

09 M.D  
D515



**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

## **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

### INTRODUCTION

Overview	1
History of Bladder Augmentation Procedures	3
Complications of Current Enterocystoplasty	6
Autoaugmentation Enterocystoplasty	8

### AIMS AND HYPOTHESES

#### *Aims*

Bladder	10
Stomach	10
Colon	10
Clinical	11

#### *Hypotheses*

Sheep	11
Clinical	12

### *Sheep Experiments*

### MATERIALS AND METHODS

<i>Anaesthesia, Analgesia and Antibiotics</i>	13
---	----

#### *Operations*

General Information	13
Autoaugmentation Gastrocystoplasty	14
Demucosalised Clam Gastrocystoplasty	16
Autoaugmentation Omentocystoplasty	17
Autoaugmentation Colocystoplasty	19
Demucosalised Clam Colocystoplasty	20

<i>Urodynamics</i>	23
--------------------	----

<i>Radiology</i>	24
------------------	----

<i>Histology</i>	26
------------------	----

#### *Animal usage and Timing of Culling*

Autoaugmentation Gastrocystoplasty	26
Demucosalised Clam Gastrocystoplasty	27
Autoaugmentation Omentocystoplasty	28
Autoaugmentation Colocystoplasty	28
Demucosalised Clam Colocystoplasty	28
Control group	28
Statistics	30

**SHEEP RESULTS**

<i>Urodynamics</i>	31
Autoaugmentation Gastrocystoplasty	34
Demucosalised Clam Gastrocystoplasty	35
Autoaugmentation Omentocystoplasty	36
Autoaugmentation Colocystoplasty	37
Demucosalised Clam Colocystoplasty	38
Control	39
Overall Urodynamic results	41
Overall Urodynamic medians	42
Statistics	43
 <i>Radiology</i>	 49
Autoaugmentation Gastrocystoplasty	50
Demucosalised Clam Gastrocystoplasty	53
Autoaugmentation Omentocystoplasty	57
Autoaugmentation Colocystoplasty	60
Demucosalised Clam Colocystoplasty	64
 <i>Histology</i>	 68
Autoaugmentation Gastrocystoplasty	69
Gastric Mucosa	69
Urothelial Survival Studies	
Immediate Sacrifice	70
Up to Four Weeks	70
Gastric Mucosal Regrowth Studies	
Five - Ten Weeks	73
Six and Twelve Months	75
Demucosalised Clam Gastrocystoplasty	
Urothelial Ingrowth Studies	76
Six and Twelve Months	78
Autoaugmentation Omentocystoplasty	
Urothelial Survival Studies	80
Inflammation and Fibrosis	81
Up to Six Months	81
At One Year	81
Autoaugmentation Colocystoplasty	
Histology of the Resected Colonic Mucosa	83
Urothelial Survival Studies	84
Colonic Mucosal Regrowth Studies	86
Demucosalised Clam Colocystoplasty	
Urothelial Regrowth Studies	87
Colonic Mucosal Regrowth Studies	89

## ***Clinical Application of Urothelial Bladder Augmentation***

### **MATERIALS AND METHODS**

Autoaugmentation Gastrocystoplasty	91
Autoaugmentation Colocystoplasty	93
Ureterocystoplasty	96
Diverticulocystoplasty	99

### **OPERATIONS**

Autoaugmentation Gastrocystoplasty	101
Autoaugmentation Colocystoplasty	105
Ureterocystoplasty	107
Diverticulocystoplasty	115

### **RESULTS**

Autoaugmentation Gastrocystoplasty	117
Autoaugmentation Colocystoplasty	124
Ureterocystoplasty	131
Diverticulocystoplasty	142

## ***Discussion***

### **SHEEP STUDIES**

Suitability of the Sheep Model	144
Comparison of Operative Techniques	145
Mucosa Regrowth	146
Urothelial Ingrowth	148
Urothelial Survival	149
Urodynamic Results	151
Histology Versus Urodynamic Results	152

### **CLINICAL APPLICATION**

Autoaugmentation Gastrocystoplasty	156
Autoaugmentation Colocystoplasty	158
Ureterocystoplasty	159
Diverticulocystoplasty	160
Comparison with Routine Enterocystoplasty	161

<b>CONCLUSION</b>	163
-------------------	-----

<b><i>References</i></b>	165
--------------------------	-----

***Publications And Presentations***

Publications	
Papers	184
Abstracts	185
Presentations	185