 1978 12:125-147.

23 Kambic H, Kay R, Chen J-F, Matsushita M, Harasaki H, Zilber S. Biodegradable pericardial implants for bladder augmentation: a 2.5-year study in dogs. *J. Urol.*, 1992 148:539-543.

24 Kelâmi A, Dustmann HO, Luedtke-Handjery A, Carcamo V, Herold G. Experimental investigations of bladder regeneration using teflon-felt as a bladder wall substitute. *J. Urol.*, 1970 104:693-698.

References - Cont'd

25 Orikasa S, Tsuji I. Enlargement of contracted bladder by use of gelatin sponge bladder. *J. Urol.*, 1970 104:107-698.

26 Kudish HG. The use of polyvinyl sponge for experimental cystoplasty. *J. Urol.*, 1957 78:232-235.

27 Stanley TH, Feminella JG, Priestley JB, Lattimer JK. Subtotal cystectomy and prosthetic bladder replacement. *J. Urol.*, 1972 107:783-787.

28 O'Sullivan DC, Barrett DM. Prosthetic bladder: in vivo studies on an active negative-pressure-driven device. *J. Urol.*, 1994 151:776-780.

29 Cartwright PC, Snow BW. Bladder autoaugmentation: early clinical experience. *J. Urol.*, 1989 142:505-508.

30 Cartwright PC, Snow BW. Bladder autoaugmentation: partial detrusor excision to augment the bladder without use of bowel. *J. Urol.*, 1989 142:1050-1053.

31 Cartwright PC, Snow BW. Autoaugmentation. *Dial. Pediatr. Urol.*, 1991 14:3-4.

32 Moorhead JD. Detrusorectomy: autoaugmentation by a different name. *Dial. Pediatr. Urol.*, 1991 14:4-5.

References - Cont'd

33 Johnson HW, Stothers L. Bladder augmentation by vesicomyotomy - clinical review and experimental aspects. *Annual Meeting of the Section of Urology,American Academy of Peditrics,San Francisco*, 1992 #47: Abstract.

34 Ehrlich RM, Gershman A. Laparoscopic seromyotomy (Auto-augmentation) for non-neurogenic neurogenic bladder in a child: initial case report. *Urol.*, 1993 42:175-178.

35 Gudziak MR, McQuire EJ, Rudy DC, Kennelly MJ, Gormley A. Detrusor myomectomy (bladder autoaugmentation): a report on 14 patients. *J. Urol.*, 1994 151 (Suppl):501A. Abstract.

36 Kennelly MJ, Gormley EA, McGuire EJ. Early clinical experience with adult bladder auto-augmentation. *J. Urol.*, 1994 152:303-306.

37 Swami ,S.K., Abrams P, Hammonds JC, Feneley RCL, Stoehrer M. Treatment of detrusor overactivity with detrusor myectomy (bladder auto-augmentation). *Société Internationale d'Urologie*, 1994 Sydney, Sept.:# 580. Abstract.

38 Rudy DC, McGuire EJ, Gudziak MR, Kennely MJ, Gormley EA. Detrusor myomectomy (bladder autoaugmentation): report of 14 cases. *Société Internationale d'Urologie*, 1994 Sydney, Sept.:#581. Abstract.

39 Snow BW, Cartwright MD. Bladder Augmentation. In King L R, Stone A R Webster G D eds; *Bladder Reconstruction and Continent Urinary Diversion* pp. 107-114. Chicago, London, Year Book Medical Publishers 1991.

References - Cont'd

40 Lim STK, Lam SK, Lee NW, Ong GB. Effects of gastrocystoplasty and serum gastrin levels on gastric acid secretion. *Brit. J. Surg.*, 1983 70:275-277.

41 Adams MC, Mitchell ME, Rink RC. Gastrocystoplasty: an alternative solution to the problem of urological reconstruction in the severely compromised patient. *J. Urol.*, 1988 140:1152-1156.

42 Hendren WH, Hendren RB. Bladder augmentation: experience with 129 children and young adults. *J. Urol.*, 1990 144:445-453.

43 Dykes EH, Ransley PG. Gastrocystoplasty in children. *Br. J. Urol.*, 1992 69:91-95.

44 Burns MW, Watkins SL, Mitchell ME, Tapper D. Treatment of bladder dysfunction in children with end-stage renal disease. *J. Pediatr. Surg.*, 1992 27:170-174.

