Prosthetic Surgery in Urology

Asif Muneer
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Editors

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Foreword

It is a great pleasure to introduce this book on prosthetic surgery in urology. Asif, Ian and David are amongst the foremost leaders in the field of prosthetics in the UK, and between them they have commissioned an impressive group of authors, encompassing the whole field of the correction of functional disorders affecting the genitourinary tract.

The reader of this book will have access to the distilled wisdom of a number of the key opinion leaders in the field. I have no doubt that this book will provide an essential addition to any library, to provide the reader with a crisp, updated, user-friendly and relevant guide to the use of prosthetics in urology.

This is a challenging field of surgery which relies upon careful evaluation of patients, adequate counselling and meticulous surgical technique. Please recall the dictum: "A good surgeon knows what to do. A better surgeon knows when to do it. The best surgeon knows when not to do it." There is no other field within urology where this is more applicable.

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Secretary General, European Association of Urology

Preface

The use of man-made materials to replace or substitute the function of damaged or absent urogenital organs has been described for well over 5000 years. The Romans described using metal catheters to drain the bladder. Also wooden sticks placed within the male urethra or under the penile skin were the earliest documented examples of penile prostheses.

Whilst there are numerous examples of relatively crude forays into the realm of urogenital prosthetic surgery, it was not until the early twentieth century that advancements in biomaterials allowed the development of either functionally proficient or in the case of testicular prostheses, cosmetically acceptable prosthetics suitable for widespread patient application.

These biomaterial advances enabled both numerous and rapid developments in penile prostheses and artificial urinary sphincters and ultimately to functional restoration for men suffering with erectile dysfunction or urinary incontinence thus ensuring that the deleterious effects of surgical treatment for pelvic cancers or benign prostatic enlargement were able to be suitably and reliably addressed.

Prosthetic surgery for female urinary incontinence, a condition afflicting approximately 30 % of the female population, has been a major breakthrough, positively changing the quality of life for women across the globe who would have previously been reliant on containment products or long-term catheters.

Despite the undoubted success, all prosthetic devices are continually subject to ongoing modifications and developments aiming to enhance their acceptability, durability, ease of implantation and functionality whilst reducing their associated complications such as erosion and potential infection risk.

Future developments in urogenital prosthetic surgery and urology in general continue to excite and with ongoing research into new biomaterials, stem cells and tissue engineering, the boundaries both functionally and cosmetically continue to be pushed further and further.

This book covers the common prosthetic surgical procedures in urology and provides clinicians with an overview of the available prostheses as well as a step-by-step guide to the surgical procedures provided by experts in each field.

This is a valuable resource for established urologists and urology trainees with an interest in prosthetic surgery, as well as nursing staff and allied healthcare professionals involved in the perioperative management of these patients.

The editors are grateful to all of the contributors who have helped to create this unique and informative guide to prosthetic surgery in urology.

London, UK — Asif Muneer
Manchester, UK — Ian Pearce
London, UK — David Ralph

Acknowledgements

The editors would like to thank all of the contributors who have given up their own time to skillfully put together their chapters. We would also like to thank everyone at Springer who has helped to finalise the project. Finally, to all our family, friends, colleagues and trainees – thank you for your patience.

A. Muneer
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Contents

An Introduction to Prosthetic Devices

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Asif Muneer and Ian Pearce

Abstract

The word "prosthesis" originates via New Latin from the Greek word "prostithenai" meaning to 'add to' or 'in addition'. Although commonly used for external limb replacements, the term also encompasses surgical prostheses used in a wide range of surgical subspecialties.

Keywords

Prosthetic surgery • Biofilms • Stem cells • Tissue engineering

Prosthetic surgery is not new, the earliest recorded examples being that of a wooden toe in the New Kingdom of Egypt (1600–1100 BC) and an iron leg made for the warrior queen Vishpala, documented in the ancient Sanskrit poem collection of Rigveda, one of the four Vedas, or sacred texts of Hinduism, (circa 1500–1200 BC). These prosthetics however, had no function and were merely anatomical in nature, it was not until approximately 800 BC that a functioning prosthesis was discovered near Thebes in Egypt.

Urological surgery has always been at the forefront of innovative developments in surgery; from the development of endoscopy, the early adoption of laparoscopy and minimally invasive surgery to the utilisation of robot assisted surgery for pelvic cancers and more recently upper tract malignancy.

The male external organs of the urinary tract namely the penis and scrotal contents are areas of the body that have become synonymous over the years with masculinity, virility, power and fertility with the emphasis varying amongst different cultures and geographical regions. Hence any functional loss related to these organs either through traumatic injury or as a result of malignancy is often linked to a loss of quality of life and self-esteem together with a negative psychological impact. It is both relevant and interesting to note that some of the first medical prostheses were developed to replace either missing testicles or to restore function, either voiding or sexual to the penis. In modern urological practice, the major technological advances have been witnessed within the areas of penile prostheses and the artificial urinary sphincter through the use of improved biomaterials and design that have also

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Table 1.1 Properties of the ideal material for prostheses

1. Durable
2. Inert
3. Negligible particle migration
4. Low infective risk
5. Functionally resilient
6. Easy to handle
7. Cost effective

led to the evolution and improvement in ureteric stents, nephrostomy tubes and urinary catheters resulting in an increasingly wide and varied range available for practical use.

An ideal prosthesis requires components and materials which can either restore or reproduce the physiological function of an organ (Table 1.1). The rapid developments in material science have provided a vast array of potential materials which are inert and therefore suitable for use within the human body and have subsequently led to an increasing number of prostheses with more indications being available in urological practice.

However, as discussed later in this book, complications still exist as with any surgical intervention and the implantation of foreign material within the urinary tract will always be at a potential risk of prosthesis infection, device malfunction and erosion as well as particle migration. Careful as well as appropriate patient selection and preparation, is of paramount importance in order to reduce the patient morbidity and patient dissatisfaction.

Surgical specialities such as Trauma and Orthopaedic surgery where prosthetic surgery forms the major component of a surgeons workload necessitate a specific theatre set up and preparation and demand that all involved personnel are well versed in protocols aimed at reducing the risk of infection, and ensuring that the handling of the prosthesis itself is performed cleanly and efficiently with a minimal risk of contamination. In contrast prosthetic surgery in urology forms a small proportion of the surgical volume and overall workload focusing almost exclusively on either mainstream core procedures such as ureteric stenting and testicular prosthesis insertion and the more complex prosthetic surgery such as inflatable penile prosthesis insertion, artificial urinary sphincter insertion and neuromodulation. These more complex procedures tend to polarize to subspecialist centres such that high volume surgeons have the necessary equipment and theatre staff well versed in these procedures.

With penile prosthesis surgery the infection risk relates to the surgeons' case volume with lower rates of infection being witnessed in high volume centres. But how do we define a high volume centre? There is currently no evidence to suggest how many procedures should be performed in order to be deemed a high volume centre, indeed, defined values for the incidence of prosthesis infection or other morbidities does not exist and thus minimum numbers associated with such figures are impossible to extrapolate and delineate.

If we take the UK practice as an example, there are approximately 500 penile prostheses inserted per annum, which are performed in over 20 centres across the country with huge variation in numbers between centres. Some will perform 1 or 2 per year whilst the largest centre performs approximately 200 per year. The remaining centres therefore average approximately 15 prostheses per year if evenly distributed although amongst some of these there will be centres performing in excess of 30. Thus, it would seam reasonable to recommend an arbitrary minimum figure based on this average of 12–24 per year equating to at least one –two penile prosthesis implantations per month. This would enable surgeons, scrub teams and ward staff to maintain the necessary skills for prostheses surgery, in addition to facilitating a compromise between high volume centralization and geographical representation thus ensuring that patients nationally can be offered prosthetic surgery closer to home.

Although this may be a model suitable for primary prosthesis surgery, revision surgery is less common, more demanding and complex and carries with it an associated higher risk of infection. For instance the quoted infection risk for a primary inflatable penile prosthesis is 4 % with a reduction in the rate to 2 % in large volume centres. With revision surgery the infection rate doubles.

However, if a center is only performing 10 penile prostheses per annum and has a single case of prosthesis infection, the infection rate increases substantially to 10 % for that year. Revision sur-

gery also requires specialized instruments, broader experience of prosthesis surgery as well as more sophisticated imaging interpretation and therefore there is a case for such surgery to be performed in the highest volume centres whereby a solitary infection amongst 100 procedures would amount to a mere 1 % infection rate. This of course must be balanced with clinical results and outcomes for each particular unit.

Clinicians and nursing staff in the field of urology routinely manage patients with various prosthetic devices on a daily basis which range from urinary catheters, stomas, ureteric stents to more complex prosthetic devices or injectables. With the more widely used prostheses such as catheters and stoma bags, very little training is often given, or indeed required in order to allow clinicians to manage complications and change or remove the prosthetic devices. However, more complex prostheses such as penile prostheses or artificial urinary sphincters do require more specialized and detailed training and this is often compounded by the relatively limited numbers of these cases performed compared to urinary catheters. In addition there is often a limited number of clinicians and nursing staff who have the required in depth knowledge or experience to troubleshoot peri and post-operative or late complications related to these devices.

In order to minimize complications when patients return to the community, it is imperative that patients undergo detailed pre-operative counseling regarding the device in order to ensure that expectations are realistic and that the patient understands the purpose of the prosthesis. In the case of sacral neuromodulation, inflatable penile prostheses and artificial urinary sphincters it is essential that the patient possesses both the mental capacity and dexterity to use the device appropriately. This aspect of a patient's care may be nurse led and aided by a standard proforma which should cover discussion of alternative options and documentation of which types of prostheses have been shown, demonstrated and discussed as potential treatment options. This also affords the opportunity to advise and optimise the patient pre operatively in terms of smoking cessation, screening for infection (urine, skin) and optimise control of their diabetes and other co-morbidities if present.

Research related to the role of biofilms has led to more interest in prophylactic measures in order to reduce the incidence of prosthetic infections by means of antibiotic coatings or developing surface materials which facilitate the absorption of antibiotics and other infection inhibiting agents. Prosthetic devices which are external such as urinary catheters will inevitably become colonized within 24 h at the latest and usually before. Although this is not problematic for short term indwelling catheters, patients with long term indwelling catheters with complicated or structurally abnormal urinary tracts often develop urosepsis if the catheters are mismanaged or, more commonly, neglected. Therefore, an understanding of biofilms has enabled researchers and clinicians to attempt to address these issues via a variety of innovations including the use of silver impregnated catheters for those who require intermittent self catheterization. The acceptance that a biofilm develops on a prosthetic device does have implications during revision surgery. Firstly the infection rate increases compared to the primary procedure and secondly, as in the case of penile prostheses and artificial urinary sphincters it is advisable to use antibiotic and antiseptic irrigants to reduce the risk of infection. In the case of penile prosthesis revision surgery, washout of the cavities with a combination of antibiotics and antiseptic agents is routinely performed, similar but not to the same extent as performing a salvage washout for an infected orthopaedic prosthesis.

There have been major advances in prosthetic surgery over the last four decades and this is likely to continue at an increasing pace as new materials are evolved and developed which have improved properties with respect to the major complications arising from such surgery.

Several exciting areas which are emerging include the use of tissue engineering to replace lost, damaged or dysfunctional tissue and to use as grafts to replicate areas within the urinary tract as well as 3D printing which offers a more personalized replacement of tissues and organs

and facilitates the replication of function. Other innovations include prostheses which respond to nerve impulses thus enhancing their utility and acceptance amongst patients and surgeons alike. These technological advances combined with the rapid growth in stem cell technology will potentially allow replacement and reconstruction of a number of areas of the urinary tract and will continue to push the boundaries as we currently know them.

The History of Prosthetic Surgery in Urology

2

Sally Deverill and Dominic Hodgson

Abstract

There have been attempts to recreate the appearance and function of the genito-urinary tract with exogenous materials for millennia; but it is only within the last half century that real success has been achieved. This has been a result, to a large extent, of advancements in material science to provide inert yet pliable products. However, materials which are both resistant to infection and offer sustained functionality are still sought. In this chapter we explore how urologists worked in conjunction with industry to develop effective prosthetic solutions to: testicular absence or loss, erectile dysfunction, urinary incontinence, and strictures within the urinary tract.

Keywords

History • Urological prostheses • Artificial testicle • Artificial urinary sphincter • Penile prosthesis • Stent • Sacral neuromodulation

Although physicians have attempted to mimic the function of the urinary tract with exogenous materials for millennia, prosthetic urological surgery is more a modern phenomenon. Its development has been possible as a consequence of surgical innovation, collaboration across specialities and with industry, leading to the production of functional yet inert artificial devices.

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Development of the Testicular Prosthesis

Testicular loss or absence occurs for a variety of reasons in both the paediatric and adult population. This may be as a result of unilateral orchidectomy (inguinal, scrotal or intra-abdominal) as a result of maldescent, malignancy, testicular trauma, infection, infarction or torsion, with bilateral orchidectomy mainly as a result of advanced prostate cancer or bilateral testicular tumours. In

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children, absence of a testicle may be as a result of testicular agenesis, intra-uterine torsion (vanishing testis), failure to descend (cryptorchidism). The loss or absence of a testicle may result in psychological distress for the individual, and therefore replacing the absent testicle with a prosthesis may lead to improved self esteem and quality of life. Prior to the introduction of synthetic materials, foreign bodies such as ivory had been used with limited success, however, the modern testicular prosthesis has undergone a number of innovative developments over the past 75 years.

The first synthetic testicular prosthesis procedure described in the literature [1] was performed by Ralph Bowers in 1940 for a patient with significant psychological distress following an orchidectomy as a result of trauma three years previously. In this case a hollow vitallium (an alloy of cobalt, chromium and molybdenum that had been successfully used in orthopaedic fixation) implant was used. After transient local oedema, the prosthesis was tolerated well and at one year follow-up the patient had no local reaction to the implant, but there was a cold metallic feel to it and considerable mobility of the artificial testicle in the scrotum. The patient's depression, however, was said to have resolved.

In the 1930s and 40s, polymethylmethacrylate (PMMA), a synthetic thermoplastic polymer which was a transparent, rigid plastic, was developed. It had been used as a substitute for glass in windows and skylights as well as signs and aircraft canopies. In 1943 Rea [2] described using PMMA (Lucite) as a testicular prosthesis, with the hope that it would produce a durable and more natural feeling product compared to vitallium. Subsequently, glass spheres [3], polyvinyl alcohol sponges and Dacron were also trialled but with little success. Interestingly, Gelfoam was also used as a filler following intra-capsular orchidectomy for metastatic prostate cancer [4].

In the 1940s silicone elastomers were developed by the chemical industry and revolutionised medical prosthetics. The first published report of these materials being implanted in humans was in 1946 when a Dr Lahey used silicone tubing for a bile duct repair [5] having obtained it from the experimental laboratory of the General Electric (GE) company. Following on from this, in 1948, Dr DeNicola used the same type of tubing to implant an artificial urethra [6] and in the 1950s, silicone was also used for creation of a ventriculo-atrial shunt for the management of hydrocephalus [7], with the aid of the other company involved in the evolution of silicone, Dow Corning. These early applications resulted in a substantial increase in interest from the medical field for both GE and Dow Corning, which led to the latter setting up a specific centre for medical research to supply scientists with research quantities of various silicone materials. In the early 1960s, as well as the production of orthopaedic implants, catheters, drains, shunts, heart valves and components in extra-corporeal technology such as haemodialysis and heart bypass machines, aesthetic implants started to also be developed. Silicone gel filled breast implants were first successfully implanted in 1963 [8]. Soon after, silicone artificial testes started to be implanted in 1964 [9]: the most significant subsequent innovation being a silicone gel filled, silicone-rubber prosthesis described by Lattimer et al. in 1973 [10]. This prosthesis was widely used until 1988 when a firmer, silicone-coated product became the standard until the mid-1990s.

The use of all silicone prostheses was called into question in 1992 in the US after the Food and Drug Administration (FDA) halted the use of gel-filled breast implants due to a number of concerns including the risk of connective tissue and autoimmune disorders, issues regarding mechanical instability and worries about the potential development of malignancy. Most of the evidence of harm was inconclusive; however, there was a perception that silicone particles migrated from the devices into the surrounding tissues. Robinson et al. analysed silicone breast implants removed from 300 consecutive patients and found that 64 % had some form of device disruption [11]. Barrett et al. also described leakage of small amounts of silicone into surrounding tissues from penile prostheses, a phenomenon known as "gel bleed" [12]. Despite this, no subsequent evidence ever found a link between the use of penile or testicular prostheses and the

development of connective tissue disorders or an increased risk of malignancy.

However, as a result of the concern and controversy surrounding silicone breast implants, there was a voluntary withdrawal of silicone-gel filled testicular prostheses in the US in 1995 (although they have remained in use within the UK) and a new silicone composite shell, but saline-filled, prosthesis was introduced by Mentor Medical Systems and has been used from that year onwards. In 2004, Turek et al. published a multi-centre prospective case-controlled trial of this new prosthesis and found no complications after one year and concluded that saline-filled prostheses appeared safe and well-tolerated in the short-term [13].

There are now a number of companies producing and supplying testicular implants: Nagor Ltd (UK); Mentor Medical Systems, now Coloplast (USA); Osteotec Plastic Surgery (UK); and Silimed (Germany). Coloplast also produce a soft-solid reinforced silicone prosthesis as well as the saline-filled prosthesis (which is the only one currently licensed by the FDA for use within the US). The other companies produce silicone gel and elastomer versions. The majority of the prostheses have a suture loop to aid fixation of the implant within the scrotum (Fig. 2.1).

More recently there have been in vivo studies investigating the development of a hormone releasing testicular prostheses which has a dual function of providing a cosmetic replacement as well as physiological function.

Early Reports of Penile Prostheses

The earliest reports of penile prostheses described the use of wooden sticks placed in the urethra or under the penile skin [14]. Sadly, as with so many of the developments in surgery, it is injuries sustained during war that provided (and still provides) much of the necessity for invention. In the sixteenth century, the greatest of war surgeons, Ambroise Paré, describes using a piece of solid wood to replace a lost penis but emphasised its function was to allow the passage of urine rather than for intercourse: *"those*

Fig. 2.1 Five sizes of modern Silimed Silicone Elastomer Prostheses 2015

that have their yards cut off close to their bellies, are greater troubled in making of urine so that they are constrained to sit downe like women for their ease." Paré created what he termed *"an artificial yarde out of firm wood"* (Yarde being an Elizabethan term for the member) that served *"instead of the yarde in making of water."* [15, 16]. (Fig. 2.2)

The first recorded attempt to restore both voiding and sexual function was by the Russian surgeon Nikolaj A Borgaraz in 1936 (cited in Gee 1975) [17]. He used an abdominal tube graft and autologous rib cartilage with the aim of providing rigidity to allow coitus. This was akin to the *os penis* or *baculum* seen in lower order animals (Fig. 2.3).

Famously the Soviet Surgeon Frumkin further developed Borgaraz's autologous technique and also described releasing the penile suspensory ligament in order to increase length [18]. He reported successful intercourse in such patients and even achievement of orgasm. Others, however, reported frequent extrusion, erosion and penile curvature following surgery [19].

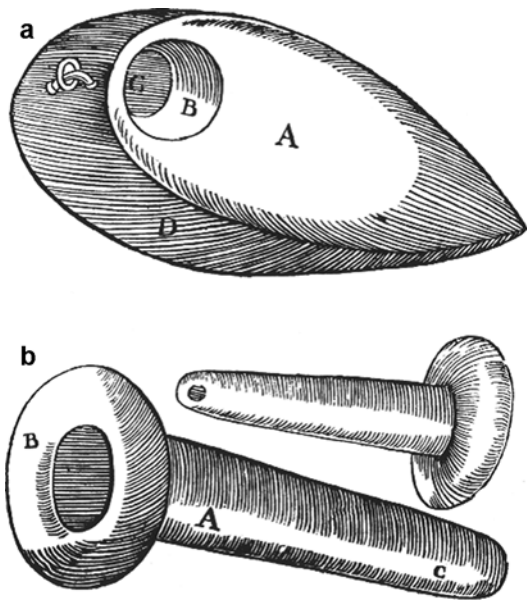

Fig. 2.2 (**a**) Urinal and (**b**) Artificial yard: examples of early incontinence and micturition devices according to Ambroise Paré (1564) [16]

Further Advancements in Penile Prostheses

The rapid post-war development in synthetic substances provided a vast array of prosthetic materials for implantation. Thus, in the 1950s stents made of acrylic materials (developed for rhinoplasties, artificial joints and testicular prostheses) were placed inside Buck's fascia but still outside the corpora cavernosa. However, many patients suffered extrusion as reported by Godwin and Scott [20].

In the late 1950s and early 1960s silicone rubber elastomers were better tolerated and less likely to induce infection when used for medical prosthetics. After being utilized for breast and testicular implants, silicone was first used in 1964 as a penile implant, using inlay methods borrowed from orthodontics, and described by Lash et al. [21]. This material provided flexibility as well as rigidity and durability with minimal tissue reaction and thus became the material of choice for future implants.

These rods were initially placed under Buck's fascia in the groove between the corpora but extrusion of the implants still remained problematic [22]. In 1972 Pearman reported an improvement by placing a single rigid silastic trimmable rod deep to the tunica albuginea (rather than Buck's fascia) dorsally between corona and suspensory ligaments [23]. This intra-cavernosal location has remained the preferred position of modern day penile prostheses.

In 1966 Beheri had also reported the use of intra-cavernosal placement of polyethene rods (an impressive 700 since 1958) [24]. However, Morales, who first reported the use of such rigid devices in the US, found that perforation and erosion were still a significant issue [25]. There was an attempt to improve on the devices by producing a larger implant filled with silicone gel, and whilst there were improved erosion rates, there was a significant risk of leaks and only a few of these were used.

In 1973 the Small-Carrion prosthesis was introduced with a silicone exterior and silicone sponge centre which permitted filling of the whole of the corpora with customized length [26].

Fig. 2.3 (**a**) Baculum- 59 cm Length (**b**) Racoon Baculum

This combination of silicone elastomer and the intra-cavernosal location proved ideal and such designs became the standard for malleable penile implants. Concealment, however, remained an issue and the Finney's Flexirod, Jonas, Omniphase and Duraphase prostheses aimed to improve this by allowing improved manipulation between the erect and flaccid state.

Although the majority of penile prostheses inserted are the inflatable devices, in certain circumstances malleable devices are preferred either for clinical reasons or cost related issues and therefore they continue to be manufactured.

