Vesicoureteric Reflux

Clinical and Laboratory Research
Including
Investigation of the Role and Risks of Plastics

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

PA DEWAN
MD MS BMedSc FRCS FRACS
Contents

Table of Contents 4
Acknowledgements 8
Summary 9
Introduction 11

PART I

Studies of the Endoscopic Management of Vescicoureteric Reflux

Introduction 21
Other Related Research 22

STUDY 1

Endoscopic Management of Primary Vescicoureteric Reflux in Irish Children 27

STUDY 2

Endoscopic Management of Vescicoureteric Reflux in Children with Spina Bifida in Ireland 31

STUDY 3

Endoscopic Management of Vescicoureteric Reflux into Duplex Ureters 36

STUDY 4

Endoscopic Correction of Vescicoureteric Reflux in Infants 41

STUDY 5

Endoscopic Management of Vescicoureteric Reflux in South Australian Children - Short-Term outcome 47

STUDY 6

Endoscopic Management of Vescicoureteric Reflux in South Australian Children - Long-Term Follow-up 52

STUDY 7

Correlation of the Endoscopic Appearance with Clinical Outcome of Submucosal Polytet Paste Injection in Vescicoureteric Reflux 55

Endoscopic Management of Vescicoureteric Reflux

Discussion 60
PART II

Risks of Plastics - Laboratory and Clinical Studies

Introduction 82

LABORATORY STUDY 1

Short-Term Response to Subcutaneously and Intravenously Injected Polytef and Bioplastique in a Rat Model

Materials and Methods 86
Results 88

LABORATORY STUDY 2

Long-Term Histological Response to Subcutaneously Injected Polytef and Bioplastique in a Rat Model

Materials and Methods 97
Results 99
Polytef 100
Bioplastique 102
Control

LABORATORY STUDY 3

Long-Term Histological Response to intravenously Injected Polytef and Bioplastique in a Rat Model

Materials and Methods 103
Results 104
Polytef 106
Bioplastique

LABORATORY STUDY 4

Histological Response to Injected Polytef and Bioplastique in the Sheep Brain

Materials and Methods 107
Results 108
Ten minutes 108
Six months

LABORATORY STUDY 5

An In Vitro Study of Silicone Migration from Intravenous Fluid Tubing as used in Paediatric Practice

Materials and Methods 111
Specimen Preparation 112
Results 113

STUDY 6: - Case Report of Migration

Skin Migration Following Periurethral PTFE Injection for Urinary Incontinence 120
STUDY 7: - Vascular Access Device

A Study of Particulate Migration In Vivo from an Implanted Vascular Access Device used in Paediatric Practice

- Introduction
- Materials and Methods
- Results
  - Detailed Patient Specimen
  - Infuse-a-port Results
  - Infuse-a-port and Sample 13 Summary

Risks of Plastics - Laboratory and Clinical Studies

- Discussion

PART III

Vesicoureteric Reflux - Clinical and Laboratory Studies

- Introduction

STUDY 1

Surgical Management of VUR

- Patients and Methods
- Results

STUDY 2

Progressive Antenatal Renal Deterioration Associated With High Grade Vesicoureteric Reflux

- Introduction
- Patients and Methods
- Results

STUDY 3

Infant Pig Model of Vesicoureteric Reflux

- Introduction
- Materials and Methods
- Results

STUDY 4

Ureteric Tunnel Incision in the Fetal Pig: A Model for Non-obstructive Prenatal Vesicoureteric Reflux

- Introduction
- Materials and Methods
- Results
Summary

The understanding of vesicoureteric reflux (VUR) has still only reached the level of "expanding ignorance". This state of affairs is because past workers have often drawn conclusions which, in retrospect, have been based on inadequate evidence. The Ransley and Risdon theory of the "big bang" is one of the best examples, where the renal injury was attributed to the first infection: it has now come to light, with the advent of frequent use of pre-natal ultrasound, that many of those with VUR have abnormal renal parenchyma before infection has occurred [1].

This study was undertaken to review the outcome of the application of new technology for the endoscopic management of VUR and, more importantly, to investigate how the subcutaneous tissue, lung and brain of animals respond to Teflon and silicone. The results, and the literature, indicate that injections under the ureteric orifice can cure VUR and that the tissue response to the plastics becomes quiescent. The question of malignant risk remains open, but the risk would appear low, possibly lower with the smaller Teflon particles than for the larger silicone microspheres.

The research into embolisation from solid implants from intravenous tubing and the possibility of antibody formation to implanted plastics were included, to place the use of injectable plastic in perspective with other clinical uses of plastics: the patient with migration of Teflon to the skin was included to highlight the need for caution in the use of plastic injection techniques. This subgroup of experiments indicates that particles are shed into the blood stream during routine paediatric intravenous infusions, and remain in the patient when the sheath around an implantable device remains in situ after removal of the implant.

The operation of open ureteric reimplant for the treatment of VUR is well established; thus there was nothing new in achieving reflux resolution for the patients thus treated
in Adelaide. However, finding improved renal growth after ureteric reimplant for high grade VUR is noteworthy, and the clarification of the debate on the issues surrounding the management of VUR is long over-due.

The next experimental step was to embark on the development of a model of fetal VUR, and the pursuit of information on pre-natal diagnosis of renal anomalies. These studies will hopefully open the door to further research which will help clarify our understanding of the pathophysiology of VUR. It would appear that kidneys do undergo progressive adverse changes in utero, possibly secondary to VUR.

The greatest achievement of this study may have been the further expansion of my ignorance! I have found more questions than answers and hope to have stimulated others to look for answers, rather than jumping to conclusions.