45 Klee LW, Hoover DM, Mitchell ME, Rink RC. Long term effects of gastrocystoplasty in rats. *J. Urol.*, 1990 144:1283-1287.

46 Churchill BM, Aliabadi H, Landau EH, McLorie GA, Steckler RE, McKenna PH, Khoury AE. Ureteral bladder augmentation. *J. Urol.*, 1993 150:716-720.

47 Bellinger MF. Ureterocystoplasty: a unique method for vesical augmentation in children. *J. Urol.*, 1993 149:811-813.

References - Cont'd

48 Wolf JS, Turzan CW. Augmentation ureterocystoplasty. *J. Urol.*, 1993 149:1095-1098.

49 Tizzoni G, Foggi A. Die Wiederherstellung der Harnblase. Experimentelle Untersuchungen. *Zentr. bl. Chir.*, 1888 15:921-924.

50 Rutkowski M. Zur Methode der Harnblasenplastik. *Zentr. bl. Chir.*, 1899 16:473-478.

51 Mikulicz J. Zur Operation der angeborenen Blasenspalte. *Zentr. bl. Chir.*, 1899 26:641-643.

52 Goldwasser B, Barrett DM, Webster GD, Kramer SA. Cystometric properties of ileum and right colon after bladder augmentation, substitution or replacement. *J. Urol.*, 1987 138:1007-1008.

53 Wespes E, Stone AR, King LR. Ileocaecocystoplasty in urinary tract reconstruction in children. *Br. J. Urol.*, 1986 58:266-272.

54 King LR, Webster GD, Bertram RA. Experiences with bladder reconstruction in children. *J. Urol.*, 1987 138:1002-1006.

55 Koff SA. Guidelines to determine the size and shape of intestinal segments used for reconstruction. *J. Urol.*, 1988 140:1150-1151.

References - Cont'd

56 Parres JA, Knopp KA. Urodynamic evaluation of the continence mechanism following urethral lengthening-reimplantation and enterocystoplasty. *J. Urol.*, 1991 146:535-538.

57 Kass EJ, Koff SA. Bladder augmentation in the pediatric neuropathic bladder. *J. Urol.*, 1983 129:552-555.

58 Sinaiko E. Artificial bladder from segment of stomach and study of effect of urine on gastric secretion. *Surg. Gynecol. & Obstet.*, 1956 102:433-438.

59 Sinaiko ES. Artificial bladder from gastric pouch. *Surg. Gynecol. & Obstet.*, 1960 111:155-162.

60 Martin DC, Schultz JI, Goodwin WE. Experimental autografting of gastric mucosa in the urinary tract to maintain persistent acid urine. *J. Urol.*, 1962 87:739-741.

61 Leong CH. Use of the stomach for bladder replacement and urinary diversion. *Ann. Royal Coll. Surg.*, 1978 60:283-289.

62 Leong CH, Ong GB. Gastrocystoplasty in dogs. *A. N. Z. J. Surg.*, 1972 41:272-279.

63 Lau JL, Richter HM, Fowler JE,Jr., Bhatti R, Ray V. Suppression of canine antral gastrin secretion by urine. *J. Urol.*, 1990 143:402-406.

64 Shoemaker WC, Maracci H. The experimental use of seromuscular grafts in bladder reconstruction. *J. Urol.*, 1955 73:314-321.

References - Cont'd

65 Shoemaker WC. Reversed seromuscular grafts in urinary tract reconstruction. *J. Urol.*, 1955 74:453-475.

66 Shoemaker WC, Bower R, Long DM. A new technique for bladder reconstruction. *Surg. Gynecol. & Obstet.*, 1957 105:645-650.

67 Blandy JP. Ileal pouch with transitional epithelium and anal sphincter as a continent urinary reservoir. *J. Urol.*, 1961 86:749-767.

68 Grotzinger PJ, Shoemaker WC, Ulin AW, Marucci HD, Martin WL. The use of inverted seromuscular grafts from the ileum and colon for reconstruction of the urinary bladder. *Ann. Surg.*, 1954 140:832-838.

69 Blandy JP, McDonald JH. Heterotopic ossification in uroepithelial regeneration on grafts of ileum and colon. *Surg. For. Urol.*, 1961 12:498-500.