Development of the Inflatable Penile Prostheses (IPP)

The charismatic Texan Urologist Brantley Scott first described an inflatable device in 1973, which consisted of two non distensible cylinders of Dacron-reinforced silicone elastomer together with a reservoir which was controlled by one pump for inflation and one for deflation [27]. This was manufactured and marketed by American Medical Systems (AMS). Such devices combined the function of non-inflatables whilst providing an acceptable appearance in the flaccid state and better concealment. This model was

further modified (including a single inflation/deflation pump) and was implanted widely throughout the following decade (Fig. 2.4).

The AMS 700 model was used from 1983 to 1987 with several modifications including thicker cylinders and kink-resistant tubing (KRT). Wilson et al. reported a 61 % complication/revision rate with the first AMS device compared with a 13 % revision rate with the later AMS 700 [28]. A further modified AMS 700 CX (1987) had an outer silicone covered woven fabric which limited expansion of the cylinder (as opposed to the more elastic corpora previously) and reduced the risk of cylinder aneurysm. Subsequent improvements included colour coded KRT and pre-connected cylinder and pump tubing to decrease intra-operative time and simplify the operation. In 2007 Wilson reported a 60 % 15 year device survival rate from his institution [29].

The 700 Ultrex, was introduced in 1990 and had a middle fabric cylinder layer that expanded in diameter and length when inflated. This was further strengthened in 1993 to reduce the risk of tearing. The device was renamed the LGX (length girth expander) to emphasise the purpose of the modification. More recently the pump has been replaced with a "momentary squeeze" (MS) pump which results in device deflation in 3–4 s and has a built in lock out valve to prevent auto-inflation. At the time of Scott's death, in a plane crash in 1991, an estimated 100,000 had already been implanted.

Mentor (now Coloplast) introduced their three-piece prosthesis in 1983. Improvements have included a change in composition with the addition of polyurethane (which has improved tensile strength without compromising the biocompatibility), and reinforced tubing. In 1989 the Mentor Alpha-1 was a connector less, single pump IPP which again improved reliability and also the risk of connector leakage (Fig. 2.5).

In 2000 the Lock-out Valve ™ stopped the flow of fluid from the reservoir as a result of increased abdominal pressure thus eliminating the risk of auto-inflation. A study revealed a 1.3 % risk of auto inflation compared to 11 % with the unmodified device. An Alpha-1 narrow-base product also allowed smaller diameter cylinders to be placed in fibrotic or scarred corpora.

Since 2000, manufacturers have impregnated the devices with antibiotics. Thus, InhibiZone™ (Minocycline and Rifampicin impregnated into the external silicone surfaces) on the AMS device conferred an 82 % lower infection rate compared to the untreated device [30] (Figs. 2.6 and 2.7).

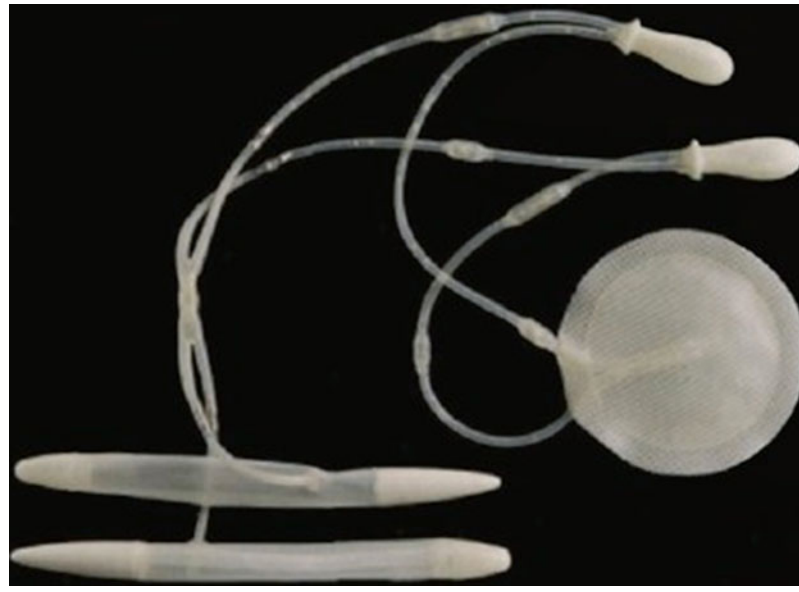

Fig. 2.4 The first inflatable penile prosthesis

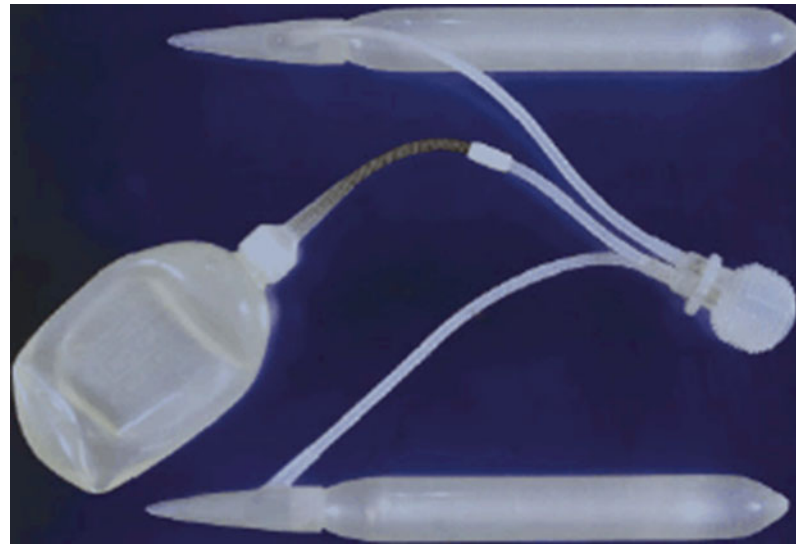

Fig. 2.5 Mentor Alpha-1 Inflatable Penile Prosthesis

Fig. 2.6 InhibiZone™ antibiotic eluting AMS IPP

Mentor's hydrophilic Titan coating was introduced in 2002, allowing absorption of antibiotics which the prosthesis is immersed in intraoperatively, with the advantage of allowing the surgeon to choose their own antibiotics. Studies have again shown a similar decrease in infection rates [31].

Further research into infections and combined with the improved knowledge of bio-films, has resulted in extensive lavage at the time of revision surgery to reduce the rate of infection.

Development of Prostheses for Urinary Incontinence

Ancient writings on urinary incontinence addressed cases of fistulae or overflow incontinence. Later there followed reports of the problem of postoperative incontinence after perineal lithotomy. The first surgical techniques to combat urinary incontinence originated with attempts at fistula repair. By the end of the nineteenth cen-

Fig. 2.7 Modern day Coloplast Titan inflatable penile prosthesis

tury procedures for stress incontinence were described, and in the late twentieth century procedures using prosthetics such as artificial urinary sphincters (AUS), prosthetic slings, bulking agents, and electro-stimulation had been introduced.

Artificial Urinary Sphincters (AUS)

The increase in the number of radical prostatectomy procedures for the management of localised prostate cancer in the latter decades of the twentieth century has had the consequence of an increase in male stress urinary incontinence. The introduction by AMS of the AUS in the early 1970s was a timely attempt to combat such male non-neurogenic stress incontinence. Its genesis was closely related to the development of the inflatable penile prostheses, borrowing many of the same technological advances, and in fact the IPP was a side-development from the AUS. The main indications for AUS insertion include: post prostatectomy incontinence; sphincter weakness incontinence due to neurogenic bladder dysfunction; intrinsic sphincter deficiency; failed female anti-incontinence surgery and rarer congenital causes of incontinence [32].

Although there have been descriptions of penile clamps to provide external compression of the urethra since the eighteenth century, the first description of an artificial urinary sphincter was credited to Foley in 1947 who described an inflatable cuff around the penile urethra controlled by a pump carried in the pocket [33]. In 1960, Vincent described the use of an externally worn belt and air-inflatable cushion to provide variable degrees of perineal compression.

The first prosthetic device in the modern era to increase urethral resistance was developed by Berry in 1961 [34]. He aimed to restore continence by using implanted acrylic blocks through the perineum in order to compress the bulbar urethra, but this technique was hindered by the implants moving and eroding into the urethra. In 1973, Kaufman described a gel filled disc shaped prosthesis designed to augment resistance by passive compression of the urethra [35].

The most significant development was in 1972 when Scott implanted the first AUS, the AMS721 (American Medical Systems, USA) [36]. This was a silicone prosthesis which consisted of an inflatable cuff for placement around the urethra or bladder neck together with separate inflation and deflation pumps and a reservoir, with valves controlling the direction of flow and the pressure within the system.

In 1978, Rosen produced an alternative sphincter consisting of a three-armed clamp, with one arm carrying a balloon attached to a reservoir bulb, and a release bulb, positioned in the scrotum. Compressing the reservoir bulb inflated the balloon which increased the urethral resistance in order to maintain continence. Failure was common as the pressure on the urethra could not be regulated and therefore the longest lasting prosthesis survived for only 26 months [37].

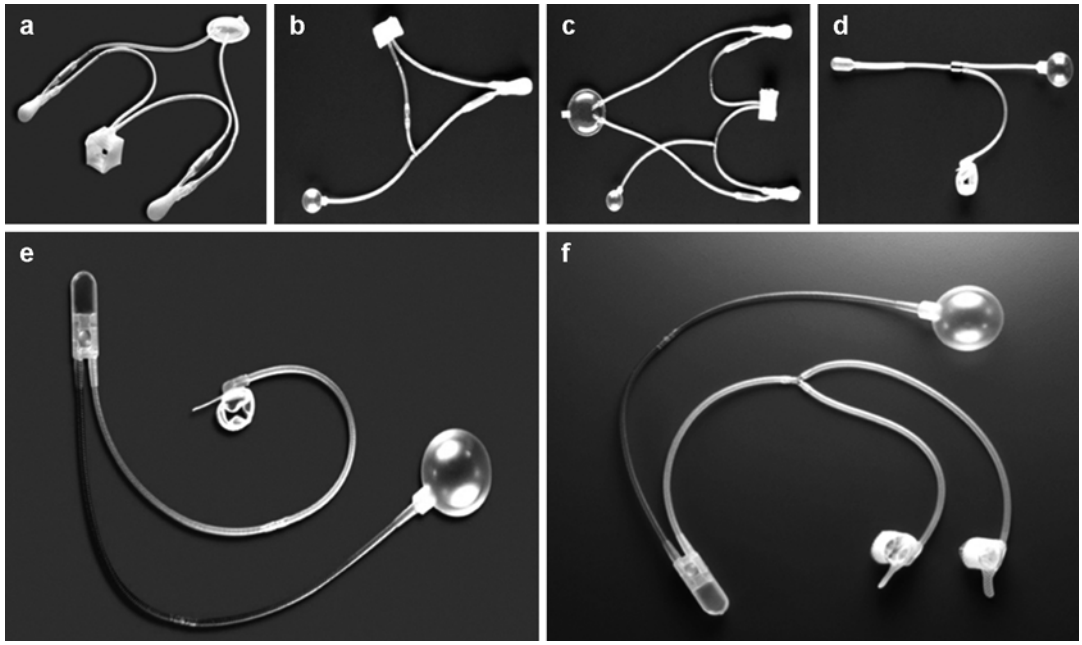

Fig. 2.8 Development of the AMS Artificial Urinary Sphincter: (**a**) 721 (1972–1979); (**b**) 742 (1974–1979); (**c**) 761 (1976–1977); (**d**) 791/2 (1977–1979); (**e**, **f**) 800 (1983/1986–)

Over the next decade and a half, the AMS model was modified to improve functionality and reduce mechanical failure. The most significant changes were the use of a balloon instead of valves to regulate the pressure, and a change to an automatic inflation device. Later models also saw the introduction of an entirely silicone based cuff instead of one of Dacron-reinforced silicone rubber. Additionally, silicone components were dip-coated to reduce the incidence of leakage, as a consequence of the concerns regarding silicone "bleed" from breast implants as previously mentioned. A deactivation button permitted periods of reduced direct urethral pressure in an attempt to prolong the life of the device, reduce mechanical fatigue and the incidence of erosion. Overall, there was a decrease in the number of components and connections, eventually leading to the currently used three-part AMS 800 AUS device. This was first introduced in 1982, reached maturity in 1987, and is still the most widely used AUS on the market, such that 25,000 had been implanted by the time of the inventor's death (Fig. 2.8).

With the increase in demand for the AUS in the last 20 years, there have been alternative devices developed to compete with the AMS 800, including the FlowSecure™ (FlowSecure, RBM-Med)[38], Zephyr ZSI 375 (Zephyr Surgical Implants, Switzerland) [39], ProACT (Uromedica) [40], Peri-urethral constrictor (Silimed, Brazil) [41], Tape Mechanical Occlusive Device (TMOD) [42] and the Versatile Automated Device [43].

Modified models and novel devices are still under investigation with innovations including the use of three smaller alternating sphincters with a microdrive control unit powered by a subcutaneous battery [44], and nanotechnology derived devices (utilising shape-memory alloys/electrically activated polymers).

Use of Sling Procedures for Urinary Incontinence

Autologus grafts for bladder neck sling procedures were first used in an attempt to restore continence in the early 1900s. Giordano used gracilis transposed beneath the bladder neck in 1907 [45]. Goebell, in 1910, described the use of pyramidalis [46] and Frangenheim in 1914 wrote

of pyramidalis with overlying fascia [47]. Stoekel in 1917 combined this same muscle-fascial sling with a plication of the bladder neck [48]. In 1933, Price first described the use of fascia lata as a sling and there have been many modifications of this technique since [49]. The "Aldridge sling" became the standard procedure for much of the last century following his publication in 1942 [50].

In 1953 Armand J Pereyra described a vaginal needle suspension which introduced the concept of minimally invasive techniques for urinary incontinence [51]. Due to the morbidity associated with graft harvesting, toward the end of the century, non-autologous biological materials (allografts and xenografts) and synthetics (Mersilene and Goretex) were used. However, there were concerns about disease transmission with the former, and erosion and rejection with the latter.

Trans Vaginal Tape (TVT)

The innovator who revolutionised this area of surgery was the Danish Gynaecologist (working in Sweden), Ulf Ulmsten. He was a rigorous scientist and his "integral" theory [52] proposed that incontinence resulted from a deficient pubococcygeus muscle incapable of lifting the anterior vaginal wall close to the urethra. His mid-urethral sling aimed to reinforce this defective mechanism. He originally called this the intravaginal sling-plasty [53], but Johnson & Johnson changed the name to TVT when they bought the patent in 1997.

Since then there have been numerous attempts to improve the original design although it is questionable as to how successful these have been.

The Use of Bulking Agents for Incontinence

In 1938, Murless reported the injection of sodium morrhuate, a sclerosing agent, into the anterior vaginal wall of 20 patients, in an attempt to treat stress incontinence [54]. Following this, other sclerosing agents including paraffin and dondren were used but complicated by the development of pulmonary emboli. Teflon (polytetrafluroethylene) was trialled in the 1970s [55, 56] but there were concerns over microparticle migration and the development of inflammatory reactions and granuloma formation. The next development was the use of collagen by Shortliffe (1989)[57], and the first bulking agent to be US FDA approved in 1993 was a Glutaraldehyde cross-linked (GAX) bovine collagen 'Contigen'. Carbon coated zirconium beads in a water based carrier gel with beta glucan (Durasphere) have also been FDA approved [58]. In the 1990s, silicones were also introduced as bulking agents, although these were not FDA approved due to the previously mentioned concerns over silicone particulate migration. Of these, Macroplastique (polydimethylsiloxane elastomer implants) has also been used to treat vesico-ureteric reflux.

Sacral Neuromodulation Development

Robert Ultzmann (1842–1889) first described the use of electrophysiology in an attempt to stimulate the detrusor muscle and sphincter muscle, by way of inserting a catheter-like electrode into the bladder or prostatic urethra [59]. Subsequently Hopkinson and Lightwood introduced electrostimulation of the pelvic floor with plug-electrodes in the 1960s [60]. However, the development of permanent intracorporeal electrodes began in 1954 when Boyce et al. described the insertion of stimulating electrodes directly onto the bladder [61]. By 1967, Burghele attached stimulators to the pelvic splanchnic nerves and Habib attached them to the segmental sacral nerves [62, 63]. In the 1970s, sacral anterior root stimulators were developed concurrently by GS Brindley's team in the UK and also by a San Francisco based group. Initial experiments were performed on baboons and the first human sacral anterior root stimulator was implanted in London in 1976 but unfortunately this resulted in no useful micturition [64].

However in 1978, two further insertions proved to be successful [64]. In 1982, the first sacral nerve stimulator (SNS) implant for refractory lower urinary tract dysfunction was inserted by Tanagho and Schmidt of the San Francisco group [65]. The first SNS implants consisted of a temporary lead placed into the S3 sacral foramen, with test stimulation for 4–7 days, followed by insertion of a permanent lead and neuromodulation as a second stage procedure. In 1997 this was developed further by using the same definitive lead for both the test phase and the permanent stimulation [66]. In 1997 InterStim received FDA approval for treatment of urge urinary incontinence and, in 1999, FDA approval was granted for the treatment of symptoms of urgency-frequency and urinary retention. In 2008, Spinelli et al. modified the insertion technique with a tined lead and moved the box to the buttock instead of the anterior abdominal wall [67].

Ureteral Stent Technology

Gustav Simon was credited with the first ureteral stent placement by inserting a tube into a ureter in the nineteenth century. In the early 1900s, Joaquín Albarrán created the first stent designed specifically for use in the ureter and this was made of fabric covered in laquer. Ureteral replacements using glass, tantalum or vitallium tubes were attempted before World War II but a combination of migration and obstruction limited their success [68, 69]. In 1967, Zimskind et al. described the first cystoscopically placed ureteric stent, which was straight and made of silicone [70]. As there was no coil at either end, these were again subject to migration. Subsequently modifications were made to prevent slippage including a shepherd's crook end (McCollough 1974) [71] and then in 1978, Finney described the double J stent design with a coil at both the proximal and distal ends to prevent migration in either direction [72]. Pure silicone does not have adequate rigidity and compresses easily therefore modern stents are composed of polyurethanes combined with silicone.

Metal Stents (MS)

Metal stents have been developed to provide long term ureteric and urethral patency in the presence of internal stricturing or external compression. Additionally trans-sphincteric urethral stents can be used to induce iatrogenic incontinence in neurogenic bladder dysfunction as an alternative to sphincterotomy [73]. Such long-term stents had first been used for vascular and biliary intervention. An ideal stent would be radio-opaque, cost effective, provide long term patency and provide resistance to migration, encrustation and infection.

Urethral Metal Stents (MS)

The first reported use of MS in the urinary system was described by Fabian in 1980 [74]. In 1988, Milroy described placement of eight stents in bulbar strictures immediately following urethrotomy [75]. Milroy's stent was a stainless steel tubular mesh. Some subsequent urethral stents have mimicked this design, while others are a short rigid titanium wire mesh (AMI), or nitinol springs. Others have attempted to produce biodegradable implants, which in contrast to long term stents don't epithelialise, but in animal models there has been failure to produce consistent results in terms of longevity. Thus far, no device has achieved all of the requisite qualities mentioned above, but after two decades of relatively widespread use, these can be considered as an alternative to catheterization in men unfit for more testing surgery.

Ureteric Metal Stents (MS)

In order to avoid the need for repeated exchanges of temporary stents, and in order to provide greater resistance to extrinsic compression, various modifications of ureteric MS have been seen since they were first described in the early 1990s [76]. Pauer was the first to use the self-expanding Wallstent in the ureter (as Milroy had in the urethra) and after multiple

adaptions this remains the most widely trialled and is normally placed after balloon dilatation. Others have attempted antegradely-placed stents that are expanded directly by a balloon but long term follow up data is absent [77]. A thermo-expandable MS (also described in the urethra) has the theoretical advantage of allowing easy removal and was first used in 1999 [78], although others have described a failure/migration rate of 60 % [79]. Other authors have written of limited experience with covered stents, which aim to make them more inert [80, 81]. Finally, full-length double-pigtailed MS aim to minimise migration whilst providing long-term patency but still have to be changed annually [82].

Conclusions

Prosthetics in urology is still a young subspecialty with ongoing developments and innovative research. This has been due to the revolution in material sciences since the Second World War which has provided materials with the requisite properties of pliability, functionality and inertness that innovative clinicians (in partnership with industry) have used to provide the devices that are available today.

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Infection and Biofilms

3

Arie S. Parnham and Vijay K. Sangar

Abstract

Prosthetics in general are susceptible to bacterial infection often with disastrous consequences, especially if not recognized and managed promptly. Consequently a good working knowledge of the underlying concepts of infections and biofilms is essential for clinicians involved in this area of urological surgery.

Keywords

Biofilm • Bacteria • Prostheses • Antibiotics • Urology • Infection • Sepsis

Biofilms

History

Although the term 'biofilm' was first published in 1975 in Microbial Ecology they were recognised much earlier [1]. The first description of a biofilm was Anthony van Leeuwnhoek, "the father of microbiology." He lived in Holland and worked as a linen salesman whose interest extended into producing microscopes using diamond shavings and also observing the natural world. In a report to the Royal Society of London regarding dental, plaques, he remarked "the number of these animalcules in the scurf of a man's teeth are so many that I believe that they exceed the number of men in a kingdom." Work by Koch in the 1800s allowed bacteria to be studied more closely, however the focus was on planktonic culture (single cells floating in a liquid medium). Although important progress was made on the more serious pathogens, as time progressed more and more scientists felt that this didn't represent the true nature of bacteria. This was later confirmed by Geesey in 1977 who confirmed that 99 % of bacteria are attached to surfaces as opposed to free floating (planktonic) [2].

In the 1940s H. Heukelekian and A. Heller wrote, "Surfaces enable bacteria to develop in substrates otherwise too dilute for growth.

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Development takes place either as bacterial slime or colonial growth attached to surfaces" [3].

Claude Zobell in the mid-1900s later described his glass bottle experiments noting that bacteria introduced into said vessel rapidly disappeared from the water contained within and seemed to rapidly colonise the walls of the container creating a microenvironment of supportive nutrients [4].

The recognition of the importance of biofilms on healthcare and industry, and the related economic costs led to the formation of the Centre for Biofilm Engineering in Montana, USA in 1990. This type of centre was subsequently mirrored in several other countries.

Introduction to Biofilms

Although a number of definitions exist, a biofilm is essentially an assemblage of microbial cells that is irreversibly associated (not removed by gentle rinsing) with a surface and enclosed in a matrix of primarily polysaccharide material [5]. It is rare for a biofilm to contain one organism in nature and usually there are many different varieties.

There are a number of advantages for bacteria to live in a biofilm.

1. A biofilm has the ability to concentrate ions and organic compounds and in nutrient poor environments where single organisms would otherwise struggle, as demonstrated by Zobell and Grant [4].
2. Within a biofilm there are a wide variety of microenvironments that can cater for different organism requirements [6]
3. Biofilms in nature are composed of multiple different species of bacteria many of which will have complementary enzyme profiles for the breakdown of nutrients.
4. They augment the transfer of genetic material through transformation (the take up and incorporation of foreign DNA), conjugation (transfer of a plasmid of DNA facilitated by an F-pilli) and transduction (a virus or phage packaged with the DNA of one bacteria is absorbed by a receiving bacterium which incorporates the new DNA into its own) [7–9]. They can also facilitate the activation of certain genes that promote transformation by allowing greater accumulation of molecules that initiate this upregulation (a process known as Quorum sensing- a phenomenon in which bacteria can chemically sense the presence of other bacteria and when bacterial populations become high enough, new suites of genes may be expressed) [10]
5. They confer a degree of resistance to phagocytes and protozoa [11]
6. They confer a degree of antibiotic resistance. A number of mechanisms have been investigated and are thought to be responsible for the increased resistance to antimicrobial agents:
   (a) In a few cases biofilms can prevent penetration; this is not the case in the vast majority of circumstances.
   (b) Biofilms allow enzymes that degrade the antibiotic to become concentrated in the microenvironment.
   (c) Due to the variable microenvironments some bacteria are quiescent and, as such have a lower metabolic activity and are less susceptible.
   (d) Biofilms are known to alter the genetic expression conferring antimicrobial resistance e.g. expression of efflux pumps.
   (e) Persister cells produce toxins that prevent critical metabolic activities. Consequently bacteria have fewer critical targets for antibiotics and disinfectants to work against. They can also produce an antitoxin that allows resumption of activity once the threat has dissipated [12]

Formation of Biofilms

Through detailed studies of biofilms we now understand that their creation is a very complex process. As a bacterium approaches a surface within a fluid, Van der Waal forces attract them. However, the closer they are to a surface the net negative electrostatic charge of bacteria and the interacting surface, results in a counteracting repulsive force. The incorporation of flagellae and pilli helps overcome this. Attachment of the bacterium is further augmented by a hydrodynamic boundary layer created by the sur-

face interaction with the suspensory fluid, creating a low turbulence and relatively calm zone. A rough surface promotes adherence compared to a smooth surface, as the surface area is increased and shear forces are diminished [13]. Once bacteria come in contact with a surface they will produce a 'conditioning film' that will build over the ensuing hours. The surface that the bacterium comes in contact with will influence the biofilm structure and properties, and no surface is immune to this process.

The attachment of bacterium to a surface occurs in two stages: reversible attachment and irreversible attachment.

As the name suggests reversible attachment is unstable and microbes under a microscope can be seen as twitching as their flagella anchors them, but the microbe body is free to be influenced by the environment. It is possible for some bacteria to move across the surface they adhere to by contracting their pilus. Eventually the bacteria become encased in a polymeric matrix, they themselves create, essentially fixing them to the surface – irreversible attachment. The time it takes for this to occur can be in the realm of minutes but is clearly organism dependent. Other species are then recruited both randomly and in some cases specifically, as well as non-living debris that can provide structural and nutritional support. An example of a developing biofilm can be seen in Fig. 3.1.

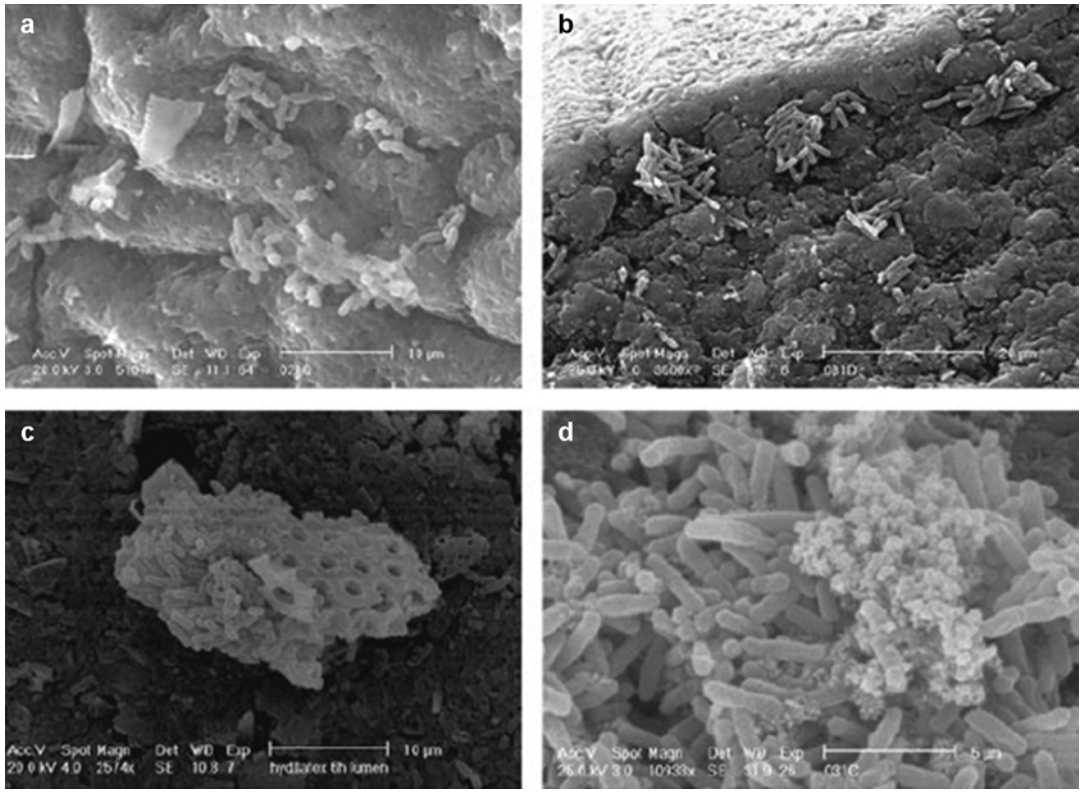

Fig. 3.1 Electron micrographs illustrating the colonization of a hydrogel-coated latex catheter by Proteus mirabilis in a laboratory model of the bladder. (**a**) This image shows bacteria trapped in crevices in the surface of the eyeholes 2 h after incubation in the model. (**b**) Microcolonies of *P. mirabilis* develop at the eyehole 4 h after incubation. (**c**) Bacteria attach to a diatom skeleton embedded in the luminal surface of the catheter 6 h after incubation in the model. (**d**) Biofilm develops at the eyehole 6 h after incubation in the model. Aggregates typical of apatite can be seen forming in the biofilm as the urine becomes alkaline (From Stickler [14]; with permission from Nature Publishing Group)

Table 3.1 Variables important in cell attachment and biofilm formation [5]

Properties of the substratum	Properties of the bulk fluid	Properties of the cell
Texture or roughness	Flow velocity	Cell surface hydrophobicity
Conditioning film hydrophobicity	pH	Fimbriae
	Temperature	Flagella
	Cations	Extracellular polymeric substances
	Presence of antimicrobial agents	

The flow of the surrounding medium can influence the structure of the biofilm; with fast flowing habitats often creating dense strongly adhered mushroom shapes whilst flat weakly attached biofilms occur in slow flow rates. Table 3.1 summarizes the important variables in cell attachment and biofilm formation.

Although biofilms confer to their 'residents' a number of advantages there are a number of circumstances in which bacteria may detach and disperse. These include passive forces including abrasion, erosion and fluid shear; or biological reasons such as nutrient limitation.

Bacteria and Biofilms in Urology

The management of biofilms is extremely important in the placement and success of prostheses in urological surgery.

Urinary Catheters

Approximately 20–30 % of patients catheterised in hospital will develop bacteriuria, with the risk increasing by 5 % each day such that by 20 days most patients, if tested, will exhibit bacteriuria [15–17]. Catheter-associated urinary tract infection (CAUTI) occurs in 2–6 % of patients [18] and is the most common hospital acquired infection, It is associated with an increased risk of mortality of as high as 30 % when associated with a bacteraemia [19, 20]. In 2012 it was estimated that there were 54,500 catheter related urinary tract infections in the United States alone [21].

A CAUTI is defined as a UTI where an indwelling urinary catheter was in place for >2 calendar days on the date of event, with day of device placement being day 1, and an indwelling urinary catheter was in place on the date of event or the day before. If an indwelling urinary catheter was in place for > 2 calendar days and then removed, the date of event for the UTI must be the day of discontinuation or the next day for the UTI to be catheter-associated [22].

CAUTIs are commonly a result of endogenous bacteria from the perineum [23]. However, a proportion (34 %) are a consequence of direct inoculation i.e. lapses in aseptic technique [23]. In some rare circumstances i.e. with Staphylococcus aureus it can be haematogenous [24].

Biofilms form both on the outer surface and inner drainage channel of a catheter within 3 days [25, 26]. The outer surface biofilm is generally populated by bacteria from the gastrointestinal tract, whilst drainage channel bacteria usually originate from cross-contamination due to a non-closed system, i.e., from a health worker's hands [27]. The presence of *Proteus mirabilis* within a biofilm generates urease, creating ammonia from urea, leading to an increase in urinary pH and subsequent crystallisation of magnesium ammonium phosphate (struvite) and calcium phosphate (hydroxyapatite), thereby causing stone formation.

The most common organisms involved depends on the duration of catheterisation as well as the location of the patient. CAUTI within 1 month of catheter placement is most commonly caused by Escherichia coli followed by Enterococcus species, Pseudomonas aeruginosa and yeast species [23]. In cases where a catheter has been in situ for longer than a month it is likely that there will be more than one microorganism cultured including enterobacteriae, gram negative and positive bacteria and yeast such as

Candida albicans. Further, these are more likely to be multiresitant [28, 29]. CAUTI in the intensive care setting are more likely to be Candida species [24].

Most patients with an indwelling catheter will have pyuria or bacteriuria whether or not they have a symptomatic urinary tact infection and do not routinely require treatment. Inappropriate use of antibiotics poses a significant risk for the development of multi-resistant organisms. Therefore the use of urine culture in the diagnosis CAUTI as an independent test is not reliable. Symptoms are therefore the most important aspect in deciding which patients have a CAUTI and require treatment [30]. In cases of CAUTI with long term catheters i.e. more than 2 weeks, the catheter should be removed and urine sent immediately from a new catheter (long-term if judged necessary or from a single intermittent self catheterisation) and empiric antibiotics initiated as per local guidelines based on epidemiological data and/or previous urinary cultures [31, 32]. Data from a randomised controlled trial suggests a shorter time to resolution and lower relapse rates with this approach rather than leaving the catheter in situ [33]. Once sensitivities return the antibiotic should be selected with the narrowest spectrum of appropriate cover [31, 32]. Duration of cover is variable dependent on the clinical situation and should be guided as per local, regional and national guidelines [31, 32].

Ureteric Stents

Although ureteric stents lie completely within the body they are not immune to the formation of biofilms or infection and rates of colonisation have been quoted as between 42 and 90% [34, 35]. However, despite this high rate few progress to develop symptomatic urinary tract infection.

The risk of bacteriuria and colonisation is directly related to the length of time the stent stays in situ, female gender and the presence of systemic disease such as diabetes mellitus, chronic renal failure and diabetic nephropathy [36].

When treating patients with a suspected urinary tract infection, with ureteric stents in situ, it is worth noting that the sensitivity of a urine culture to the presence and characterisation of colonisation is low and therefore a negative culture does not rule out a colonised stent [34]. Further the bacteria are often more resistant as previously described [34].

Both the American Urological Association and the European Association of Urology recommend prophylactic antibiotics prior to the insertion of ureteral stents however no RCTs exist to guide decision making [37]. However, there is RCT and meta-analysis data from transurethral resections of the prostate and transurethral resections of bladder tumour, favour prophylaxis to reduce sepsis episodes and bacteriuria [38–40].

Penile Prostheses

One complication related to penile prostheses which requires removal of the device. The most common bacterium causing medical device and penile implant infections is Staphylococcus epidermidis [41, 42]. Chapter 19 (“Complications of Penile Prosthesis Surgery”) covers the management of such complications but overviews of the steps that currently are employed to reduce the risk of infection are outlined in the next section.

Pre-operative and Perioperative Preparation

Pre-operative assessment is crucial in patients undergoing implant insertion. Patients undergoing revision surgery, impaired host defences, diabetes mellitus, spinal cord injury and penile fibrosis are all at a higher risk of infection and as such should be optimised where possible and appropriately counselled.

Parenteral antibiotics are recommended 1 h prior to incision and continuing for 24 h (American Urological Association [AUA] best practice statement 2008), although the guidance acknowledges that there are no randomised controlled trials regarding antimicrobial prophylaxis for insertion of penile prosthesis and is based on meta-analyses of mesh hernia repair and orthopaedic surgery [37]. The choice of antibiotic varies but the AUA recommend an Aminoglycoside

and a 1st or 2nd generation Cephalosporin or Vancomycin [37].

A Cochrane review in 2006 found no difference in surgical site infections (SSIs) among patients who have had hair removed prior to surgery and those who have not, however if it is necessary to remove hair then clipping resulted in fewer SSIs than shaving using a razor [43]. There was insufficient evidence regarding depilatory cream compared with shaving using a razor and there was no difference in SSIs when patients were shaved or clipped 1 day before surgery or on the day of surgery [43].

Many implanters have adopted a 10 minute timed surgical scrub of the patient although there is little in the literature to recommend this. However, the choice of scrub used appears to make a difference with Chlorhexidine appearing to be more efficacious [44].

The theatre should ideally have a laminar flow system and traffic in and out of theatre should be limited.

Device

Currently the main three-piece penile prosthesis manufacturers are American Medical Systems (AMS, Minnetonka, MN now part of Boston Scientific Mens Health), and Coloplast Corporation (Humlebaek, Denmark). Both companies have taken different approaches to reducing the risk of infection and biofilm formation.

In 2001 AMS introduced Inhibizone™ to their implants, a combination of the antibiotics minocycline and rifampicin impregnated into all the components of the prosthesis, which elute maximally for 3 days and continue to elute to a lesser extent over a 14- to 21-day period [45, 46].

In 2002 Coloplast Corporation released a device coated in polyvinylpyrrolidone (PVP), a hydrophilic polymer that covers the whole device including the reservoir. The PVP-coated implant allows the surgeon to select their own antibiotic combinations at the time of surgery by simply immersing it in a bath of the antibiotic(s). In addition the coating prevents bacterial adherence.

A systematic review in 2012 of 9910 implants found that the infection rates for non-coated versus coated penile implants were 2.32 % and 0.89 % respectively ($P = <0.01$) firmly establishing their role [47].

Surgical Technique

Contamination of the implant with Staphylococcus epidermidis is most likely from the patient's own skin. Consequently a "no touch" technique has been shown in a large single surgeon series using historical controls, to reduce infection rates to 0.48 % [48]. This technique requires gloves and instruments to be changed and an additional sterile drape to be placed once the incisions in the corpora are made.

Artificial Urinary Sphincters

Many issues surrounding the use of artificial urinary sphincters mirror those of penile implants. The most commonly employed artificial sphincter is the AMS 800® produced by American Medical Systems (AMS, Minnetonka, MN). Like its penile implant equivalent the sphincter is coated with Inhibizone™. It should follow that with the convincing data from penile implants, there should be an improvement in infection rates with Inhibizone use in sphincters but there is a paucity of data pertaining to its clinical benefits in this setting. In a retrospective review of 426 consecutive patients (213 without and 213 with Inhibizone™) implanted by a single surgeon, the rates of infection were identical 3.3 %, $P = 0.99$ [49]. Further, in a subgroup of complex patients there was no statistically significant difference between the coated and non-coated devices (2 of 38 patients or 5 % vs. 3 of 50 or 6 %, $P = 0.42$) [49]. However a lower incidence of infection in patients with diabetes was noted in the coated group vs non-coated, although this was not statistically significant (0 of 42 or 0 % vs. 4 of 40 or 10 %, $P = 0.052$) [49].

Conclusions

Careful consideration of biofilms when placing prostheses is of upmost importance to the serious implanter and ultimately the patient. A clearer understanding of how biofilms and

bacteria work and the mechanisms by which they survive and proliferate has lead to a number of important changes in surgery which have resulted in fewer complications and ultimately better patient outcomes.

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Patient Selection and Assessment for Surgery

4

Arie Parnham and Sachin Malde

Abstract

To ensure the best outcomes and highest rates of patient satisfaction, a thorough patient assessment and selection of procedure and prosthesis is required.

Keywords

Prostheses • Patient selection • Assessment • Co-morbidity

General Considerations

Background

The importance of correctly identifying a patient that will benefit from surgery and subsequent assessment cannot be overstated. The vast majority of the operations described in this book have the potential to dramatically transform a carefully selected patient's quality of life for the better, allowing them to re-engage with society and ameliorate the imposition of their condition. However, in a poorly selected patient where inadequate care has been afforded in the work up, surgery can have disastrous implications to both the patient in terms of quality of life as well as the surgeon in terms of medico-legal issues. The following section aims to identify and discuss some of these specific issues.

Elderly Patients

The definition of elderly depends on which source you choose to use as well as the patients place of origin. What is defined as elderly in developing countries is probably not appropriate in developed countries. Consequently, the definition of what constitutes elderly may not be a simple concept. Both the United Nations (UN) and World Health Organisation (WHO) have made attempts to clear the issue by creating their

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own definitions. The WHO refers to patients of 65 and above as elderly whilst the United Nations uses 60 years of age and above.

Worldwide, 1 in 9 people are aged over 60 and this is projected to increase to 1 in 5 by 2050 [1]. In the United Kingdom alone there are now nearly 14.7 million people aged over 60 and this is set to rise to 20 million in 2030 [2, 3]. Approximately 23 % of all procedures performed in the UK are in patients over 75 [4].

The impact of age on the assessment and selection of patients for prostheses is clear. Older people are at a higher risk of adverse postoperative outcomes. This is as a consequence of numerous factors including multiple co-morbidities, polypharmacy, age-related physiological decline and geriatric syndromes including frailty. Therefore any assessment or selection should be detailed enough to detect these factors and take account of them where possible.

However, age should seldom be a barrier to prosthetic surgery in a properly assessed and counselled patient.

Comorbidities

The importance of assessing co-morbidities is set out in the next few paragraphs. A number of scales exist that help quantify the burden of co-morbidity on the patient.

The American Society of Anaethesiologists Score (ASA Score) was proposed in 1963 as a result of a working group set up to create a system to quantify the overall health status of patients pre-operatively [5]. It currently has six grades as shown in Table 4.1. The letter E is added to the grade to denote that the operation is an emergency.

A number of studies have demonstrated a correlation between ASA score and clinical outcomes in a number of specialties. Wolters et al. interrogated the correlation between ASA perioperative risk factors and outcomes in patients undergoing general or vascular surgery. Univariate analysis showed a significant correlation ($P<0.05$) between (1) ASA class and perioperative variables (intraoperative blood loss, duration of postoperative ventilation and duration

Table 4.1 ASA physical status classification system

Grade	Definition	Description
1	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
2	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30<BM<40), well controlled DM/HTN, mild lung disease
3	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA <60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
4	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (<3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis
5	A moribund patient who is not expected to survive without the operation	Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction
6	A declared brain-dead patient whose organs are being removed for donor purposes	

Adapted from Delegates AHo [6]

of intensive care stay) and (2) postoperative complications and mortality rate [7].

Critics of this score point out that it does not account for the whole picture and excludes both patient and procedure related factors including age, sex, weight, pregnancy, type of surgery, surgeon/anaesthetist experience and postoperative care [8, 9]. There is also evidence of inter-observer variability, some of which can be levied at the ambiguity of the term 'systemic disease' [10, 11].

A number of other scoring systems exist although it is worth noting that many were designed for use on patients with malignancy and not those undergoing prosthetic surgery. These include the Karnofsky Score, Eastern Cooperative Oncology Group Score (ECOG).

Diabetes

The pre-operative identification, assessment and management of the diabetic population is extremely important in patients considering prosthetic surgery.

Diabetes is associated with a two to four times increase in the risk of cardiac disease [6, 12]. Nephropathy and neuropathy are also common in this group of patients as a consequence of microvascular disease placing such patients at a higher risk of fluid overload and other complications. Patients with diabetes mellitus are at higher risk of infection and impaired wound healing which are both important issues when considering the insertion of any type of prosthesis [13]. The increased risk of infection is probably multifactorial including reduced T-cell and neutrophil function and an altered humoral response [14–16].

At the pre-operative clinic, the degree of long-term diabetic control should be assessed. The measurement of HbA1c gives an indication of how well the patient's diabetes has been controlled over the last 3 months. Glucose in high concentrations irreversibly binds and glycosylates haemoglobin. The more glucose that is present in the blood stream, the more glycosylated haemoglobin there is, which in turn can then be measured as a percentage.

There is evidence that a raised HbA1c preoperatively is associated with adverse outcomes in a range of surgical procedures [17, 18]. The evidence in prosthetics is less clear. For penile implants, Bishop et al. studied 90 patients undergoing penile implantation. Of the five infections, four had an HbA1c >11.5 % [19]. However Wilson (et al.) found no correlation between an HbA1c greater than 11.5 % and an increased risk of infection [20].

The recommended HbA1c varies for good diabetic control. However, patients with HbA1c greater than 69 mmol/mol (8.5 %) should be referred to a diabetologist to gain tighter control of the diabetes [21].

Patients with diabetes should ideally be placed at the beginning of a morning list where possible in order to minimise the starvation time and allow continuation of a normal feeding pattern as early as possible. Patients that are anticipated to have a long starvation period should be started on a variable rate insulin infusion. Patients that are expected to be day cases and miss no more than one meal can be managed without a variable rate insulin infusion but a close eye should be kept on their blood glucose levels [21].

The capillary blood glucose should be monitored regularly peri-, intra-, and postoperatively to identify any hypo/hyperglycaemia (6–10 mmol/L) and consider a variable rate insulin infusion or subcutaneous insulin if outside of this range [21].

Immunocompromised Patients

Immunocompromise can be broadly characterised as either congenital or acquired, of which the majority of patients are the latter [22]. A number of causes for acquired immunodeficiency exist and are listed in Table 4.2.

Patients with human immunodeficiency virus (HIV) are not precluded from prosthetic surgery. However, specific considerations must be made when considering intervention. HIV is a lentivirus that binds to the CD4 molecule on T4 lymphocytes and subsequently incorporates its own RNA into the cell's DNA via reverse transcriptase. This

Table 4.2 Causes of acquired or secondary immunodeficiency

Category	Example
Endocrine	Diabetes mellitus
Gastrointestinal	Hepatitis, hepatic insufficiency
Haematological	Aplastic anaemia, cancer, graft-versus-host disease
Iatrogenic	Immunosuppression, radiation therapy, splenectomy
Infectious	Cytomegalovirus, Epstein-Barr virus, HIV infection
Nutritional	Alcoholism, malnutrition
Renal	Nephrotic syndrome, renal insufficiency, uraemia
Rheumatological	Rheumatoid arthritis, SLE
Miscellaneous	Burns, critical or chronic illness, sarcoidosis

From Neskovic [23]; with permission

results in a reduction in the CD4 exhibiting immune cells. Patients whose CD4 counts fall below 200 cells/mm^3 or who exhibit 1 of any 20 defining conditions, are considered to have Acquired Immunodeficiency Syndrome (AIDS) [23, 24].