70 Heeg MM, Chappell SM, Pories WJ. The use of intact colon to expand bladder capacity. *J. Urol.*, 1968 99:436-438.

71 Motley RC, Montgomery BT, Zollman PE, Holley KE, Kramer SA. Augmentation cystoplasty utilizing de-epithelialized sigmoid colon: a preliminary study. *J. Urol.*, 1990 143:1257-1260.

72 Mráz JP, Sutory M. An alternative in surgical treatment of the post-irradiation vesicovaginal and rectovaginal fistulas: the seromuscular intestinal graft (patch). *J. Urol.*, 1994 151:357-359.

References - Cont'd

73 Harada N, Tanimura M, Kadowaki H. Construction of a urothelial urinary conduit by a free graft of bladder mucosa to the peritoneum. *Plast. Reconstr. Surg.*, 1960 26:57-68.

74 Gordon E, Malone PR, Duffy PG, Capps S. The place of autocystoplasty in the management of the neuropathic bladder.(Abstract). *Br. J. Urol.*, 1991 68:644.

75 Diamond DA, Blight A, Samuell CT, Ransley PG. Ammonia levels in paediatric ureterosigmoidostomy patients: a screen for hyperammonaemia. *Br. J. Urol.*, 1991 67:541-544.

76 Goldwasser B, Webster GD. Augmentation and substitution enterocystoplasty. *J. Urol.*, 1986 135:215-224.

77 Jahnson S, Pedersen J. Cystectomy and urinary diversion during twenty years - complications and metabolic implications. *Eur. Urol.*, 1994 24:343-349.

78 Davidsson T, Åkerlund S, Fossel-Aronsson E, Kock NG, Månsson W. Absorption of sodium and chloride in continent reservoirs for urine: comparison of ileal and colonic reservoirs. *J. Urol.*, 1994 151:335-337.

79 Sheiner JR, Kaplan GW. Spontaneous bladder rupture following enterocystoplasty. *J. Urol.*, 1988 140:1157-1158.

References - Cont'd

80 Elder JS, Snyder HM, Hulbert WC, Duckett JW. Perforation of the augmented bladder in patients undergoing clean intermittent catheterization. *J. Urol.*, 1988 140:1159-1162.

81 Crane JM, Scherz HS, Billman GF, Kaplan GW. Ischemic necrosis: a hypothesis to explain the pathogenesis of spontaneously ruptured enterocystoplasty. *J. Urol.*, 1991 146:141-144.

82 Mundy AR, Nurse DE. Calcium balance, growth and skeletal mineralisation in patients with cystoplasties. *Br. J. Urol.*, 1992 69:257-259.

83 Tanagho EA. A case against incorporating of bowel segments into closed urinary systems. *J. Urol.*, 1975 113:796-802.

84 Kälble T, Amelung F, Busse K, Staehler G. Prophylaxis of carcinomas following urinary diversion by surgical methods. *J. Urol.*, 1994 151 (Suppl):500A. Abstract.

85 Canning DA, Perman JA, Jeffs RD, Gearhart JP. Nutritional consequences of bowel segments in the lower urinary tract. *J. Urol.*, 1989 142:509-511.

86 Parsons CD, Thomas MH, Garrett RA. Colonic adenocarcinoma: a delayed complication of ureterosigmoidostomy. *J. Urol.*, 1977 118:31-34.

87 Moorcraft J, DuBoulay CEH, Isaacson P, Atwell JD. Changes in the mucosa of colon conduits with particular reference to the risk of malignant change. *Br. J. Urol.*, 1983 55:185-188.

References - Cont'd

88 Kirsch AJ, Hensle TW. Symptomatic cholelithiasis following continent urinary diversion using ileocolonic bowel segments. *J. Urol.*, 1994 151:859-860.

89 Gregoire M, Kantoff P, DeWolf WC. Synchronous adenocarcinoma and transitional cell carcinoma of the bladder associated with augmentation: case report and review of the literature. *J. Urol.*, 1993 149:115-118.

90 Piser JA, Mitchell ME, Kulb TB, Rink RC, Kennedy HA, McNulty A. Gastrocystoplasty and colocystoplasty in canines: the metabolic consequences of acute saline and acid loading. *J. Urol.*, 1987 138:1009-1013.