Performing surgery in HIV-positive patients clearly raises issues for both patient and surgeon safety. It is estimated that the risk of contracting HIV after mucous membrane exposure is in the order of 0.09 % [25]. Clearly all precautions should be undertaken including hand washing, personal protective equipment and careful disposal of surgical sharps.

Patients with HIV should be preoperatively assessed in the same manner as patients without HIV. However, it is worth noting that a number of conditions are more prevalent in this patient population including:

- Coronary artery disease
- Coagulopathy, thrombocytopenia and neutropenia
- MRSA
- Drug allergies
- Substance abuse
- Hepatic and renal dysfunction

High-quality guidelines exist which have been accepted into the National Guideline Clearing house for the perioperative assessment of patients with HIV [26].

The general health of the HIV infected patient, the nutritional status and the presence of organ failure are the most important factors in predicting the outcome of any surgery. There is evidence that CD4 counts of fewer than 300 cells/cm^3 are associated with poorer surgical outcomes however this appears to be inconsistent [27–29]. Further, reduction of blood viral load <30,000 copies/ml by antiretroviral therapy (ART) may improve outcomes [30]. ART should also be optimised prior to surgery.

Spinal Injury

Spinal injury patients present a number of challenges for surgeons planning a surgical procedure such as artificial sphincter insertion, sacral neuromodulation or penile prosthesis. A thorough history of the injury level and functional status should be sought, especially where a degree of manual dexterity is required. Care should be taken in those patients with injuries above T5/6 as these patients can develop profound hypertension and in severe cases can lead to death as a consequence of autonomic dysreflexia.

In patients with both complete and partial spinal cord injuries, there is a higher incidence of urinary tract infections as a consequence of altered urinary tract function [31]. Consequently patients should be assessed for the presence of UTI and consideration should be made to prophylactic antibiotics prior to surgery.

In the case of penile prostheses the main concerns are infection and erosion. Both Wilson and Dietzen demonstrated that patients with spinal injuries are at an increased risk of developing infections. In Wilsons retrospective review of 823 primary penile implants, he found that those with spinal cord injuries as their primary aetiology for erectile dysfunction had a 9 % chance of developing an infection compared with 3 % of all primary implants for all causes ($p = 0.037$) [32]. Dietzen retrospectively looked at 30 men with spinal cord injuries that underwent penile implantation with 9 (30 %) becoming infected [33].

The rate of erosion of implants in spinal cord patients is also higher, probably as a consequence of altered sensation in the penile and perineal area [34]. The rate of erosion is higher in semi-rigid implants compared to that of inflatable implants in this group of patients [35].

Artificial urinary sphincters, like penile implants, also demonstrate a higher complication and revision rate as well as reduced continence rates compared to those patients without a spinal injury. Murphy et al. [36] compared a total of 30 incontinent patients with and without a neurogenic aetiology implanted with an AMS 800 artificial urinary sphincter. His group found only 15 % of patients with a neurogenic aetiology remained with the implant without any revisions compared with 41 % in the non-neurogenic group (p = <0.05). Furthermore, the continence rates of those in the neurogenic group were lower than those in the non-neurogenic group (23 % vs 64 %, p = <0.05) [36]. The rate of non-mechanical failure was statistically higher in the neurogenic group with cuff erosion being the most common issue (92 % vs 41 % p = <0.05).

In another study with a 10-year follow-up, continence rates in a group composed predominantly of neuropaths was 75 %. However this was countered by the fact that 79 % of patients required at least one revision procedure [37].

The pattern of increased complications and revision rates versus reasonable short term and long-term continence is seen in a number of studies although modifications in technique continue to improve long term outcomes [38].

Patients with spinal injury or a neurogenic aetiology should therefore be adequately counselled as well as having the necessary precautions taken to reduce complications particularly attributed to their underlying medical condition.

Medications

Anticoagulants

Many patients are now taking anticoagulants for a range of cardiac conditions and whereas, until recently, the choices were fairly limited to aspirin, clopidogrel and warfarin, the introduction of novel anticoagulants (NOACs) for atrial fibrillation has led to a plethora of new brands (Table 4.3). The NOACs have been licensed for stroke prevention in patients with atrial fibrillation by the European Medicines Agency and approved by the National Institute for Health and Care Excellence in the United Kingdom. The attraction of the NOACs is that they do not require the expensive monitoring and service costs that are required with warfarin.

Clearly anticoagulants should be stopped prior to surgery. The pharmacokinetics of each agent will dictate the length of time that the medication needs to be withheld before its effect is no longer present. Most hospitals will have guidelines on the advised length of time. Depending on the

Table 4.3 Anticoagulants

	Warfarin	Dabigatran (Pradaxa®)	Rivaroxaban (Xarelto®)	Apixaban (Eliquis®)
Coagulation factor target	Vitamin K dependent factors II, VII, IX and X	Direct factor IIa (thrombin) inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Dose	Variable	110 or 150 mg	10–20 mg	5 mg
Half-life	~40 h	11–17 h	9–15 h	9–14 h
Renal excretion	–	80 %	33 %	25 %
Specific coagulation tests	INR	Dilute thrombin time (Hemoclot®)	Anti-Xa assay	Anti-Xa assay
Antidote	Vitamin K Prothrombin Complex Concentrate (Octaplex®)	None	None	None

indications for the anticoagulation, bridging therapy may need to be instigated. However, each individual hospital will have its own policy on this and it is therefore beyond the scope of this text.

Patients Treated with Steroids

Steroids are used in medicine in a wide variety of disciplines. First used by Hench in 1949, they suppress inflammation, oedema and the immune system. The effect of long-term steroid use can result in suppression of the hypothalamo-pituitary adrenal axis (HPA) resulting in a reduction of cortisol and an Addisonian state. In cases of stress, such as surgery, the failure to release corticosteroids can result in profound refractory hypotension and shock. There is significant controversy regarding the management of patients on steroids. The need for supplemental exogenous steroids at the time of surgery is based on two case reports published in the 1950s concerning patients who were taking steroids and subsequently died after surgery [39, 40]. At autopsy their histology demonstrated complete adrenal cortical atrophy.

Many have taken the approach that patients should be given a supplemental steroid as advocated by Kehlet's physiological approach which is based on the magnitude of surgical stress i.e. minor or major surgery [41]. This was taken further by Symreng who pre-operatively tested patients' responses to corticotrophin stimulation and consequently only gave those with an impaired response an additional low dose hydrocortisone therapy to those with an impaired response [42]. His results suggested that patients receiving steroids might have had a preserved adrenal function and a comparable response to those not taking steroids. The definitive need for supplemental steroid cover in surgery has been questioned by many through evidence mounted in both animal models and clinical studies [43–45]. However, most would take a risk reduction approach to adhere to the principles outlined above and in Table 4.4 [46].

There is evidence that suggests that the use of steroids can result in (1) impairment of wound healing, (2) increased risk of infection, respiratory, renal, cardiac events and (3) mortality especially for those on steroids long term [47, 48].

Lifestyle Choices

Smoking

Patients who smoke have a higher risk of poorer surgical outcomes including post-operative infection and impaired wound healing. Furthermore patients are at a higher risk of lung and heart complications, being admitted to intensive care, mortality, readmission and increased hospital stay. The minimum abstinence period for smokers is difficult to define although most would advocate 2 months. For those unable to stop smoking they should at least refrain on the day of surgery [49]. Patients should be given the support to help them quit smoking.

Table 4.4 A suggested regimen for the management of patients on steroids [46]

Patients on steroids	<10 mg/day	Assume normal HPA response	Not required
	>10 mg/day	Minor	25 mg hydrocortisone at induction
		Moderate	25 mg hydrocortisone at induction + 100 mg/day for 24 h
		Major	25 mg hydrocortisone at induction + 100 mg/day for 48–72 h
		High dose immunosuppression	Give usual doses
Patients stopped taking steroids	<3 months	Treat as if on steroids	
	>3 months	No perioperative steroids necessary	

Procedure-Specific Considerations

Urinary Catheters

Selection

It is estimated that between 15 and 25 % of patients are catheterised during an inpatient hospital stay [50–54]. Catheter Associated Urinary Tract Infections (CAUTI) are covered in Chap. 3 ("Infection and Biofilms") and are the most common healthcare-associated infection (19 %) with between 43 and 56 % of UTIs associated with a urinary catheter. The use of urinary catheters should therefore only really be considered once alternative options have been fully assessed. Once inserted, the need for the catheter should then be reviewed at regular intervals.

Sacral Neuromodulation

Selection

Both the European Association of Urology (EAU) and the American Urological Association (AUA) recommend that sacral neuromodulation (SNM) is reserved primarily for those patients that have failed or could not tolerate conservative management options with the following conditions:

- Overactive bladder
- Non-obstructive urinary retention
- (Chronic faecal incontinence- which will not be covered in this chapter)

Sacral Neuromodulation is not appropriate for patients who:

- Have not demonstrated an appropriate response to the evaluation (screening test)
- Have predominant stress incontinence
- Are unable to operate the neuromodulation system
- Are not appropriate candidates for surgery
- Have experienced urinary retention due to mechanical obstructions such as benign prostatic hypertrophy, cancer, or urethral stricture disease.

Safety and effectiveness of the InterStim System have not yet been established for:

- Bilateral stimulation
- Pregnancy, unborn fetus, and delivery
- Pediatric use under the age of 16
- Or for patients with neurological disease origins such as multiple sclerosis or diabetes.

Assessment

History and Examination

Patients that are being considered for sacral neuromodulation should be reviewed prior to implantation and the indication for the procedure defined along with the general considerations outlined above.

A thorough history to ascertain the type of urinary incontinence should be sought including an evaluation of the impact of the symptoms on the patient's quality of life, their desire for treatment, and previous treatments that have been trialled. In cases of urinary retention details of precipitating factors and symptoms suggestive of a structural (e.g. peri-urethral mass) or neurological aetiology should be excluded.

A thorough past medical history should also be sought. In particular, a history of prior chronic back or neurological issues that may require serial MRI scans of the spine in the future should be identified as this would preclude them from SNM. An MRI of the head is possible but only with certain models under specific conditions and advice should be sought directly from the manufacturer in this regard.

It is important to consider that the procedure is usually performed prone and consequently the patient should ideally be assessed for neck, respiratory and cardiovascular issues as well as their weight. Furthermore, patients with an extremely low BMI should be informed that the device may be palpable and uncomfortable.

Patients whose lifestyle/occupation requires regular travel should be identified and counselled appropriately as the device can be affected by pulse induction metal detectors. These can cause the device to turn on and off (although it will not

change the settings). Consequently patients should be advised to turn the device off prior to passing through the detector. Such patients should also be advised to take their Interstim identification card with them.

Investigations

Urinalysis

A urinalysis should be performed to identify any underlying urinary tract infection that could be responsible for the patient's symptoms and to exclude infection prior to insertion of the device. In women of child-bearing age a negative pregnancy test should also be confirmed as the implantation procedure requires the use of ionising radiation and furthermore the safety of this device during pregnancy is unknown.

Validated Questionnaires

The use of a validated questionnaire is recommended in the EAU, AUA guidelines and NICE guidance, as part of the initial assessment of patients with overactive bladder and it should be used prior to implantation of SNM. A variety of questionnaires exist although none of the guidelines go so far as to recommend one over the other. It is important to be aware that different questionnaires examine different populations and aspects of voiding dysfunction.

Voiding Diary

Three different types of voiding diaries have been identified [55, 56]:

- **micturition time charts** which simply record the times of micturition (but not volumes) over a 24 h period.
- **frequency volume charts** which record volumes and time of voiding.
- **bladder diaries** which are more detailed and document other variables including, volume intake, pad usage, incontinence episodes.

The EAU, AUA and NICE guidelines recommend the use of a Bladder Diary. Patients should aim to complete between 3 and 7 days of the diary.

The bladder diary is especially important in patients undergoing SNM as it allows objective assessment of response and ultimately is one of the arbiters to second stage/permanent placement of the SNM- if patients have a ≥50 % improvement in symptoms based on their voiding diary following the test phase they are considered suitable for implantation of the permanent device.

Pad Testing

See section "Artificial Urinary Sphincter and Male Urethral Slings" later in this chapter.

Urodynamics

Although evidence is lacking to support the use of urodynamics in predicting those patients that will respond well to sacral neuromodulation, many would consider it mandatory. It can confirm the presence of detrusor overactivity and help elucidate the cause of obstruction in those patients undergoing SNM for urinary retention (Fig. 4.1). In those patients with suspected Fowler's syndrome, cystometry generally demonstrates a prolonged filling phase with reduced sensations of filling; there is typically only limited detrusor pressure increase during the voiding phase. Furthermore, sphincteric tone can be assessed with urethral pressure profilometry to measure the maximum urethral closure pressure (MUCP) (Fig. 4.2). A high MUCP is suggestive of a functional sphincteric obstruction and these patients may benefit from SNM for their voiding dysfunction.

The AUA, EAU and National Institute of Health and Care Excellence (NICE) all recommend the use of urodynamics in patients with overactive bladder symptoms prior to invasive therapy.

Sphincter Electromyography (EMG)

In cases of neurogenic bladder dysfunction, detrusor-sphincter dyssynergia or Fowler syndrome, sphincter EMG may be considered for evaluation of inappropriate pelvic floor muscle behaviour with the classic finding of decelerating bursts and complex repetitive discharges suggestive of a failure of relaxation of the urethral sphincter. However this is a highly specialised test, is invasive, and in most centres the MUCP

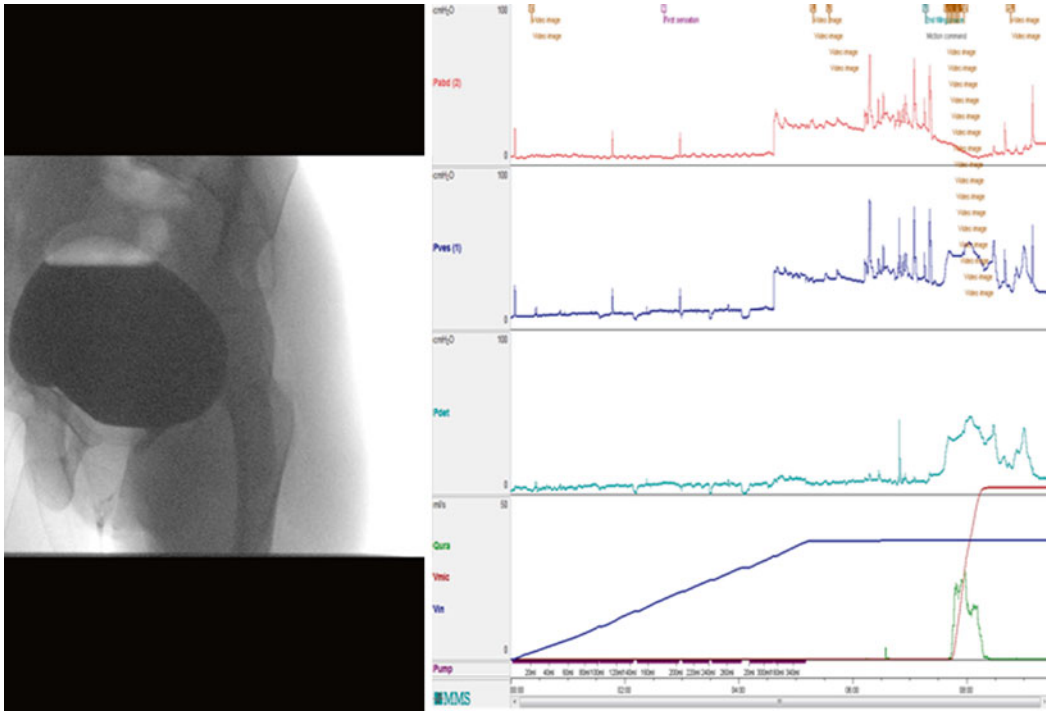

Fig. 4.1 Video urodynamics showing bladder outflow obstruction at the level of the mid-urethra suggestive of functional sphincteric obstruction that may be treated with SNM

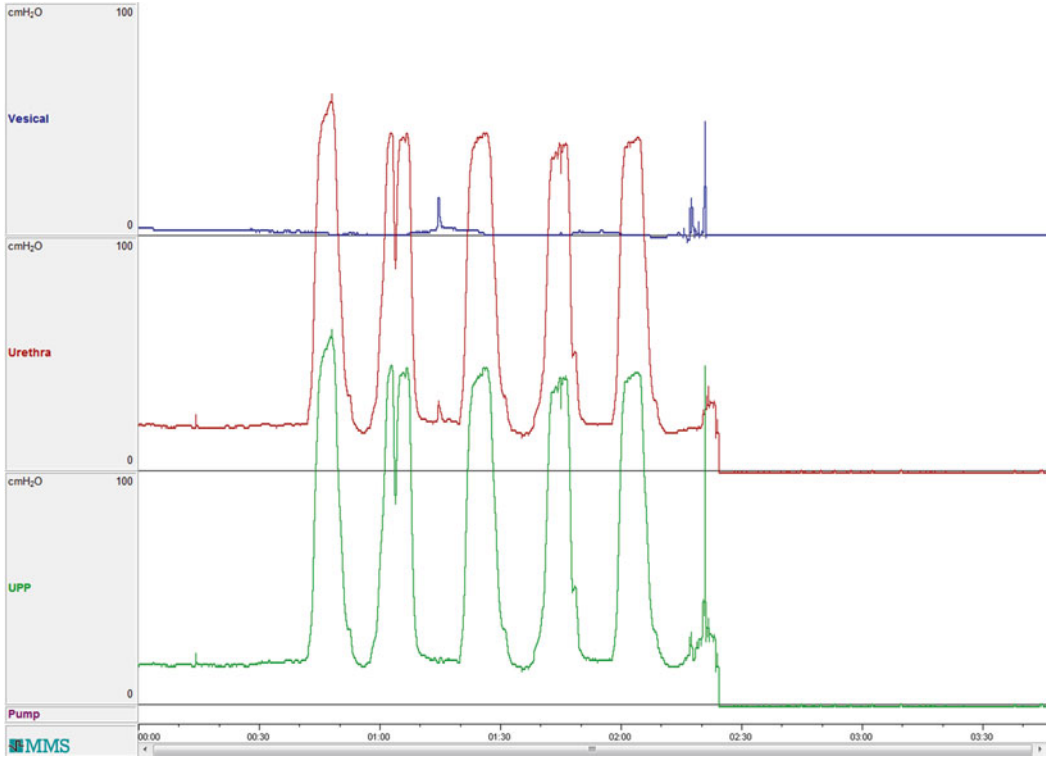

Fig. 4.2 Urethral pressure profilometry of the same patient trace showing elevated MUCP confirming high-tone non-relaxing sphincter as cause of bladder outflow obstruction

alone is used to diagnose a functional sphincteric obstruction [57].

Artificial Urinary Sphincter and Male Urethral Slings

Selection

The most commonly implanted artificial urinary sphincter (AUS) worldwide is the AMS 800, which has undergone a number of improvements since its original description over 40 years ago. The indication for implantation is stress urinary incontinence due to reduced outlet resistance (intrinsic sphincter deficiency) in post prostatectomy patients, or for intrinsic sphincter deficiency stress incontinence in women who have failed all other therapies.

Contraindications include:

- Patients deemed to be poor candidates for surgical procedures and/or anaesthesia due to physical or mental conditions.
- Patients with urinary incontinence due to or complicated by an irreversibly obstructed lower urinary tract.
- Patients with irresolvable detrusor overactivity or bladder instability.
- The implantation of the InhibiZone version of this device is contraindicated in patients with a known allergy or sensitivity to Rifampicin, Minocycline or other tetracyclines.
- The implantation of products with InhibiZone is contraindicated in patients with systemic lupus erythematosus because Minocycline has been reported to aggravate this condition

The male sling procedure is indicated in those patients suffering from male stress urinary incontinence that have failed conservative management.

Contraindications include:

1. Severe incontinence, which is unlikely to be resolved with a sling procedure (although this is currently being investigated in the MASTERS trial, a multi-institutional randomised-controlled trial in the UK).
2. Bladder dysfunction that can jeopardize renal function, such as loss of compliance and vesicoureteric reflux at low bladder pressures.
3. Inadequate tissue integrity of the bladder neck or urethra.
4. Active urinary tract infection.

Relative contraindications include:

1. Previous history of radiotherapy
2. Perceived need for future instrumentation of the urethra e.g. patients with bladder cancer or with refractory urethral strictures, as repeated instrumentation may increase the risk of erosion or infection.

Assessment

History and Examination

The history should aim to expand upon the type of urinary incontinence, the precipitating events and the degree and severity of the condition. The differentiation between stress and urge urinary incontinence is essential to ensure correct identification of surgical candidates as well as appropriate counselling. The effect on their quality of life should also be assessed. Physical examination should be conducted of the abdomen and genitalia as well as a thorough neuro-urological examination including perineal sensation, anal tone, voluntary contraction, relaxation of the anal sphincter and elucidation of the bulbocavernosous reflex. Patients being considered for an AUS should be shown the device and should have adequate manual dexterity in order to operate the control pump successfully.

Investigations

Urinalysis and Mid Stream Urine (MSU)

A urinalysis should be performed to exclude a urinary tract infection prior to insertion of these prosthetic devices. In those patients with

demonstrable non-visible haematuria, further investigation should be arranged as appropriate prior to proceeding with either a male sling or AUS.

Post Void Residual

The post void residual volume should be measured using either ultrasound or by catheterisation. Serial measurements should be taken, as there can be considerable variations in the volume. Persistently high residual volumes imply a weak detrusor relative to outflow obstruction and are a good estimation of voiding efficiency. What constitutes a raised PVR is unclear, however volumes >50 ml are likely to be significant and >200–300 ml are likely to have poorer outcomes from bladder outflow surgery.

Questionnaires

The ICIQ-Sf has been used in RCTs on post prostatectomy incontinence in males and is recommended by the ICS for the assessment of incontinence in men.

Voiding Diary

(See under section "Sacral Neuromodulation") A Voiding Diary can help to quantify as well as help differentiate between stress and urge urinary incontinence, and can provide information on functional bladder capacity and daytime and night-time frequency.