91 Vaughan ED, Tiffany P. The use of gastrocystoplasty. *Dial. Pediatr. Urol.*, 1988 11:6.

92 Kennedy HA, Adams MC, Mitchell ME, Rink RC, Piser JA, McNulty A. Chronic renal failure and bladder augmentation: stomach versus sigmoid colon in the canine model. *J. Urol.*, 1988 140:1138-1140.

93 Guan Z, Ricard G, Charest-Boule L, Neilson K, Kiruluta G. Augmentation cystoplasty in rats: development of an animal model. *J. Urol.*, 1990 144:461-465.

94 Goodwin WE, Cockett ATK. Surgical treatment of multiple, recurrent, branched, renal (staghorn) calculi by pyelo-nephro-ileo-vesical anastomosis. *Trans. Amer. Assn. Genito-Urin. Surg.*, 1960 52:102-110.

References - Cont'd

95 Muraishi O, Ikado S, Yamashita T, Yamaguchi K, Ogawa A. Gastrocystoplasty in dogs: an ulcerating effect of acid urine. *J. Urol.*, 1992 147:242-245.

96 McLaughlin KP, Rink R, Adams MC, Keating MA. The use of stomach in combination with other intestinal segments in pediatric lower urinary tract reconstruction. *J. Urol.*, 1994 151 (Suppl):234A. Abstract.

97 Lockhart JL, Davies R, Cox C, Mcallister E, Helal M, Figueroa TE. The gastroileoileal pouch: an alternative continent urinary resevoir for patients with short bowel,acidosis and/or extensive pelvic radiation. *J. Urol.*, 1993 150:46-50.

98 Buson H, Castro Diaz D, Manivel JC, Jessurun J, Dayanc M, Gonzalez R. The development of tumors in experimental gastroenterocystoplasty. *J. Urol.*, 1993 150:730-733.

99 Castro-Diaz D, Froemming C, Manival JC, Long R, Buson H, Reinberg Y, Gonzalez R. The influence of urinary diversion on experimental gastrocystoplasty. *J. Urol.*, 1992 148:571-574.

100 Gilbert MG, Pace W, Izant G. Uroepithelium transplantation to intestinal segments: an experimental study. *J. Urol.*, 1958 80:237.

101 Pompino H-J, Loeffler W, Oerthel-Haid D, Scheiner M. The neurogenic bladder; an experimental study. *Progr. Pediatr. Surg.*, 1973 5:135-161.

References - Cont'd

102 Mau H. *Die neurogene Blase - tierexperimentelle Untersuchungen zur Restauration der Blasenfunktion* pp. 1-300. Habilitationsschrift, Humboldt-Universität zu Berlin 1980.

103 Dewan PA. Double lumen suprapubic urodynamic catheter. *A. N. Z. J. Surg.*, 1995 In Press.

104 Robinson RG, Delahunt B, Pringle KC. Autoaugmentation gastrocystoplasty. *J. Urol.*, 1994 151 Suppl:500A. Abstract.

105 Horowitz M, Mitchell ME, Nguyen DH. The DAWG procedure, gastrocystoplasty made better. *J. Urol.*, 1994 151 Suppl:503A. Abstract.

106 Gonzalez R, Reid C, Reinberg Y, Buon H. Seromuscular enterocystoplasty lined with urothelium (SELU): experience with urothelium in 16 patients. *Urol.*, 1995 45:124-129. Abstract.

107 Tasker JH. Ileo-cystoplasty: a new technique. *Br. J. Urol.*, 1953 25:349-357.

108 Norris MA, Cohen MS, Warren MM, Becker SN, Baur PS, Seybold HM. Bladder reconstruction in rabbits with glutaraldehyde-stabilized amniotic membranes. *Urol.*, 1982 19:631-634.

109 Buson H, Manivel JC, Dayanç M, Long R, Gonzalez R. Seromuscular colocystoplasty lined with urothelium (SCLU): experimental study. *Urol.*, 1994 44:743-748.

110 Yanez R, Schalper J Torres P. *Non secretory gastrocystoplasty, a new option* 1994. UnPub.

111 Turner WR,Jr., Ransley PG, Bloom DA, Williams DI. Variants of the extrophy complex. *Urol. Clin. Nth. Am.*, 1980 7:493-501.