Pad Testing

Pad testing can be used to identify and quantify the severity of the incontinence both pre and post operatively. A number of pad tests have been described including but not limited to 20 min, 1, 24 and 48 h pad tests. The ICS currently recommend the use of a 24 h pad test, as it is the most reproducible. However, the ICS also concede that the 1-h pad test is more easily performed and standardised despite the tendency to underestimate sphincter weakness towards the end of the day. Although the capability of pad testing to predict outcome is poor, it is sensitive to intervention and therefore is a good tool to assess response to treatment.

Cystourethroscopy

Flexible or rigid cystourethroscopy are useful adjuncts in the assessment of male incontinence. They allow assessment of any urethral sphincteric defect as well as visual confirmation of its contraction in those patients that are awake i.e. flexible cystoscopy. The bladder can also be assessed at the same time for evidence of bladder neck stenosis, diverticulae, trabeculation and other pathology that may contribute to incontinence or affect the decision to perform surgery.

Urodynamics

Although not mandatory, urodynamics is used in men with incontinence that have failed conservative management. There are currently no RCTs examining the usefulness of urodynamics in the management of post-prostatectomy patients [58, 59]. Its ability to discriminate between those patients that may do well or poorly is uncertain although it can help identify patients with detrusor overactivity that may be contributing to or may be the primary cause of the incontinence. Detrusor overactivity may be present in up to 50 % of patients with incontinence following prostatectomy.

The abdominal leak point pressure (defined by the ICS [55] as the intravesical pressure at which urine leakage occurs due to increased abdominal pressure in the absence of a detrusor contraction), acts as an indication of the competence of the bladder neck and urethral sphincter mechanism to resist increases in intra-abdominal pressure. The ALPP can be measured either by asking the patient to cough (CLPP) or perform a Valsalva (VLPP) to increase the intra-abdominal pressure. The CLPP is thought to be more accurate although the rapid nature of the test sometimes makes identification more difficult.

An ALPP <60 cmH_2O as well as symptoms of stress incontinence correlates with sphincter incompetence although it is diagnostic.

Bladder compliance can also be assessed. Patients with reduced compliance as previously stated are contraindicated to receive

male slings. Compliance can be an issue in patients following prostatectomy especially if accompanied with pelvic radiotherapy. In one study of 19 patients' post radical prostatectomy (prior to artificial sphincter placement) 17.5 % were found to have reduced compliance [60]. However the presence of low compliance does not necessarily indicate a poor outcome following surgery in post prostatectomy patients [58].

The presence of bladder outflow obstruction or detrusor underactivity can also be assessed during the voiding phase and a formal assessment made using the ICS nomogram, Abrams-Griffiths number or Bladder Outlet Obstruction Number (BOOI). $BOOI = P_{det}@Q_{max} - 2Q_{max}$. Using this nomogram, men can be divided into obstructed, equivocal, and unobstructed according to their BOOI: BOOI >40 = obstructed; BOOI 20–40 = equivocal; and BOOI <20 = unobstructed [61].

The use of video urodynamics can help identify reflux as well as demonstrating sphincter incompetence and urinary incontinence.

Penile Prostheses

Selection

Penile prostheses are often employed in patients who have exhausted all other medical therapies to resolve their erectile dysfunction. Indications for the placement of a penile prosthesis include:

- Refractory erectile dysfunction
- Failure to tolerate and/or dissatisfaction with alternative therapies
- Refractory ischaemic priapism
- Peyronie's disease with concurrent erectile dysfunction
- Patients with a buried penis or problems using a condom sheath for incontinence

Care should be taken in those patients with neurological deficits/spinal cord injury or diabetes due to the increased risk of infection.

Assessment

History and Examination

Prior to the insertion of a penile prosthesis, the patient should undergo a thorough medical and sexual history to identify the potential underlying pathophysiology, risk factors, complicating comorbidities (including diabetes) spinal cord injury and functional status.

In patients with Peyronie's disease the clinician should take steps to reassure themselves that the disease is stable.

The clinician should be confident that the patient has the dexterity and cognitive ability to operate the device once implanted. The patient should also have been screened for cardiovascular risk factors.

An examination should identify any genitourinary, endocrine, vascular and neurological signs that might contribute to the patient's erectile dysfunction.

In the case of Peyronie's disease, the plaque should be identified and its location and size documented. The degree of angulation should be recorded if present either by the use of good quality digital photographs with consent or with a goniometer (in clinic) once an artificially induced erection has been achieved using intracavernosal prostaglandin. Any local skin infections should be noted and treated prior to surgery in order to reduce the risk of post operative implant infection.

In all cases, an appropriate questionnaire should be completed prior to surgery – this documents pre-existing dysfunction using the IIEF or Peyronies Disease Questionnaire (PDQ).

Investigations

Urinalysis and Mid Stream Urine (MSU)

Prior to surgery the patient must have a urine sample taken to ensure that the urine is sterile.

Questionnaires

A number of questionnaires exist for erectile dysfunction. However, the more commonly used are the International Index of Erectile Function

(IIEF) as well as the shorter IIEF-5 otherwise known as the Sexual Health Inventory for Men (SHIM). Both have been extensively validated. The IIEF is constructed from 15 questions that are split into five domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. The SHIM uses 4 of the 6 questions from the erectile function domain of the IIEF as well as an overall intercourse satisfaction domain. These questions were selected as they were found to be the most reliable for discriminating between men with and without erectile dysfunction. Patients are classified into five groups dependent on severity: Severe erectile dysfunction (5–7), moderate erectile dysfunction (8–11), Mild to moderate erectile dysfunction (12–16), mild erectile dysfunction (17–21), and no erectile dysfunction (22–25).

For patients with Peyronies Disease, the Peyronies Disease Questionnaire (PDQ) has been developed on the back of pharmaceutical trials to look at the effectiveness of collagenase in Peyronies disease. It consists of three domains: (1) Psychological and physical subscale (six items), (2) Symptom bother scale (six items) and (3) Penile pain subscale (three items).

The questionnaires are primarily used to document the presence and severity of disease as well as provide an objective measure of response.

Conclusions

Correct patient selection and careful general as well as procedure-specific work-up, will ensure that patients undergo the most appropriate operation for their condition and limit their complications.

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Patient Consent for Surgery

5

Howard P. Marsh

Abstract

In the United Kingdom consent is described by the Department of Health as a principle that is an important part of medical ethics and international human rights law. All surgeons should be able to obtain valid informed consent for the procedures that they intend to perform. Legally, the process of obtaining consent for the treatment of the competent adult is governed by common law i.e. by case law, rather than by statute. There is a common law duty of care for the surgeon to inform the patient of what a specific procedure entails and the risks involved.

Keywords

Consent • General Medical Council • Royal College of Surgeons

In the United Kingdom consent is described by the Department of Health as a principle that is an important part of medical ethics and international human rights law [1].

All surgeons should be able to obtain valid informed consent for the procedures that they intend to perform. Legally, the process of obtaining consent for the treatment of the competent adult is governed by common law i.e. by case law, rather than by statute. There is a common law duty of care for the surgeon to inform the patient of what a specific procedure entails and the risks involved.

Professionally, guidance is supplied by the Department of Health, the General Medical Council (GMC), and The Royal College of Surgeons (RCS).

The GMC guidance outlines the duty of a doctor in 'Good Medical Practice' [2], and makes clear that "You are personally responsible for your professional practice and must always be prepared to justify your decisions and actions".

In Good Medical Practice (2013), the GMC also states "you must keep up to date with, and follow, the law, our guidance and other regulations relevant to your work." In addition, it states that "You must be satisfied that you have consent or other valid authority before you carry out any examination or investigation, provide treatment

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or involve patients or volunteers in teaching or research".

Further guidance from the GMC is provided in 'Consent: patients and doctors making decisions together' [3], which states that serious or persistent failure to follow the guidance will put a doctor's registration at risk. The Royal College of Surgeons expands on the guidance of the GMC in 'Good Surgical Practice' (2013) [4].

What Constitutes Valid Consent

In order for consent to be valid, there are three main elements-it must be voluntary and informed, and the person consenting must have the capacity to make the decision [1].

The Consent Must Be Given Voluntarily

The decision either to consent or not to consent to treatment must be made by the person himself or herself, and must not be influenced by pressure from medical staff, friends or family.

The Patient Must Have Capacity

The person must be capable of giving consent, which means that they understand the information given to them, and they can use it to make an informed decision. They must therefore have the ability to comprehend and retain information. It is important to be aware that capacity may fluctuate and to take this into account during the consent process.

It is necessary to ensure that the patient has capacity to give consent as described in the Mental Capacity Act (2005), and to take practical and appropriate steps to help patients make the decision themselves.

Where a patient lacks capacity, Good Surgical Practice advises acting in the patient's best interests and where relevant seeking consent from a person with a lasting power of attorney to give consent on the patient's behalf. Otherwise no adult may give consent for another, including relatives.

Where intervention is required in a patient's best interest without consent, then it is advisable to get agreement with a consultant colleague and to discuss with the patient's next of kin.

If an adult has the capacity to make a voluntary and informed decision to consent to or refuse a particular treatment, their decision must be respected. This still stands even if refusing treatment would result in their death, or the death of their unborn child [1].

For children and young people, the GMC provides guidance for 0–18 years: guidance for all doctors [5]. Young people are presumed to have capacity to give consent at 16 years of age. Below 16 years, the doctor must make an assessment of the child's capacity to give consent. Children and young people should be involved in discussions and decisions around their care as much as possible, even if they are not able to make decisions on their own [3].

The Patient Must Have Received Enough Information

Surgeons have an overriding duty to ensure that patients are given enough information about the treatment proposed, the alternative options and the main risks, side effects and complications *at the time that the decision to operate is made*.

This means that consent is a process, and *starts* when the decision is made. It does not start in the pre-admission clinic the week before surgery, or on the day of surgery [6].

Good Surgical Practice advises that surgeons should "Recognise that seeking consent for surgical intervention is not merely the signing of a form. It is the process of providing the information that enables the patient to make a decision to undergo a specific treatment. Consent should be considered informed decision-making, or informed request. It requires time, patience and clarity of explanation."

A signature on a consent form alone, is *not* proof that consent has been obtained, as Justice

Bristow emphasised in *Chatterton v Gerson* [1981] [7]:

> …getting the patient to sign a proforma expressing consent to undergo the operation 'the effect and nature of which has been explained to me'…. should be a valuable reminder of the need for explanation and consent. But it would be no defence to an action….if no explanation had in fact been given. The consent would have been expressed in form only, not in reality.

Obtaining consent avoids an action in trespass against the person [7]:

> Once the patient is informed in broad terms of the nature of the procedure which is intended…the consent is real, and the cause of the action on which to base a claim for failure to go into risks and implications is negligence, not trespass

However, consent can be real, but still invalid, if not enough information has been given. Traditionally this was determined by applying the *Bolam* test. Mr Bolam suffered severe fractures during electroconvulsive therapy for depression, a risk known to his doctor, but not communicated to Mr Bolam. He alleged that the failure to warn was negligent. Justice McNair found that the amount of information given to Mr Bolam accorded with accepted medical practice at the time [8]:

> …in the case of a medical man negligence means failure to act in accordance with the standards of reasonably competent medical men at the time….. there may be one or more perfectly proper standards; and if a medical man conforms with one of those proper standards then he is not negligent.

Actions based on one opinion do not equate to negligence if those actions can be shown to be reasonable as judged against the standards of the doctor's peers.

Elsewhere in the world however, the emphasis has been on what a reasonable patient can expect rather than what a reasonable doctor might do.

In *Canterbury v. Spence* [1972] [9] the US Appeal Court described the failure to warn of the risk of paralysis following spinal surgery as: "a prima facie case of violation of the physician's duty to disclose."

The case became known as the 'reasonable patient test' and enshrined in US law the patient's right to know, obliging doctors to disclose to their patients any material risk inherent in a proposed treatment, a material risk being one that a reasonable person would attach significance to [6].

In *Reibl v Hughes* [1980] (Mr Reibl suffered a massive stroke after carotid artery surgery, but was not warned of this possible risk), the Canadian Supreme Court held that [10]:

> What is under consideration here is the patient's right to know what risks are involved in undergoing or forgoing certain surgery or other treatment…Respect for the patient's right of self-determination on particular therapy demands a standard set by law…The duty to disclose or inform cannot be summarily limited to a self-created custom of the profession.

In *Rogers v. Whittaker* [1992] [11], Dr Whittaker, an ophthalmic surgeon was judged to be negligent in failing to warn Mrs Rogers that there was a chance that surgery to her right eye could lead to a risk of loss of sight in her left eye (through the process of sympathetic ophthalmia). Despite evidence from a body of reputable medical practitioners that they too would not have warned of the danger, the High Court of Australia emphasized that *the court, and not the medical profession*, set the standard of care (and not just in respect of disclosure):

> There is no need to consider the practices of medical practitioners in deciding how much information should be given to a particular patient.

In English law the first real move away from Bolam came with Sidaway [1985]. Mrs. Sidaway, who was paralysed following surgery to her spine, alleged that her surgeon had failed to warn her of this possibility. In the House of Lords, Lord Scarman stated that disclosure was necessary [12]:

> …where the risk is such that in the court's view a prudent person in the patient's situation would have regarded it as significant.

In *Pearce* [1999], Lord Woolf stated [13]:

> If there is a significant risk which would affect the judgment of the reasonable patient…it is the responsibility of a doctor to inform the patient of that significant risk, if the information is needed so that the patient can determine for him or herself as to what course he or she should adopt.

Chester v Afshar [14] was a particularly significant case in which Miss Chester consented to spinal surgery but post operatively suffered paralysis. The surgeon had not warned the patient beforehand of this risk. Lord Steyn found that "the surgeon had not been negligent in performing the operation: he did not increase the risks inherent in surgery. On the other hand, if the claimant had been warned she would not have agreed to the operation".

He went on to state that:

> ….In modern law medical paternalism no longer rules and a patient has a prima facie right to be informed by a surgeon of a small, but well established, risk of serious injury as a result of surgery..….Surgery performed without the informed consent of the patient is unlawful. The court is the final arbiter of what constitutes informed consent.

It is essential, therefore, that surgeons are mindful of this conclusion when determining for themselves whether or not a patient has received enough information to constitute informed consent.

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Theatre Preparation and Equipment

6

Asif Muneer

Abstract

The operating theatre environment should be comfortable for the theatre personnel to work in, yet minimize the risk of bacterial contamination during prosthetic surgery. This chapter will provide an overview of the key considerations required to minimize post operative complications related to prosthetic surgery.

Keywords

Operating theatre • Bacterial contamination • Prosthetic surgery

The Operating Theatre

When performing prosthetic surgery it is of paramount importance that the operating theatre provides a safe and user-friendly environment which minimizes bacterial contamination which in turn reduces the risk of prosthesis infection. Steps should be taken in order to reduce the theatre traffic and notices are placed on the theatre entry doors to indicate that a prosthetic operation is being performed as it has been demonstrated that the bacteria count in theatre is directly related to the number of personnel in theatre and the movement of people in theatre. Ideally the theatre suite should also incorporate the theatre sterile supply unit. A theatre user committee within the hospital which consists of surgeons, anaesthetists, microbiologists as well as theatre managers should meet regularly and discuss improvements in the theatre design and ensure that infection rates are regularly audited.

Minimising Contamination

Post operative prosthesis infection is a disastrous and unwanted complication and therefore all possible measures to minimize this risk should be implemented. The theatre suite should incorporate the concept of zones such that around the operating table there is an aseptic zone.

An example of this zonal concept includes:

1. An outer zone – this can be a patient waiting or reception area near to the operating suite
2. A clean zone – this is the area connecting the reception area to the theatre suite

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3. Aseptic zone – the operating theatre itself
4. A dirty zone – area for disposal of used equipment and a corridor to allow transfer of this equipment for cleaning and resterilising.

Theatre Environment and Staff Behavior

Laminar Air Flow

Directional or laminar air flow can be either vertical or horizontal. This increased rate of air exchange reduces the number of contaminated particles around the patient and uses air which is pumped into the room through filters and passed out through vents. The number of air changes is variable with most theatres using 20–40 air changes per hour which can increase to over 400 if a vertical system is being used. The prefiltered air delivered to the theatre is free of pathogens such as *Staphylococcus aureus* and therefore the airborne bacteria in theatre is mainly derived from the personnel within the operating theatre.

Theatre Clothing, Gowns and Masks

Cotton theater wear does very little to prevent the passage of bacteria through clothing as the diameter of the holes in the cloth itself is approximately 80 μm. Therefore additional theatre gowns must be worn when performing surgical procedures. Ideally disposable reinforced theatre gowns should be used in order to reduce the dispersal of bacteria laden particles emanating from the body. Breathable membrane fabrics such as Goretex consisting of fabric in which a layer of polytetrafluoroethylene (PTFE) is laminated are also available.

Although there is debate regarding the necessity for masks when performing abdominal surgery, masks are still recommended for all the theatre personnel if a prosthesis is being inserted with a fresh mask required for each case. Masks should stop small droplets from air passages contaminating the front of the theatre gown, gloves and ultimately the wound itself. If there is an unexpected number of infections following prosthesis surgery particularly if associated with MRSA, theatre personnel and surgeons should also undergo nasal swabs and treatment if they are found to be persistent carriers.

Operating Tents

Although these are commonly used for orthopaedic prosthetic surgery, the use in urology is currently very limited. However, when combined with body exhaust suits this may allow infection rates to reduce even further.

Theatre Temperature and Humidity

The theatre temperature should be kept to a comfortable level with minimal variation. The temperature within the operating theatre needs to be increased for elderly patients and also for procedures which are likely to be prolonged. Patients can become hypothermic if the temperature is below 21 °C and most staff prefer a comfortable working temperature of 22–23 °C. Patients can be kept warm by using warming blankets or a Bair Hugger®.

Operating Table

The operating table should be heavy and steady yet easy to maneuver. Adjustability for different surgical procedures is also required and most operating suites utilize a hand held control to adjust the table. The surface should be made of padding which adjusts to the contours of the patient and it is essential to ensure that the patient is not in contact with any of the metallic structures of the table in order to prevent inadvertent diathermy burns. The lower end of the table should have the facility to be removed to allow leg supports to be fitted if patients are to be placed in the lithotomy position as well as allowing a radiolucent section to be added if additional fluoroscopy or X-Ray is required intraoperatively such as for stent insertion or sacral

neuromodulation procedures. Precautions should be taken to protect the ulnar nerve at the elbow and the lateral popliteal nerve in the lower limb which are commonly at risk due to compression after positioning the patient.

Using X-Ray Equipment in Theatre

Medical staff who are directing X-Rays should have a certificate to confirm that they have received basic training in radiation protection. The X-Ray equipment is normally mobile and comprises a mobile image intensifier mounted on a 'C' arm. All theatre personnel should be protected with lead aprons and the screening time should be recorded. As the patient also 'scatters' the X-ray beam, staff should remain as far as possible from the patient. In prosthetic surgery, ureteric stents comprise the largest group of patients requiring X ray screening although occasionally screening is required for missing needles and instruments from the instrument tray.

Diathermy Safety

The principles and safety of diathermy is ubiquitous to all surgical disciplines and the surgeons should familiarize themselves with the diathermy settings for their machine (Fig. 6.1). Surgeons should remember that the responsibility for diathermy lies with them and although they rarely attach the diathermy plate or set the diathermy settings, all surgeons should ensure that these are checked before starting the surgical case. Since the majority of prosthetic procedures require a thorough iodine or chlorhexidine based scrub prior to surgery followed in some cases by an alcohol based preparation, diathermy burns may occur if the alcohol has not been allowed to evaporate completely and the skin allowed to dry. Any spirit being used should be dabbed on with a swab as opposed to being splashed onto the skin. There is also a tendency to use the cutting diathermy to incise the skin. Our recommendation is to avoid this and the initial skin incisions performed using a scalpel to prevent damage to the skin surface which may impair wound healing.

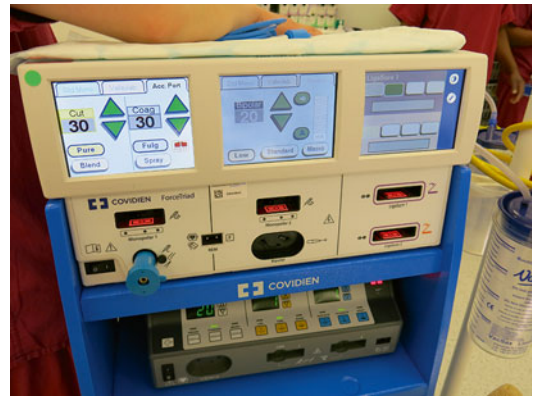

Fig. 6.1 Diathermy settings and familiarity with the diathermy machine is recommended to prevent intraoperative malfunction

Theatre Instruments

Before starting a case the surgeon should ensure that specialized instruments and the prostheses to be used are readily available (Fig. 6.2). This is particularly important for prostheses which require differing sizes and multiple components such as inflatable penile prostheses. Individual specialized instruments will be discussed within the relevant chapters.

Fig. 6.2 Theatre instruments for each individual case should be recorded on a preference card and checked before starting the procedure

Conclusions

Although the principles of theatre preparation before prosthetic surgery are straightforward, surgeons still need to be aware of the sources of infection within the theatre environment in order to ensure that post operative outcomes remain satisfactory.

Patient Preparation for Surgery

7

Ivor M. Cullen and Paul Hegarty

Abstract

There is a wealth of evidence to support best practice in terms of effective patient operative field preparation prior to prosthetic urological surgery. The main focus of these steps is to eradicate commensal bacteria and minimize the risk of surgical site and prosthetic infection, which is the prosthetic surgeon's worst fear. These techniques include a combination of skin scrubbing, preparation, depilation and management of the urethra prior to commencement of the prosthesis surgery.

Keywords

Pre-operative • Bathing • Scrub • Depilation • Skin preparation

Introduction

Surgical site infections (SSI) following prosthetic urological procedures remain a substantial economic burden to the patient, the treating institution, and the health care system.

Skin preparation is defined as the removal of as many bacteria as possible from the patient's skin through depilation, washing and chemical disinfection. The purpose of skin preparation is to reduce the number of microorganisms in the operative field and prevent infection.

Traditionally Staphylococcus epidermidis has been the primary organism responsible for genitourinary prosthetic infection. However, the increasing prevalence of Staphylococcus aureus infection poses a serious problem [1].

Similarly, the most common organism associated with penile implant infections is coagulase negative staphylococcus comprising 58 % in one large series [2]. Other bacteria less commonly seen were Pseudomonas aeruginosa, Serratia marcescens, enterococcus, Proteus mirabilis, and methicillin-resistant Staphylococcus aureus (MRSA). Fungal infections such as Candida albicans and anaerobic infections such as Bacteroides fragilis are rarely be seen in these circumstances.

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Pre-operative Bathing

Preoperative bathing or showering with an antiseptic skin wash product is a well-accepted procedure for reducing skin bacteria (microflora). It is less clear whether reducing skin microflora leads to a lower incidence of surgical site infection.

Webster and Osborne performed a Cochrane review meta-analysis of randomised controlled trials comparing any antiseptic preparation used for preoperative full-body bathing or showering with non-antiseptic preparations in patients undergoing surgery [3]. Seven trials involving a total of 10,157 participants were included. Four of the included trials had three comparison groups. The antiseptic used in all trials was 4 % chlorhexidine gluconate (Hibiscrub). Three trials involving 7791 participants compared chlorhexidine with a placebo. Bathing with chlorhexidine compared with placebo did not result in a statistically significant reduction in SSIs. Three trials of 1192 patients compared bathing with chlorhexidine with no washing, one large study found a statistically significant difference in favour of bathing with chlorhexidine (RR 0.36, 95 % CI 0.17–0.79). The authors concluded that their review provides no clear evidence of benefit for preoperative showering or bathing with chlorhexidine over other wash products, to reduce surgical site infection.

Although we do not ask our patients to perform dedicated chlorhexidine bathing prior to the surgery, we do request the patient to have a thorough bath/shower on the morning of surgery.

Depilation

The origin of the practice of shaving hair from operative sites is not clearly documented. However, Smith's account of surgical practice at Bellevue Hospital in the United States of America dates the practice as being late eighteenth century in origin: 'The patient was often put on the (operating) table unbathed and grimy with dirt, superfluous hair was sometimes shaved off' [4]. The surgeons of the time believed that wounds might heal more quickly if hair could be prevented from becoming entangled in the sutures and wound during closure. The preparation of people for surgery has traditionally included the routine removal of body hair from the intended surgical wound site. However, there are studies, which claim that pre-operative hair removal is deleterious to patients, perhaps contributing to SSIs, and should not be carried out [5].

Recently Tanner et al. conducted a meta-analysis of randomised controlled trials or quasi randomised trials that compared: (1) hair removal with no hair removal; (2) different methods of hair removal; (3) hair removal at different times before surgery; and, (4) hair removal in different settings (e.g. the ward, the anaesthetic room) [5].

Six trials, two of which had three comparison arms, (972 participants) compared hair removal (shaving, clipping, or depilatory cream) with no hair removal and found no statistically significant difference in SSI rates however the authors noted that the comparison was underpowered. Three trials (1343 participants) that compared shaving with clipping showed significantly more SSIs associated with shaving (RR 2.09, 95 % CI 1.15–3.80). Seven trials (1213 participants) found no significant difference in SSI rates when hair removal by shaving was compared with depilatory cream (RR 1.53, 95 % CI 0.73–3.21), however this comparison was also noted to be underpowered. One trial compared two groups that shaved or clipped hair on the day of surgery compared with the day before surgery and found no statistically significant difference in the number of SSIs between groups.

The authors concluded that hair removal has no statistically significant effect on SSI rates but highlight that insufficient numbers of people have been involved in this research to allow confidence in this conclusion.

When it is necessary to remove hair, the existing evidence suggests that clippers are associated with fewer SSIs than razors.

Many studies show that hair removal with a razor or clippers can cause skin abrasion, even nicks which can lead to the development of pseudofolliculitis and subsequent SSIs and thus it is imperative that the procedure is undertaken with care (Fig. 7.1) [6].

Depilatory creams have an advantage in areas that are difficult to be shaved. The use of depila-

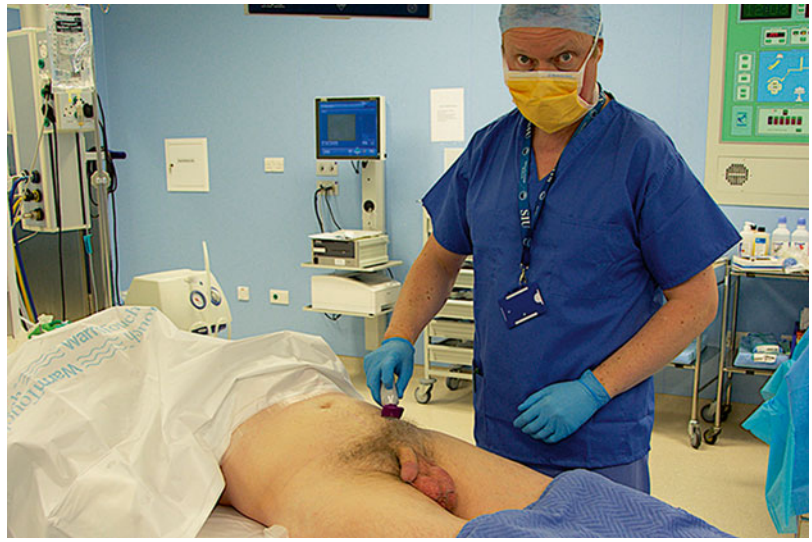

Fig. 7.1 Pre operative depilation with a hair clipper prior to penile prosthesis surgery. Skin abrasions should be avoided by careful use of the clippers particularly around the scrotum

tory cream produces clean, intact skin without the risk of developing lacerations or abrasions. It can, however, cause skin irritation or rash, especially in the groin area. If possible, long hair should be cut with a pair of scissors before applying the cream so that a reduced amount of cream is used. The chemical in the hair removal cream affects the chemistry of the individual hair strands. The active chemicals in the cream break down keratin, the principal protein, which normally requires a blade for depilation or any other harsh treatment. The effects of the cream vary, based on the strength, colour and coarseness of the hair being removed as well as the length of time the cream is left undisturbed on the hair to act. Most common complications with creams are rashes and erythema, which can also increase the risk of post-operative infection.

A small, discrete area in the same region of the body should be tested with the depilatory cream before a more wide-spread application is attempted. This helps determine how long the cream should be left in situ and also helps discern any negative skin reactions. The cream should be applied thickly and evenly over the area to be treated and should be left undisturbed for the recommended period of time. After the appropriate time has elapsed, a small portion of the cream should be removed to test the effectiveness of the treatment, and if the hair comes off easily, the remaining cream should then be removed. The hair removal cream should neither be applied over small abrasions, scratches or cuts nor on sunburned areas.

The timing of preoperative shaving has been shown to have an important effect on postoperative wound infection rates [7]. Removal of hair immediately before an operation results in lower infection rates than removal of hair the day before an operation. A possible explanation for this is that bacteria do not have as long to infect the traumatised dermis during a shorter preoperative period.

We therefore recommend that the surgical field be shaved after administering the anesthetic. This avoids any small nicks in the skin being colonized with bacteria.

We feel the presence of hair can interfere with the exposure of the incision and subsequent wound, the suturing of the incision and the application of adhesive drapes and successful wound dressing.

Skin Preparation

Preoperative skin antisepsis using antiseptics is performed to reduce the risk of surgical site infections by removing transient organisms from the skin where a surgical incision will be made. Antiseptics are thought to be toxic to bacteria and therefore aid their mechanical removal. The

effectiveness of preoperative skin preparation is thought to be dependent on both the antiseptic used and the method of application. Skin lesions such as comedones should be eliminated before the prep so that their contents are not expressed into the wound during penile and scrotal manipulation.

Aqueous-based iodophors, such as povidone-iodine, contain iodine complexed with a solubilizing agent, allowing for the release of free iodine when in a solution. Iodine acts in an antiseptic manner by destroying microbial proteins and DNA. Iodophor-containing products enjoy widespread use because of their broad-spectrum antimicrobial properties, efficacy, and safety on nearly all skin surfaces.

More recently alcohol containing preparations have gained traction in the urological community performing prosthesis surgery because of its perceived benefits over the iodine containing solutions. A limitation to the use of alcohol in the operating room is its flammability on skin surfaces prior to evaporation. Flammability can be avoided by allowing the skin to completely dry and by avoiding preparation of areas with excessive body hair that can delay alcohol vaporization.

A comprehensive review of current evidence found some evidence that preoperative skin preparation with 0.5 % chlorhexidine in methylated spirits was associated with lower rates of surgical site infections following clean surgery than alcohol-based povidone iodine paint [8]. Thirteen studies were included in this review (2623 participants). These evaluated several different types of skin antiseptics – leading to 11 different comparisons being made. Although the antiseptics evaluated differed between studies, all trials involved some form of iodine. A mixed treatment comparison meta-analysis was conducted and this suggested that alcohol-containing products had the highest probability of being effective – however the authors of this study note that the quality of this evidence was low.

Yeung et al. recently compared chlorhexidine-alcohol to povidone-iodine skin preparation before urological prosthetic device implantation [9]. Patients undergoing virgin placement of a penile implant, an artificial urinary sphincter, mid urethral sling or testicular implant were included in the study.

Patients were randomized in a 1:1 ratio to surgical site skin antisepsis with a standard povidone-iodine 10-min scrub and paint process or a 2-min chlorhexidine-alcohol scrub. The two agents were compared in terms of decreasing the rate of positive bacterial skin cultures at the surgical skin site before prosthetic device implantation. A total of 100 patients were randomized, with 50 patients in each arm. Pre-preparation skin cultures were positive in 79 % of the patients. Post-preparation skin cultures were positive in 8 % in the chlorhexidine-alcohol group compared to 32 % in the povidone-iodine group ($p = 0.0091$). Coagulase-negative staphylococci were the most commonly isolated organisms in post-preparation cultures in the povidone-iodine group (13 of 16 patients) as opposed to propionibacterium in the chlorhexidine-alcohol group (3 of 4 patients). Interestingly, clinical complications requiring additional operations or device removal occurred in 6 patients (6 %) with no significant difference between either group. No urethral or genital skin complications occurred in either group.

It is the author's preference to perform a traditional 10 min povidone-iodine scrub of the genitalia prior to the commencement of formal draping (Fig. 7.2). It is essential that this be performed adhering to principles of moving from the outer areas towards the area where the incision is to be made and we feel that stop watch measurement of the time ensures strict adherence to the

Fig. 7.2 Timer to assist with the traditional 10 min povidone-iodine scrub of the genitalia prior to the commencement of formal draping

10 min duration. Thereafter we 'paint' the operative site with 0.5 % chlorhexidine in methylated spirits, allowing to dry before draping (Figs. 7.3 and 7.4).

Protective Adhesive Drape

As most organisms are introduced into the wound from the skin at the time of surgery, a recent series compared the infection rate using a no-skin-touch technique with the standard insertion procedure by the same surgeon in respect to penile prosthesis surgery. In the former group a protective adhesive skin drape was applied, the incision made through the drape, and skin hooks immediately placed in the edges of the wound to give surgical exposure without touching the skin during the entire procedure. The infection rate in the no-skin-touch group (0.7 %) was less than one-third of that in the control group (2.2 %) [10]. It is essential to ensure that the antiseptic of choice has dried adequately prior to placement of the adhesive drape to ensure good adherence to the skin.

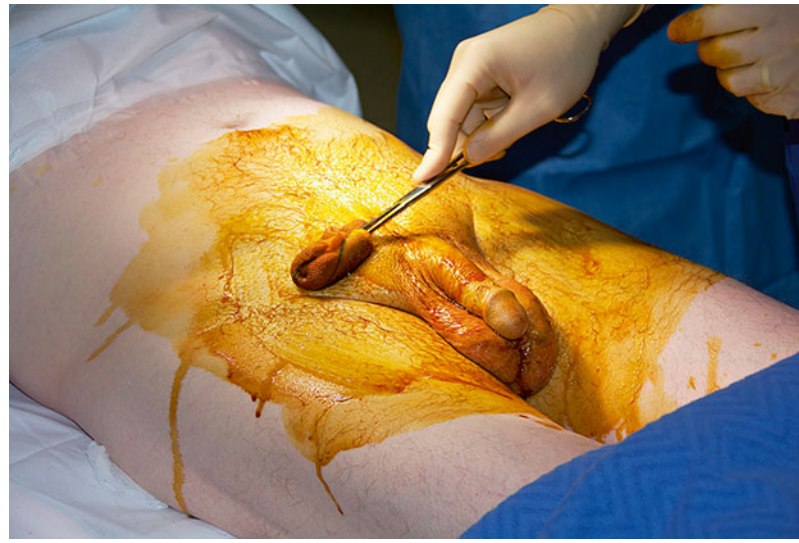

Fig. 7.3 Povidone-iodine scrub of the genitalia prior to the commencement of formal draping

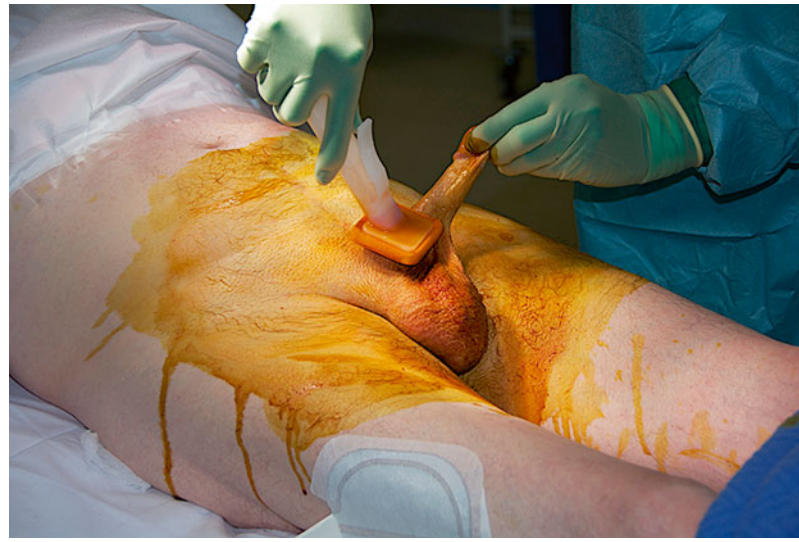

Fig. 7.4 Continuing the povidone-iodine scrub

The Urethra

Urinary tract infections should be eradicated before surgery. The urinary tract is not entered during implant placement, but leakage of urine onto the operative field is a possibility. Patients with a neurogenic bladder are more prone to develop urinary tract infections, and it might be prudent to place these patients on prophylactic culture appropriate oral antibiotics for a few days prior to the surgery to minimize the chance of such an infection developing.

Patients who have had a previous radical prostatectomy may have stress urine leakage. Placing a urethral catheter during the operation will reduce the chance of urine spillage and also provide guidance to the location of the corpus spongiosum during scrotal dissection. Similarly urethral catheterization is of significant benefit in penile prosthesis surgery for anatomical identification of the urethra and also to ensure urine spillage over the wound is minimized in the post operative period.

We the authors feel that another potential source of pathogens is from the urethra during catheterization. Our practice is to gently pass the catheter per urethra with the catheter tip lubricated rather than injection of lubricant into the urethra. This minimizes the potential for leakage of lubricant into the operative field, which could potentially harbor urethral bacteria. Similarly, once the catheter balloon is inflated, a spigot is applied and the catheter is withdrawn so that the balloon rests at the bladder neck. The distal length of catheter that remains external to the tip of the urethra is pulled through a swab soaked in Gentamicin and Rifampicin solution. This technique ensures that all possible contaminants from the catheristation procedure are addressed. Re-gloving is essential after this procedure (Fig. 7.5).

Current International Practice

Katz et al. [11] performed an anonymous Web-based survey sent to members of the Sexual Medicine Society of North America (SMSNA) and the International Society of Sexual Medicine (ISSM). They identified great variation in perioperative strategies utilized to prevent penile implant infections. 40% and 50% of SMSNA and ISSM members did not perform routine urine culture, respectively. Similar percentages of surgeons from each society request a daily preoperative antimicrobial scrub. About two-thirds of ISSM members use razors for the preoperative shave compared with one-third of SMSNA members. Most ISSM surgeons preferred povidone-iodine for hand and skin preparation while most SMSNA surgeons

Fig. 7.5 Use of double gloving during the procedure. This is particularly important when setting up the operative field and during catheter placement

chose this only for skin preparation. Two-thirds of SMSNA members prepared the skin for at least 10 min compared with 34 % of ISSM surgeons.

Conclusions

Strict adherence to skin preparation is important to reduce SSI. As the majority of infections are from skin commensals, the 'no touch' technique or similar variation should be used where possible.

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Urinary Catheters, Drains and Stomas

8

Suzanne M. Biers and Nikesh Thiruchelvam

Abstract

This chapter gives an overview of the different types of catheter available for bladder drainage, with details of their composition, size and style. We include technical tips on the insertion and the recognition and management of catheter complications, with an emphasis on catheter associated urinary tract infections and antibiotic stewardship. A description of the different types and indications for surgical drains is also provided, and a comprehensive overview of the types of stoma used in urological practice, including continent catheterisable channels (Mitrofanoff and Yang-Monti), ileal conduit, double-barrelled wet colostomy, vesicostomy and ureterostomy.

Keywords

Catheter • Urethral • Suprapubic • Drain • Stoma • Ileal conduit • Mitrofanoff • Monti • Ureterostomy • Vesicostomy

History of Urinary Catheters

The word catheter is derived from the Greek word 'to send or let down'. Devices for draining the urinary bladder were described as early as 400BC in the Hippocratic text on disease, and have subsequently been available in many guises including the use of reeds, long hollow Allium (onion) leaves, and manipulation of paper, leather and wax soaked cloth. Metal tubes (copper, brass, gold and silver) were used in the sixteenth century until natural rubber became available in the eighteenth century, bringing with it the advantage of malleability of shape and design. In 1837, Frederick Foley developed the first 'self-retaining bag catheter for use as an indwelling catheter for constant drainage of the bladder' [1] and also added a catheter balloon to the design. Other early self-retaining catheters had expanded shoulders (de

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Pezzer) or wings (Malecot) and were tied to the genitalia. Mercier described the single (coudé) and double curved (bicoudé) tip catheters in 1863 to help negotiate the challenging curves of the male urethra [2].

Attitudes to catheterisation and bladder management have evolved over the years. In World War I it was the rule not to insert a catheter in spinal cord injured (SCI) soldiers, but simply to let the bladder overflow in the belief that this would reduce urinary tract infection (UTI). This resulted in an 80 % mortality rate from UTI in soldiers rendered paraplegic from gunshot wounds [3]. This management changed in World War II, with SCI patients being evacuated from the battlefield with a suprapubic cystotomy in place. Over time, this was replaced by the suprapubic catheter (SPC), a technique advanced by Riches in 1943, with a formal introducer and Malecot catheter [4]. Later the classic Bard SPC was to be introduced in 1966.

Intermittent sterile catheterization was developed by Guttman in 1966 [5], and later modified to a less onerous clean intermittent self-catheterisation (CISC) technique by Lapides in 1972 [6]. This approach was more acceptable to the patients and produced fewer complications compared to indwelling catheters [7], and still remains the gold standard.

Indications for Catheterisation

Although the main indication for catheterisation was to use an external conduit to drain urine, there are other indications shown below where catheterisation is required.

- Drainage of the bladder (in urinary retention, detrusor underactivity, incontinence, perioperatively and after urethral or bladder trauma)
- Instillation of intravesical therapeutic and diagnostic agents (e.g. Mitomycin C, BCG, methylene blue)
- Monitoring of urine output
- Instillation of fluid and vesical pressure measurements during urodynamic studies
- Bladder washout
- For intermittent self dilatation (in cases with urethral strictures or bladder neck stenosis)
- Urine collection for microbiology analysis and urine culture
- Radiology studies such as urethrography and cystography
- Accurate measurement of the volume of urine in the bladder (e.g. post void residual volume)

Cautions and Contraindications

Although the utilisation of latex or silicone based catheters has led to easier urethral catheterisation which is relatively atraumatic, there are some situations whereby additional care or special manoeuvres are required.

Cautions

Artificial Urinary Sphincter

In the presence of an **artificial urinary sphincter** (AUS) (*see* Chap. 14), the cuff component should be deactivated prior to urethral catheter insertion. When inserting a SPC, care must also be taken to locate the site of the AUS reservoir component to avoid inadvertent puncture and therefore it is safer to perform this under ultrasound guidance.

Urethral Trauma

Urethral trauma is associated with visible blood at the external meatus in 75 % of anterior and 98 % of posterior urethral injuries [8]. In the emergency situation where the patient is unable to void, most guidelines advocate one gentle attempt at urethral catheter insertion by a urologist [9]; however, if this fails, the recommendation is for retrograde urethrography with radiological or cystoscopic guided insertion of a urethral catheter over a guidewire, or to proceed to insertion of an SPC.

Lower Urinary Tract Reconstruction

After lower urinary tract reconstructive surgery either at the level of the bladder neck following urethral anastomosis at the time of radical

prostatectomy or following urethral reconstruction for stricture disease, accidental loss of a urethral catheter should be replaced under direct vision with the use of a cystoscope to avoid disruption of the anastomosis.

Contraindications

Insertion of a SPC is contraindicated where the patient has known urothelial carcinoma of the bladder, visible haematuria or is on active anticoagulant therapy or has an untreated coagulopathy. Where patients have undergone lower abdominal surgery through an open approach, it is prudent to perform an open cystotomy to insert an SPC as opposed to a blind puncture, due to the increased risk of bowel lying in an aberrant low pelvic position and subsequent risk of bowel injury. Blind insertion of a SPC is reported to have a 2.4 % risk of bowel injury, and a 1.8 % 30 day mortality risk [10]. However, ultrasound guided insertion of a SPC provides another safe option with the risk of inadvertent bowel injury being reported as 0 % [11, 12].

Types of Urinary Catheter

Urinary catheters can be broadly categorised into indwelling (urethral, suprapubic), intermittent (inserted via the urethra or a continent catheterisable channel), and according to their size, number of channels, tip shape, material and coating.

Catheter Size

Joseph-Frederic-Benoit Charrière was a surgical instrument maker in nineteenth century Paris who introduced the Charrière (Ch) or French (Fr) scale. One Fr is equivalent to 0.33 mm, and is the measure of external diameter (rather than the lumen size). Three French is equivalent to 1 mm in diameter, and hence 30 Fr is equal to a 10 mm diameter. The internal diameter of the catheter lumen is smaller, with a 14 Fr catheter having an external diameter of around 4.7 mm, and an internal diameter of 3 mm in a silicone catheter and only 1.8 mm in a latex catheter [13]. Figure 8.1 demonstrates the difference in lumen sizes in 16 Fr catheters made from different materials. Female catheters are approximately 20–25 cm in length whereas male catheters are 41–45 cm long. The shorter female catheter has been withdrawn in many UK hospitals because of inadvertent insertion of the shorter female catheter into the male patient resulting in trauma to the male urethra following balloon inflation.