112 Koch MO, Gurevitch E, Hill DE, McDougal WS. Urinary solute transport by intestinal segments: a comparative Study of ileum and colon in rats. *J. Urol.*, 1990 143:1275-1279.

113 Rapoport A, Nicholson TF, Yendt ER. Movement of electrolytes across the wall of the urinary bladder in dogs. *Am. J. Physiol.*, 1960 198:191-194.

114 Chelsky MJ, Rosen SI, Knight LC, Maurer AH, Hanno PM, Ruggieri MR. Bladder permeability in interstitial cystitis is similar to that of normal volunteers: direct measurement by transvesical absorption of 99m Technetium-Diethylenetriaminepentaacetic Acid. *J. Urol.*, 1994 151:346-349.

115 Gearhart JP. Mucous secretions in augmented bladder. *Dial. Pediatr. Urol.*, 1987 10:6.

116 Gleeson MJ, Cunnane G, Graiger R. Spontaneous perforation of an augmented bladder. *Br. J. Urol.*, 1991 68:655.

117 Maloney SA, Bauer SB. Bladder perforation in augmentation cystoplasty. *Dial. Pediatr. Urol.*, 1991 14:2-3.

References - Cont'd

118 Mevorach RA, Hulbert WC, Merguerian PA, Rabinowitz R. Perforation and intravesical erosion of a ventriculoperitoneal shunt in a child with an augmentation cystoplasty. *J. Urol.*, 1992 147:433-434.

119 Rushton HG, Woodard JR, Parrott TS, Jeffs RD, Gearhart JP. Delayed bladder rupture after augmentation enterocystoplasty. *J. Urol.*, 1988 140:344.

120 Bauer SB, Hendren WH, Kozakewich H, Maloney S, Colodny AH, Mandell J, Retik AB. Perforation of the augmented bladder. *J. Urol.*, 1992 148:699-703.

121 Reinberg Y, Manivel JC, Froemming C, Gonzalez R. Perforation of the gastric segment of an augmented bladder secondary to peptic ulcer disease. *J. Urol.*, 1992 148:369-371.

122 Gosalbez R,Jr., Woodard JR, Broecker BH, Parrott TS, Massad C. The use of stomach in pediatric urinary reconstruction. *J. Urol.*, 1993 150:438-440.

123 Kinahan TJ, Khoury AE, McLorie GA, Churchill BM. Omeprazole in post-gastrocystoplasty metabolic alkalosis and aciduria. *J. Urol.*, 1992 147:435-437.

124 Gosalbez R,Jr., Woodard JR, Broecker BH, Warshaw B. Metabolic complications of the use of stomach for urinary reconstruction. *J. Urol.*, 1993 150:710-712.

125 Tiffany P, Vaughan ED,Jr., Marion D, Amberson J. Hypergastrinemia following antral gastrocystoplasty. *J. Urol.*, 1986 136:692-695.

References - Cont'd

126 Nguyen DH, Bain MA, Salmonson KL, Ganesan GS, Burns MW, Mitchell ME. The syndrome of dysuria and hematuria in pediatric urinary reconstruction with stomach. *J. Urol.*, 1993 150:707-709.

127 Sethia KK, Brading AF, Smith JC. An animal model of non-obstructive bladder instability. *J. Urol.*, 1990 143:1243-1246.

128 Choudhury A, Mittra S. Transection denervation of the urinary bladder: an experimental study. *Br. J. Urol.*, 1980 52:193-195.

129 Staskin DR, Parsons KF, Levin RM, Wein AJ. Bladder transection - a functional, neurophysiological, neuropharmacological and neuroanatomical study. *Br. J. Urol.*, 1981 53:552-557.

130 Gold BD, Bhoopalam PS, Reifen RM, Harvey E, Marcon MA. Gastrointestinal complications of gastrocystoplasty. *Arch. Dis. Child.*, 1992 67:1272-1276.

131 Lima SVC, Araujo A, Vilar DOF Lima KCE. *Non Secretory sigmoid-cystoplasty: experimental and clinical results* 1994. UnPub.

132 Eckstein HB, Martin MRR. Uretero-cystoplastik. *Act. Urol.*, 1973 4:255-257.

133 Jarow JJ, Brendler CB. Urinary retention caused by a large bladder diverticulum: a simple method of diverticulectomy. *J. Urol.*, 1988 139:1260-1263.

134 Lytton B, Green DF. Urodynamic studies in patients undergoing bladder replacement surgery. *J. Urol.*, 1989 141:1394-1397.

References - Cont'd

135 Williams MPL, Katz Z, Rickwood AMK. Combined bladder augmentation and bladder neck suspension for neuropathic incontinence in girls. *J. Pediatr. Surg.*, 1988 23:212-215.

136 Nasrallah PF, Aliabadi HA. Bladder augmentation in patients with neurogenic bladder and vesicoureteral reflux. *J. Urol.*, 1991 146:563-566.

137 Cher ML, Allen TD. Continence in the myelodysplastic patient following enterocystoplasty. *J. Urol.*, 1993 149:1103-1106.

138 Smith RB, Van Cangh P, Skinner DG, Kaufmann JJ, Goodwin WE. Augmentation enterocystoplasty: a critical review. *J. Urol.*, 1977 118:35-39.

139 Kockelberger RC, Tan JBL, Bates CB, Bishop MC, Dunn M, Lemberger RJ. Clam enterocystoplasty in general urological practice. *Br. J. Urol.*, 1991 68:38-41.

140 Cheng C, Hendry WF, Kirby RS, Whitfield HN. Detubularisation in cystoplasty: clinical review. *Br. J. Urol.*, 1991 67:303-307.

141 Sethia KK, Webb RJ, Neal DE. Urodynamic study of ileocystoplasty in the treatment of idiopathic detrusor instability. *Br. J. Urol.*, 1991 67:286-290.

142 Sidi AA, Aliabadi H, Gonzalez R. Enterocystoplasty in the management and reconstruction of the pediatric neurogenic bladder. *J. Pediatr. Surg.*, 1987 22:153-157.

References - Cont'd

143 Woodhouse CRG. Reconstruction of the lower urinary tract for neurogenic bladder: lessons from the adolescent age group. *Br. J. Urol.*, 1992 69:589-593.

144 Pagani JJ, Barbaric ZL, Cochran ST. Augmentation enterocystoplasty. *Radiol.*, 1979 131:321-326.

145 Ngan JHK, Lau JLT, Lim STK, Chan K-W, Tam P-C, Li M-K. Long-term results of antral gastrocystoplasty. *J. Urol.*, 1993 149:731-734.

146 Atala A, Bauer SB, Hendren WH, Mandell J, Retik AB. The effect of gastric augmentation on bladder function. *J. Urol.*, 1993 149:1099-1102.

PUBLICATIONS AND PRESENTATIONS

Papers Resulting from the Study

1. Dewan PA, Byard RW. Autoaugmentation gastrocystoplasty in a sheep model. *Br. J. Urol.*, 1993 72:56-59.

2. Lorenz C, Dewan PA. The evolution of autoaugmentation gastrocystoplasty. *Pediatr. Surg. Int.*, 1993 8:491-495.

3. Dewan PA, Stefanek W, Lorenz C, Byard RW. Autoaugmentation omentocystoplasty in a sheep model. *Urology*, 1994 43:888-891.

4. Dewan PA, Nicholls, EA Goh DW. Ureterocystoplasty: an extraperitoneal, urothelial bladder augmentation technique. *Eur. Urol.*, 1994 26:85-89.

5. Dewan PA, Lorenz C. Bladder incorporation of large paraureteric diverticula: diverticulocystoplasty. *A. N. Z. J. Surg.*, 1994 64;731-734.

6. Dewan PA, Stefanek W. Autoaugmentation colocystoplasty: a case report. *Pediatr. Surg. Int.*, 1994 9:526-528.

7. Dewan PA. Autoaugmentation gastrocystoplasty. *Dial. Pediatr. Urol.*, 1994 17(9):7-8.

8. Dewan PA, Stefanek W. Autoaugmentation gastrocystoplasty: early clinical results. *Brit. J. Urol.*, 1994 74:460-464.

9. Dewan PA, Lorenz C, Stefanek W, Byard RW. Urothelial lined colocystoplasty in a sheep model. *Eur. Urol.*, 1994 26: 240-246.

10. Dewan PA, McMullin ND, Barker AP. Renal allograft survival in patients with congenital obstruction of the posterior urethra. *A. N. Z. J. Surg.*, 1995 65:27-30.