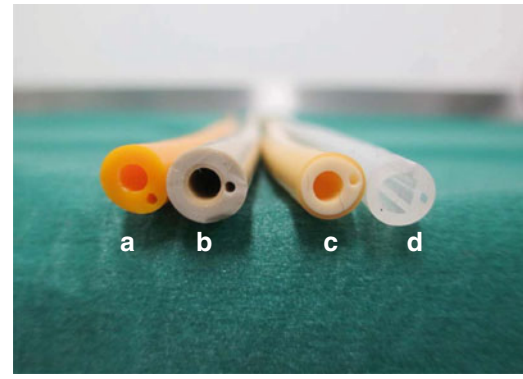

Fig. 8.1 Differences in the internal lumen size of 16Fr catheters manufactured by different companies in different materials: hydrogel coated latex (**a** and **b**), silicone coated latex (**c**) and silicone (**d**)

Number of Channels

Single channel catheters are for intermittent use. Two-way catheters are indwelling with a lumen for urinary drainage (also allows instillation of fluid), and a narrower parallel channel for inflation of the catheter retention balloon. Three-way catheters have an additional lumen for bidirectional flow to allow bladder washouts to be performed or to perform continuous irrigation following endoscopic resection surgery (see Fig. 8.2). Balloons on two-way catheters accommodate 10 ml of water and 20–30 ml in three-way catheters, although slightly larger volumes can be used without rupture and this is sometimes utilised following transurethral prostate surgery for haemostasis. Sterile water should be used for inflation as saline can precipitate into crystals

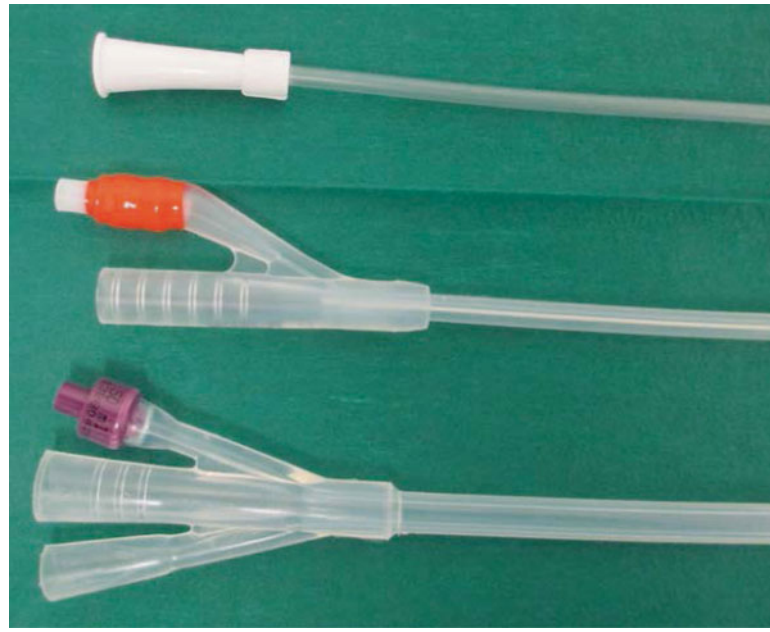

Fig. 8.2 Different numbers of catheter channels. From *top to bottom*: single, two-way and three-way catheter ends

and block the catheter lumen, making it difficult to deflate the balloon. The internal diameter of the main outflow lumen in a three-way catheter is smaller compared to the equivalent French gauge two-way catheter, in order to accommodate the extra inflow lumen. Likewise, the diameter of the two-way catheter is smaller than the equivalent French gauge single lumen catheter.

Catheter Tips

Standard catheters are straight, with a rounded, closed end with side holes for drainage. Non-retained straight catheters include Jacques, Nelaton and Robinson styles. Council-tip catheters have a straight flat open-ended tip, which allows the insertion of a guidewire within its lumen (see Fig. 8.3). Whistle-tip catheters have a large hole in a bevelled-style tip (see Fig. 8.4). Whereas Foley catheters are retained by inflated balloons, Malecot catheters have two to four small wings that protrude around the tip to retain the device in the bladder or renal pelvis, and the de Pezzer style 'mushroom' catheters have a flattened wider head (see Fig. 8.4); both can be used for suprapubic or nephrostomy drainage. The

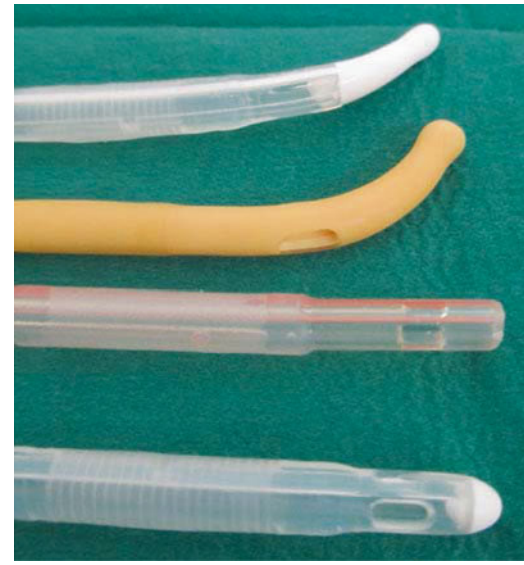

Fig. 8.3 Different styles of catheter tip. From *top to bottom*: silicone Tiemann tip, silicone coated latex Tiemann tip, silicone Council tip, and silicone closed/rounded tip

Roberts catheter has drainage holes both above and below the balloon to optimise emptying of the bladder residuals. A short self-retaining intra-urethral catheter (IUC) is used in prostatic obstruction (Puroflex, Urosoft®, Bard). It is

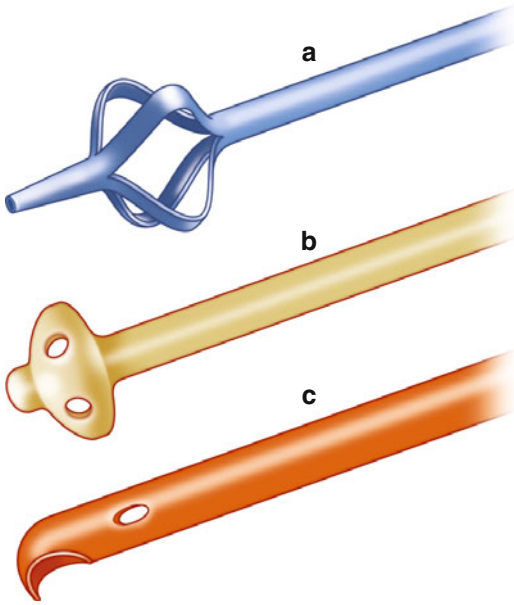

Fig. 8.4 Different styles of catheter tip: Malecot (**a**), de Pezzer (**b**), and Whistle-tip (**c**)

deployed via an introducer and is designed to sit along the bladder neck and prostatic urethra, being retained in place with Malecot type projections at each end. Curved tip catheters are useful for navigating the male urethral particularly during difficult male urethral catheterisation and include the Coudé, Tiemann and Carson tips (see Fig. 8.3).

Catheter Materials

Rubber and latex catheters tend to be for short-term use only. Silicone, polytetrafluoroethylene (PTFE) and hydrogel are materials which are used to coat latex catheters in order to enhance their longevity as it has been shown that catheter surface irregularities appear to facilitate bacterial colonization and crystal deposition [14]. Silicone catheters have the advantage of a smoother luminal surface, a larger internal luminal diameter, a reduced risk of kinking, with maintenance of better flow properties compared to latex-based catheters. As silicone is a relatively inert material there is less risk of bacterial adherence and tissue reaction [15], and they are more resistant to encrustation [16], and have reduced infection rates as compared to latex [17]. However, greater retention forces are recorded for both the inflated and deflated conditions, meaning that more force is required to remove the silicone catheters [18].

Coated Catheters

Single use, intermittent catheters are often hydrophilic and coated with polyvinylpyrrolidone (PVP), which binds water to the catheter surface, providing a smooth, slippery interface, and reduces the friction coefficient. These properties decrease mucosal friction, and act as a potential barrier to bacterial adhesion, resulting in reduced infection rates [19].

Silver has the ability to destroy both gram positive and gram negative bacteria, including antibiotic-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant *enterococci* (VRE). It can also treat *Candida albicans* infection. Its antimicrobial action is due to the silver cation which targets bacterial cells at multiple sites causing structural and functional changes, cell membrane rupture, binding and inhibition of cellular enzymes, and binding to DNA, thus interfering with the replication and cell division of pathogenic bacteria. The combination of silver alloy with hydrogel on catheters appears to be most effective, with a 47 % relative reduction in catheter-associated urinary tract infection (CAUTI) rates as compared to standard catheters over 3 months [20]. An earlier Cochrane review in 2008 [21] evaluating short-term catheter use reported that silver alloyed catheters reduced bacteriuria and symptomatic UTI compared to standard catheters. Subsequent reviews comparing antibiotic impregnated, standard and silver alloyed catheters could not identify which catheters are best for which group of patients [22].

Rates of symptomatic UTI in patients undergoing short-term catheterisation with either nitrofurazone coated catheters, silver alloy catheters or standard PTFE catheters were compared in a large randomised study of 6394 patients [23]. At 6 weeks follow-up, the risk of a symptomatic

CAUTI was lowest in the nitrofurazone group (10.6 %), which also proved the most cost effective, however there were higher reports of discomfort whilst the catheter was in situ and upon removal, and also the rate of reduction of CAUTI was not deemed clinically significant.

Trials looking at chlorhexidine and triclosan impregnation of catheters have reported effective prevention of bacterial colonization for 20–30 days compared to control catheters, which appear to be colonised within 1–2 days [24]. Triclosan has been used for inflation of the catheter balloon and reduces catheter encrustation for 7 days in laboratory bladder models infected with *Proteus mirabilis* [25]. Conversely, instillation of chlorhexidine into urinary drainage bags every time they were emptied (along with daily chlorhexidine skin cleansing) resulted in an outbreak of a chlorhexidine resistant multidrug resistant strain of *Proteus* [26].

Catheter Insertion Techniques

Urethral Catheterisation

Aseptic technique and sterile preparation of the field should be performed prior to urethral catheterisation. The smallest catheter size that is appropriate is chosen, and the balloon tested prior to insertion. Currently there is no good quality evidence for the use of prophylactic antibiotics in asymptomatic low risk patients. With the patient in a supine position, topical anaesthetic gel is inserted into the urethra, which also aids lubrication and reduces mucosal trauma. To optimise the anaesthetic effect in men, ideally slow instillation of 20–30 ml of 2 % lignocaine gel should be undertaken, and held in situ for a minimum of 10 min (by hand or penile clamp). In clinical practice, 10ml of gel is usually instilled over 1 min. Instillagel® is a commonly used anaesthetic lubricant. It containes lignocaine 2 %, chlorhexidine 0.25 %, methyl hydroxybenzoate 0.06 %, and propyl hydroxybenzoate 0.025 %. Systemic absorption is minimal, and toxicity is rare. Hypersensitivity reactions to the chlorhexidine component are possible, and repeat exposure in susceptible individuals can cause anaphylaxis, but this is rare [27].

Standard Male Catheterisation

The male urethra is approximately 20 cm long, and sigmoidal in its course. Therefore the left hand is used to retract the prepuce and the penis gently stretched at an angle of 60–90° to the abdominal wall, whilst the right hand introduces the catheter. After insertion of the first 10 cm, the penis is gradually angled towards the feet and the catheter is advanced past the resistance of the membranous urethra and into the bladder. Once urine is seen draining, the balloon is inflated with 10 ml of water, at which point a sterile closed drainage bag can be applied and positioned below bladder level. The foreskin should finally be replaced forwards to avoid a paraphimosis.

Difficult Male Catheterisation

A number of techniques can be used to aid difficult urethral catheterisation. A 60 ml syringe of saline can be placed on the end of the catheter, and fluid instilled as the catheter is advanced into the urethra. Alternatively, curved tip catheters can help to negotiate difficult prostatic urethras or a high bladder neck. Curved thin, metal introducer devices can be placed either within the lumen of a straight catheter to create the curve tip (Guyon introducer) (see Fig. 8.5a, b). Alternatively, the Maryfield introducer can be used, which hooks into the eyeholes at the tip of the catheter, and then has a convex surface which can accommodate the catheter tubing to create a curve. It is unhooked and removed once the catheter is in the bladder. Catheter introducers should be used with caution due to the risk of urethral trauma which can lead to urethral stricture formation. Flexible cystoscopy can be used to visualise the path to the bladder and a guidewire placed into the bladder, over which a Council tip catheter can be inserted. Short urethral strictures can be dilated with urethral sounds or dilators over a guidewire although a SPC insertion is required if urethral techniques fail.

Female Catheterisation

The female urethra is approximately 4 cm long. Again, anaesthetic gel can be applied to the

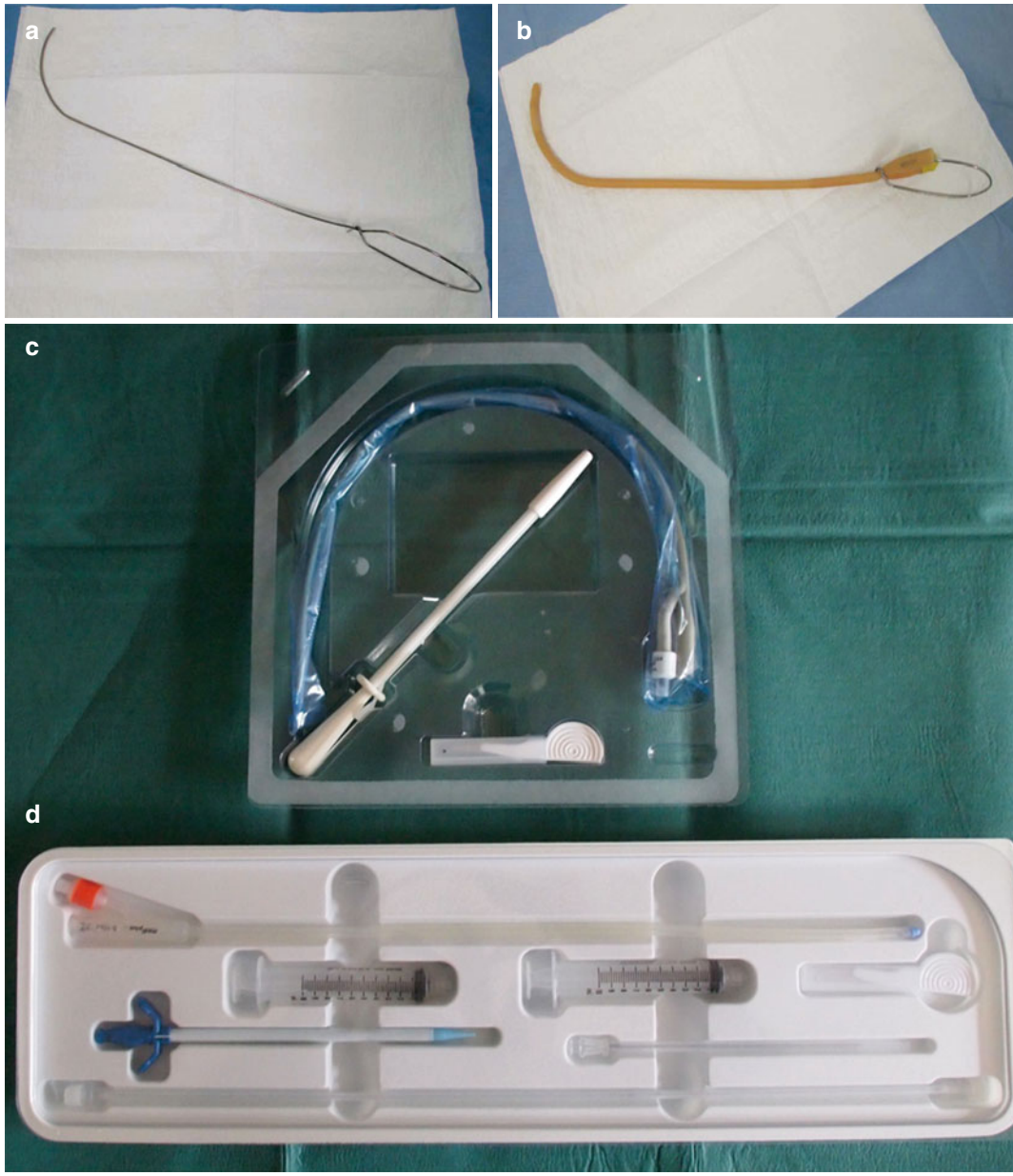

Fig. 8.5 (**a**) Long thin metal curved catheter introducer (Guyon style). (**b**) Metal introducer inserted and held within a straight tipped Foley catheter. (**c**) A BARD® trocar suprapubic catheter set, and (**d**) Mediplus® seldinger suprapubic catheter set

urethral meatus or tip of the catheter. With the patient's ankles together and knees bent to the sides, the left hand is used to part the labia, and the right sterile hand is used to introduce the catheter. Once urine begins to drain, the balloon is inflated, and the catheter withdrawn so that the balloon sits at the level of the bladder neck. Difficulty in identifying the meatus can be overcome by tilting the pelvis forward using a pillow under the buttocks, or placing the patient in the left lateral position and using a Sims speculum on the posterior vaginal wall for retraction to more clearly identify the anatomy. Alternatively in atrophic vaginitis where the urethral meatus is drawn into the anterior vaginal wall, the catheter can be guided in blindly using the index finger.

SPC Insertion

SPCs are indicated in the presence of significant urethral strictures, bladder neck stenosis, traumatic urethral disruption, for urinary drainage after bladder reconstructive surgery, and for long-term catheter use. Relative contraindications to SPC insertion include underlying bladder cancer, uncorrected coagulopathy, and undiagnosed macroscopic haematuria. Current UK guidelines recommend ultrasound guided SPC insertion where practical [28]. The risks associated with SPC insertion include bleeding, infection and injury to surrounding viscera (bowel injury in 2.4 %) [10].

Several approaches can be used for SPC insertion such as percutaneous or open, under direct vision with a cystoscope, ultrasound guided, or in some situations a 'blind' approach. Previous abdominal surgery is an indication for an open cystotomy approach or ultrasound guided approach. Local anaesthetic infiltration 3–4 cm above the symphysis pubis in the midline should be administered after antiseptic skin preparation. Trocar SPC insertion (Bard) (see Fig. 8.5c) involves a small suprapubic incision, aspiration of urine from the bladder followed by percutaneous insertion into the bladder whilst standing on the left hand side of the patient and angling the trocar slightly towards the pelvis. Withdrawal of the trocar will result in visible urine into the sheath following which, the catheter can be inserted within the outer sheath and directed into the bladder, and the balloon inflated. The outer sheath is then peeled off. The Seldinger technique (Mediplus) [29] (see Fig. 8.5d) involves inserting a hollow-bore 18g needle into the bladder to aspirate urine. The floppy end of the three-stage 0.035in. guidewire is fed through the needle and into the bladder, followed by withdrawal of the needle. An incision is made in the skin (and fascia), the trocar is placed over the guidewire and into the bladder. The guidewire and inner sheath are then removed, and the catheter fed into the bladder. Whilst SPCs are associated with a lower risk of urethral injury and stricture, there is little evidence that SPC reduces the risk of UTI compared to other catheters [30, 31]. However, SPCs are favoured for long-term use as they are easier to change in the community, result in less trauma to the urethral meatus and allow patients to potentially resume sexual intercourse.

Catheter Management

The interval of catheter exchange should be adapted to the individual, aiming to avoid catheter blockage or complications. Exchanges tend to be every 8–12 weeks although urine collection bags are changed weekly. If patients have satisfactory manual dexterity and cognition, and have a low pressure bladder, catheter valves can be used (e.g. FLIP-FLO® Catheter Valve by Bard). These are exchanged every 5–6 days. Relative contraindications include detrusor overactivity, renal impairment or vesicoureteric reflux. Purple discolouration of the drainage bag can sometimes be encountered [32]. It is thought to originate from tryptophan being metabolised by gut bacteria to indole, which is converted to indoxyl sulphate in the liver. This is excreted into the urine, and further broken down into indirubin (red) and indigo (blue), which combine to make a purple colour. It is associated with bacteriuria, but in itself does not cause any clinical problems.

Complications of Catheters

Difficulty in Removing a Catheter

Catheter knotting is rare but can occur if an excessive length is inserted into the bladder and forms a loop. Subsequent withdrawal of the catheter can tighten the knot. Rigid cystoscopy and piecemeal removal of the catheter is required. Difficulty with deflating the balloon can be due to a faulty valve, blockage of the inflation channel, or crystallization within the balloon. Rarely, the catheter might be caught within a suture at the bladder neck. After balloon deflation, a cuff of material can form making removal difficult. In a survey of community practice, 14 % experienced difficulty with catheter removal in the last 12 months; 8 % of all the urethral and 22 % of SPCs, of which 68 % of all problems were with all-silicone catheters [33].

Stepwise Approach to Problem Solving Issues with Balloon Deflation

- Add a further 1–2 ml of fluid or air to the balloon, and then attempt deflation again
- If this fails, the inflation channel can be opened by passing a guidewire into its lumen
- The next step is to cut off the end of the inflation port (plus or minus the whole catheter end, whilst ensuring that it is secure), to open the lumen and allow the balloon fluid to escape
- If this fails, ultrasound guided percutaneous needle puncture of the balloon can be performed.

Catheter Biofilm and Encrustation

Biofilms are associated with the urease-producing bacteria (*Proteus mirabilis*) which colonise the catheter surface, and hydrolyse urea to carbon dioxide and ammonia thus alkalinising the urine. As the pH rises, crystals of calcium and magnesium phosphate precipitate in the urine (at the nucleation pH), and crystals form on the catheter surface which contribute to the biofilm [34], causing encrustation, catheter blockages and difficulty with catheter removal. On balloon deflation, fragments of crystalline debris are shed into the bladder, which can act as a nidus for bladder stone formation. However, encouraging patients to increase their fluid intake leads to dilution of the urine, increases the urinary pH, and helps to slow catheter encrustation rates [35, 36]. Citrate (potassium citrate and lemon juice) inhibits the crystallization of calcium and magnesium phosphates, increases the urinary pH and can also inhibit encrustation [36]. In clinical studies, lemon juice is better tolerated by patients than potassium citrate, and can be taken as 60 ml of concentrated PLJ Lemon juice in 1 L water [37]. A community survey of long-term catheter complications over a 6 month period reported 48 % suffered catheter blockages and 37 % experienced bypassing [38]. Blockages were associated with a higher urine pH, urine cultures positive for *Proteus* and the presence of bladder stones. Interestingly, a Cochrane review investigating the role of regular catheter washout (assessing saline, acidic and antibiotic solutions) as compared to no washout for the prevention of catheter blockages, was unable to identify any clear benefit or preventative role for regular washouts [39].