11. Dewan PA, Stefanek W, Lorenz C, Byard R. Autoaugmentation gastrocystoplasty and demucosalised gastrocystoplasty in a sheep model. *Urology*, 1995 45:291-295.

12. Dewan PA, Owen, AJ, Stefanek W, Lorenz C, Byard RW. Late follow-up of autoaugmentation omentocystoplasty in a sheep model. *A. N. Z. J. Surg.*, 1995 (In Press).

13. Dewan PA, Stefanek W. Double lumen suprapubic catheter. *A.N.Z.J.Surg.*. 1995. (In Press).

Abstracts Resulting from the Study

1. Lorenz C, Dewan P. Gibt es alternativen zur enterozystoplastik? *Kinder Heilkunde*, 1993 141:#245.

2. Byard RW, Lorenz C, Dewan PA. The histological response to auto-augmentation gastrocystoplasty (AAGC) in a sheep model. *Pathol.*, 1993 25 Suppl 2.

3. Nicholls EA, Dewan PA, Boucaut HAB. A double lumen suprapubic catheter for urodynamic studies. *Br. J. Urol.*, 1993 71:77.

4. Byard RW, Lorenz C, Dewan PA. The short term histological response to gastric patch cystoplasty (CP), omental CP and auto-augmentation gastro-CP, in a sheep model. *Pathol.*, 1994 26:15.

5. Dewan PA, Byard RW. Autoaugmentation gastrocystoplasty in a sheep model. *J. Urol.*, 1994 151:1130.

6. Dewan PA, Stefanek W, Lorenz C, Byard R. Autoaugmentation gastrocystoplasty and demucosalised gastrocystoplasty in a sheep model. *J. Urol.*, 1994 151 (Suppl): 449A.

7. Dewan PA, Nicholls, EA Goh DW. Ureterocystoplasty: an extraperitoneal, urothelial bladder augmentation technique. *J. Urol.*, 1995 153:277.

Presentations Resulting from the Study

1. The early results of Autoaugmentation Gastrocystoplasty in a sheep model. Australasian Urological Society, South Australian Sectional Meeting, Burra, October 1991.

2. Follow-up studies on Autoaugmentation Gastrocystoplasty in a sheep model. Australasian Urological Society, 35th Annual Scientific Meeting, Adelaide, March 1992.

3. The histological changes in the Autoaugmentation Gastrocystoplasty in a sheep model. 11th Asian Association of Paediatric Surgeons Congress, Tokyo, March 1992.

4. Autoaugmentation Gastrocystoplasty in a sheep model. 3rd Annual European Society of Pediatric Urologists Conference, Cambridge, England, March 1992

5. Urothelial bladder augmentation. Royal Australasian College of Surgeons, GSM, Canberra, May 1992 (Invited).

6. Autoaugmentation gastrocystoplasty in a sheep model, American Association of Paediatrics, Urology Section, October, San Fransisco, 1992.

7. Patients with Autoaugmentation gastrocystoplasty; the early clinical experience. Urological Society of Australasian 46th Annual Scientific Meeting, Hobart, February 1993.

8. Ureterocystoplasty and urothelial bladder augmentation 3rd Annual Australasian Paediatric Urology Club meeting, Adelaide, November 1993.

9. Autoaugmentation Colocystoplasty: the early clinical experience. Royal Australasian College of Surgeons, GSM, Hobart, May 1994.

10. Autoaugmentation gastrocystoplasty and demucosalized gastrocystoplasty in a sheep model. 89th American Urological Association meeting, San Fransisco, May 1994.

11. Ureterocystoplasty. RACS SA Annual state meeting, Adelaide, August, 1994.

12. Autoaugmentation Colocystoplasty: the early clinical experience. International Urology Society, Sydney, September 1994.

13. Autoaugmentation Colocystoplasty: the early clinical experience. South Australian Urology Club meeting, Glenelg, October 1994.

14. Autoaugmentation Colocystoplasty: the technique. Australasian Paediatric Urology Club, Brisbane, November 1994.

15. Ureterocystoplasty - the ideal bladder augmentation. Asian Association of Surgeons, Bali, March, 1995.

16. Ureterocystoplasty - the ideal bladder augmentation. International pediatric Surgery and Radiology Congress, Melbourne, March, 1995.