Catheter-Associated Urinary Tract Infection

UTIs accounts for 40 % of all hospital acquired infections, most of which are catheter related [40, 41]. Bacteriuria develops in up to 25 % of patients who have had a urinary catheter for ≥1 week, with a daily risk of 5–7 % [42, 43]. The commonest uropathogen is *E. coli* and other bacteria include *Enterococci*, *Pseudomonas aeruginosa*, and *Klebsiella* [44]. Approximately 67 % of CAUTIs in hospitalised patients are due to bacteria ascending from the external urethral meatus along the catheter-urethral interface (extraluminal). Around 33 % are due to bacteria migrating into the catheter lumen as a result of disconnecting the catheter system (intraluminal) [45, 46].

Risk Factors for CAUTI

A number of factors have been identified as risk factors for CAUTI. These include a urethral catheter being *in situ* for more than 6 days, female patients, elderly patients, other sites of infection, other medical comorbidities, malnutrition, renal insufficiency, and the drainage bag or tubing being placed above the bladder [42, 45].

Complications

Clinically CAUTIs manifest as cystitis, prostatitis, urethritis, pyelonephritis, urinary sepsis, and periurethral abscess. In high risk patients, gram negative urinary sepsis and abscess formation need to be treated promptly in order to avoid a systemic inflammatory response and potential multi organ failure. Complications also include catheter encrustation, catheter blockage and bypassing of urine which is reported in 11 % of short-term catheter users and up to 52 % of long-term catheters [47]. Urethral stricture rates are quoted as 3.4 % with short-term catheterisation [47]. Patients in nursing homes are a high risk group where catheterisation increases both the morbidity and mortality risk [48].

Reducing the Risk of CAUTI

Clinical vigilance over catheter care is essential in order to avoid complications. Therefore unnecessary catheterisation should be avoided, and catheters should be removed at the earliest opportunity [49], as well as considering alterative options such as CISC. The type of catheter used for CISC (hydrophilic, gel reservoir, and non-coated) does not alter the risk of symptomatic UTI [50]. A closed drainage system is preferable, with the collection tubing and bag remaining below the level of the bladder, and the drainage tubing above the level of the collection bag. This system should be manipulated as little as possible, and urine output should be monitored hourly only when clinically indicated. There is some evidence that separating catheterized patients geographically in a hospital ward may also reduce the risk of cross infection with multidrug-resistant nosocomial organisms [42]. Proactive programmes to prompt removal of catheters by means of reminders or stop orders decreases catheterisation times, and reduces infection rates by 52 % according to a systematic review [51].

The Role of Antibiotics

Urine and blood specimens should be sent for culture prior to starting antibiotics in a symptomatic patient. Of note, febrile episodes are reported in up to 10 % of patients with a long-term catheter, so it is essential to exclude other causes. In asymptomatic *Candida* infection of the urine, antifungal therapy is not always indicated, although a catheter exchange is advised. In symptomatic CAUTI, the catheter should be replaced before starting antibiotic treatment if it has been in situ for >7 days.

Limited evidence exists for the use of antibiotic prophylaxis in reducing CAUTI [30, 52]. In a systematic review (including 6 RCTs) investigating the role of antibiotic prophylaxis at the time of catheter insertion [53], the absolute reduction in the risk of UTI was 5.8 %, however, the number needed to treat to prevent one UTI was 17. Benefits need to be weighed up against the risk of side effects, cost of antibiotics, and risk of antimicrobial resistance. Most guidelines do not recommend antibiotic prophylaxis to cover routine insertion or removal of catheters and long-term antibiotic therapy is not effective in reducing the risk of CAUTIs. Asymptomatic CAUTIs should not be treated with antibiotics, except if the patient is due to undergo urological surgery or a urinary tract intervention. Studies have also indicated that bladder washouts with antibiotic (Neomycin-Polymyxin) solution has no effect on the degree of bacteriuria, pyuria or inflammation [54].

Urinary Tract Stones

Bladder and upper tracts stones are reported to develop with long-term catheter use. In SCI patients with an indwelling catheter, 16 % (all asymptomatic) were found to have bladder stones on cystoscopic surveillance [55]. In patients who suffer recurrent catheter blockages, bladder stones were identified in 40 % of patients with SPCs and 22 % with urethral catheters [55]. In a study of 316 SCI patients, with the majority managing their bladder with a catheter, at a mean follow-up of 18.3 years, upper tract stones were documented at least once in 35.1 % of patients, and bladder stones in 14.6 % [7].

Bladder Cancer

Chronic bladder irritation and inflammation related to catheter use has been considered a risk factor for developing bladder cancer. Nitrosamine in combination with infected urine may contribute to the pathogenesis [56]. This risk was initially reported as higher in SCI patients [2], where both the presence of a catheter and/or a neuropathic bladder are both considered as risk factors [57]. Previous studies reported a lifetime incidence of bladder cancer occurring in 2–10 % in SCI patients [58]. A prospective study of 3670 SCI patients has calculated the risk of bladder cancer as 77 per 100,000 person-years for those with

indwelling catheters [59]. This corresponded with an age- and gender-adjusted standardized morbidity ratio of 25.4 when compared to the general population. Squamous cell carcinoma (SCC) is more frequent in SCI, and in patients with indwelling catheters compared to those using CISC, convene drainage or spontaneously voiding [57]. Contemporary studies indicate that this trend is changing, reporting that bladder cancer risk is now declining to match that of the general population [60]. The most common presenting symptoms are haematuria and recurrent UTI [56]. A recent systematic review and meta-analysis reported a 13.5 % risk of visible haematuria, and a 1 % risk of bladder cancer with long-term catheter use [57]. Therefore urgent investigation of SCI patients is recommended if they have new onset haematuria with some clinicians also advocating routine cystoscopic bladder surveillance for patients with a long-term catheter [55].

Quality of Life

The impact of long-term catheterisation on quality of life (QoL) was studied in 1201 multiple sclerosis patients, using a specifically designed North American Research Committee of Multiple Sclerosis (NARCOMS) questionnaires [61]. Patients who reported a negative impact in 25 % and a positive impact in 52 % with a neutral effect on QoL in 22 %. The impact from different types of catheter (intermittent versus indwelling) did not differ significantly, suggesting that catheters are an acceptable bladder management option.

Drains

A number of different types of drain are routinely used in urological practice, for both therapeutic and prophylactic indications, including surgical abdominal drains, nephrostomy drains and urinary catheters. The role of surgical drains remains controversial. Several studies fail to show significant benefit from the placement of drains after surgical procedures [62, 63], and even report an increased risk of surgical site infection (SSI) [64, 65] therefore advising against the routine use of drains unless a strong indication exists. General rules are that drains should be placed away from the operative incision, as drains placed through the incision site increase the risk of SSI [66]. This also allows the wound and drain to be dressed separately. The risk of SSI is lower with closed suction drains compared to open drains [67]. Timing the removal of the drain should be optimised, as bacterial colonisation of the drain tract increases with the length of time the drain is left *in situ* [68]. We will review the use of drains in urological practice, including their advantages and disadvantage (see Table 8.1).

Indications for Surgical Drains

- To remove existing or potential collections (such as post-operative lymphocele, haematoma, urinoma, air or pus)
- Diversion of fluids
- Irrigation of a cavity
- Reduce seroma formation

Table 8.1 Advantages and disadvantages of the use of surgical drains

Advantages	Disadvantages
Removal of fluid collection to avoid infected collections	Drains may act as a route for bacterial invasion and surgical site infection
Prevents re-accumulation of fluid collections	Suction may damage tissues and delay wound healing
Allows surveillance and characterisation of the fluid type (blood, pus, bowel anastomotic leak)	Drains do not always successfully drain certain material (faeces, pus, clot)
After removal, the tract may remain patent for a limited time, allowing residual fluid to drain	

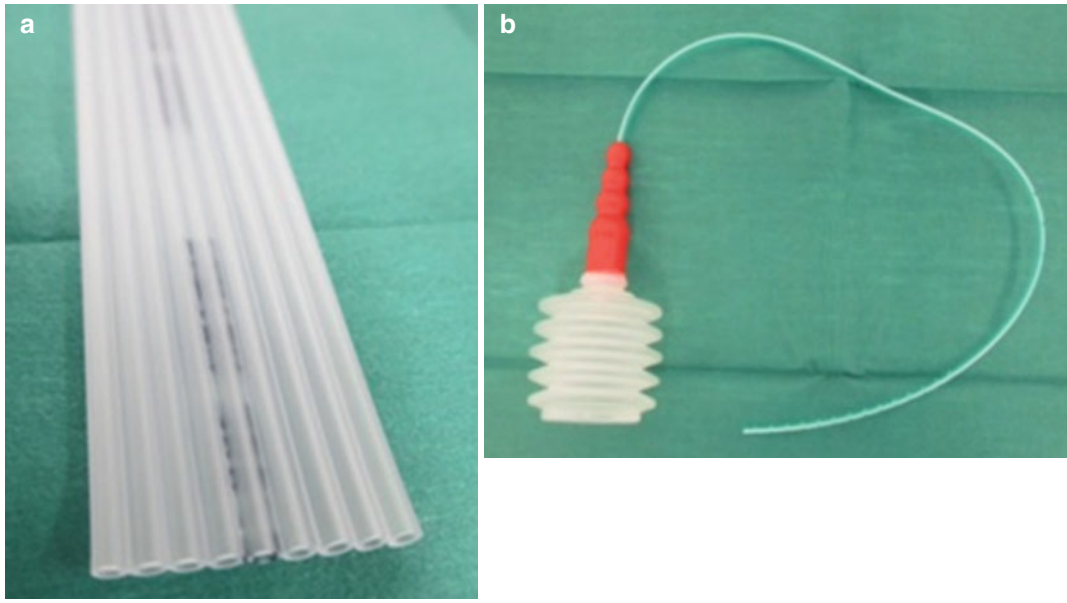

Fig. 8.6 Examples of drains. Yeates drain (**a**) and Minivac drain (**b**)

Types of Drains

Drains can be categorised into open or closed and passive or active. They can be inserted electively at the time of surgery for pelvic and abdominal operations (open or laparoscopic), after scrotal or genital surgery, and after percutaneous nephrolithotomy (PCNL) using a nephrostomy tube (pigtail or Malecot). They can also be placed electively or in the emergency situation with radiological guidance (ultrasound or CT imaging) into abdominal (retroperitoneal or intraperitoneal) collections of fluid (blood, lymph, pus, urine).

Open Passive Drains

Open drains allow drainage directly into a sterile dressing or stoma bag. They are also passive, in that they do not use suction, but drain due to a differential pressure between the higher pressure in the body compared to the lower pressure exteriorly, and are dependent on gravity or capillary action. They can be used when quantification of the volume of fluid loss is not required for monitoring purposes. They are easier to remove and often better tolerated by patients, but are also associated with an increased risk of infection, as fluid movement can be reversed with the risk of introducing bacteria into the wound. Examples include corrugated drains that may be used in scrotal surgery, Yeates drain (flat drain containing a series of capillary tubes) (see Fig. 8.6a), wicks (such as ribbon gauze) and Penrose drains. The latter are soft tubes often made from rubber, but are also available as silicone tubes, with the inner lumen ribbing to prevent complete collapse, also designed to be detectable on x-ray. Corrugated and Penrose drains are usually held in place with a long (Mersilk) suture or safety pin.

Closed Drains

These consist of tube systems which allow drainage of fluids directly into a bag or bottle (with or without suction). Common materials that are used include silicone, polyurethane and polyvinylchloride. Benefits of a closed system include the ability to visualise and so characterise the drainage fluid, accurately quantify fluid volumes and also avoid contamination and soiling of the surgical site. They are commonly utilised for pelvic and intraperitoneal drainage.

Closed Passive Drains

These drain fluid by gravity or capillary flow into a closed container. Examples include the Robinson drain. This tends to be manufactured from clear silicone elastomer, and can come in a variety of

sizes, with an external diameter ranging from 9 to 36 Fr, attached to a 600 ml closed drainage bag with an internal anti-reflux valve to prevent backflow of fluid. The tubing is radio-opaque with elliptical, atraumatic eyeholes for drainage.

Closed Active Drains

These generate high or low (negative) pressure suction to move fluid into a closed vacuumed container, aiding removal of fluid and eliminating deadspace. Examples include the Jackson Pratt drain, Redivac® and Minivac® drains (see Fig. 8.6b). They have a sharp trocar for insertion of the tubing (which is later removed) with either a bulbous or concertinaed collecting bottle, which can be squeezed to evacuate the air and create a vacuum. They are useful for post-operative removal of blood from potential dead space. Jackson-Pratt devices are low pressure, and Redivac® drains are higher pressure. When the drainage system container is full, it needs to be exchanged and the vacuum reapplied. A sump drain consists of a suction drain tube with a double lumen, incorporating an intake tube which supplies air to the bottom of the main tube to which suction is applied, so assisting the drainage of fluid whilst the flow of air helps to avoid blockages.

Maintenance of Drains

After insertion, the drain should be secured to avoid displacement, and placed below the surgical site. Surgical drains are typically sutured in place temporarily with Mersilk. The drain output (volume and fluid type) should be recorded daily, with checks to ensure there is no blockage, kinking or leaking. Surgical drains should be removed as soon as possible in order to reduce the risk of SSI [68], either once drainage has stopped completely or has reduced to less than 25–50 ml/day. The vacuum should be released prior to removal of suction drains, and any stay suture cut. The drain can be removed in total or shortened by withdrawing it gradually by around 2 cm per day to allow gradual healing of the tract. However, having a patent tract can be helpful to allow any residual fluid to continue to drain after the tubing has been removed. This can be collected into a stoma bag if the fluid output volume is high, or onto a dry covered dressing. Drain removal can be uncomfortable for some patients, and manual pressure should be applied initially to the drain site with sterile gauze after the tubing has been removed in order to stop bleeding and collect excess fluid. If there is concern regarding ongoing infection, the end of the drain can be cut off and sent to microbiology for culture after drain removal.

Complications of Drains

Complications of drain placement include a risk of damage to surrounding organs and structures during open or radiologically guided insertion of drains as well as bleeding from the drain site. Active (suction) drains have the potential to cause pressure related injury to surrounding structures, including adjacent bowel. Drains can also cause skin irritation, pain, and reduced mobility post-operatively with the infection risk reported to be higher in open (passive) drainage systems, although one study reports limited evidence that the use of a Penrose drain after different types of genital surgery (including hydrocele repair, epididymectomy and excision of spermatocele) did not alter the infection risks [69]. It should also be noted that drains do not always effectively evacuate fluid or blood, and so can provide false negative results. Intraperitoneal drains can collapse or block, and therefore these drains do not always effectively drain faeces or pus [70], thus giving false reassurance after bowel anastomosis. Whilst pelvic drains can act as early indicators of anastomotic bowel leak, it is considered that prophylactic drains are not necessary for many types of gastrointestinal surgery, including bowel resection and primary anastomosis [71], as there is no evidence that they prevent anastomotic leak or other related complications [63]. Very rarely, drains that have been left *in situ* for prolonged periods can result in erosion into surrounding structures such as bowel [72]. Inadvertent suturing of the drain into the wound can also occur, and manifests as difficulty in removing the drain which requires reopening of the wound in order to release the suture. Following drain removal, complications such as scar formation, herniae, chronic pain and re-accumulation of fluid have been reported.

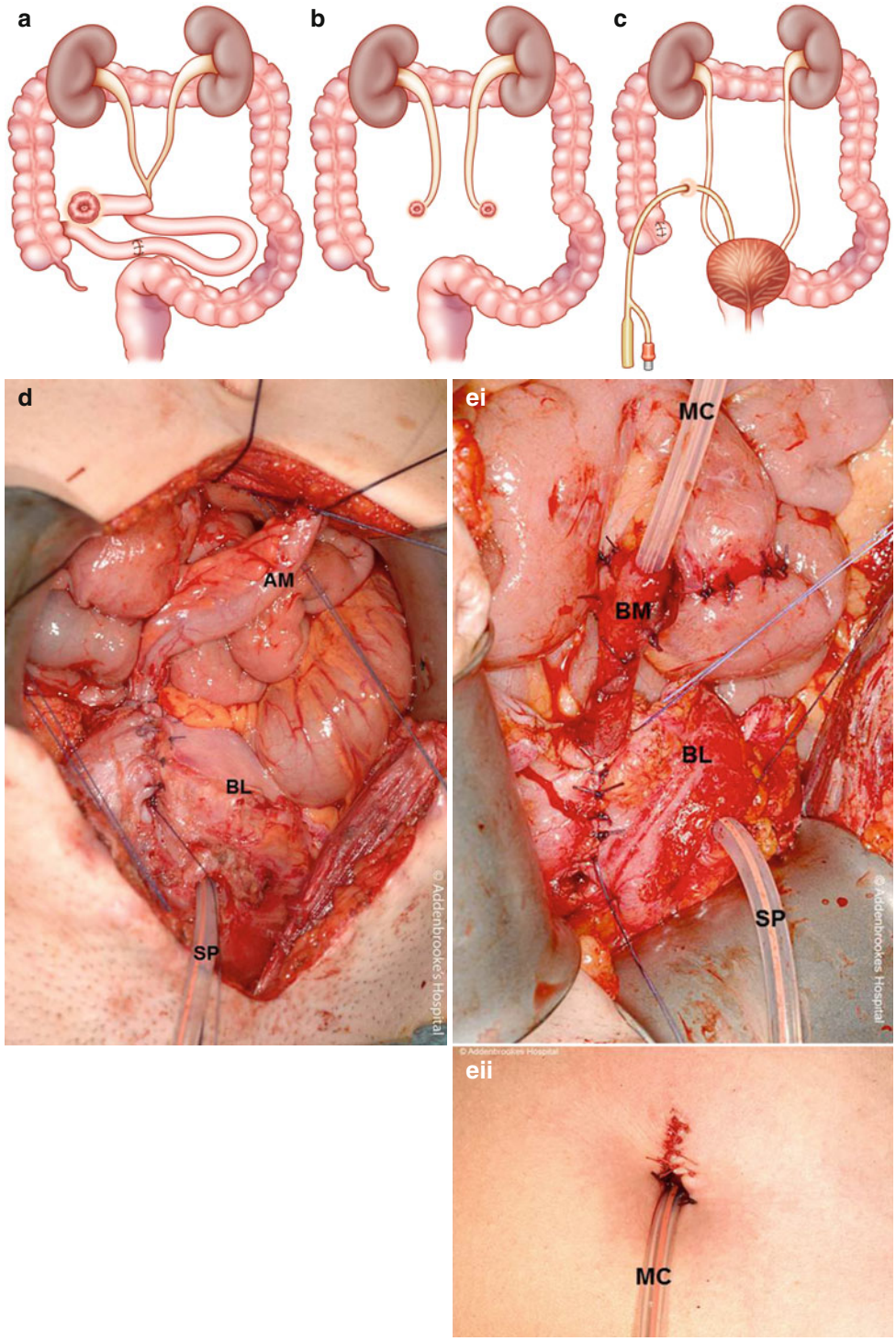

Fig. 8.7 Stomas. (**a**) Diagrammatic representation of an ileal conduit urinary stoma. (**b**) Diagrammatic representation of bilateral cutaneous ureterostomies. (**c**) Diagrammatic representation of a Mitrofanoff catheterisable conduit. (**d**) Photo during creation of a Mitrofanoff catheterisable conduit created using an appendix. (**ei**) Photo during creation of a Mitrofanoff catheterisable conduit created using small bowel. (**eii**) Mitrofanoff stoma. *BL* bladder, *AM* appendix Mitrofanoff, *SP* suprapubic catheter, *MC* Mitrofanoff catheter, *BM* bowel Mitrofanoff

Stomas

Types of Stomas Used in Urology
(*See* Fig. 8.7)

Examples of urinary diversion techniques with a non-continent stoma draining urine cutaneously into a collection appliance include the ileal conduit, double-barrelled wet colostomy, vesicostomy and cutaneous ureterostomy. Continent urinary diversion operations, where the patient needs to empty the bladder themselves with a catheter, include the Mitrofanoff and Monti catheterisable channels. Stomas can be made using the urinary tract alone (vesicostomy, ureterostomy), or in combination with a segment of bowel.

Principles of Bowel Harvesting in Urinary Reconstruction

Bowel Choice and Harvesting

The small intestine is approximately 6.7 m long; with the duodenum having the largest diameter, and the ileum the smallest diameter. The ileum is most frequently used for urinary tract reconstruction, followed by the colon. The ileum receives its blood supply from the superior mesenteric artery and therefore during harvesting an ileal segment, the attached mesentery is divided ensuring that a good blood supply is included from a vascular arcade supplied by a robust artery in the base of the mesenteric pedicle. When harvesting the bowel segment, ileum should be taken 20 cm proximal to the ileocaecal valve in order to avoid taking the terminal ileum and therefore reduce the risk of Vitamin B_{12} and bile salt malabsorption. Bowel that has been exposed to radiotherapy should also be avoided, and an alternative non-irradiated segment chosen. To avoid metabolic complications, limited segments of bowel should be taken from patients who cannot acidify the urine (<pH 5.8), are unable to concentrate urine (to >600 mOsm/kg), or who have a poor glomerular filtration rate (<35 ml/min). There is no evidence that bowel preparation is required or beneficial prior to ileal resection (and ileal conduit formation) [73].

Principles of Intestinal Re-anastomosis

The aims are to achieve adequate surgical exposure, ensure a good blood supply, avoid faecal contamination and have accurate serosal apposition of the two segments of bowel with correct tensioning of sutures and accurate alignment of the mesentery. Gastrointestinal anastomosis (GIA) staple devices can also be used as an alternative to suturing of the bowel. For a summary of the complications relating to the use of intestinal segments, please see Table 8.2.

Ileal Conduit

Reconstruction of the ureters into an isolated segment of the gastrointestinal tract, which is then brought onto the abdominal skin surface to drain urine freely into an appliance, has been described using stomach [74], jejunum [75], ileocaecum [76], transverse [77] and sigmoid [78] colon. Whilst it appears earlier in the literature, the ileal conduit technique was refined and popularised by Bricker in 1950 [79]. Overall, it remains the most commonly performed urinary

Table 8.2 Complications related to the use of bowel

Complications of intestinal anastomosis	Leak
	Fistula formation
	Infection and sepsis
	Ileus, bowel obstruction and pseudo-obstruction
	Haemorrhage
	Intestinal stenosis
Complications of the isolated intestinal segment	Intestinal stricture
	Elongation of the segment
	Necrosis
Complications of intestinal stoma	Bowel necrosis, requiring revision
	Bleeding
	Parastomal hernia or prolapse
	Obstruction
	Stomal retraction
	Stomal stenosis
	Dermatitis

diversion technique used after radical cystectomy [80, 81].

Indications for Surgery

The purpose is for diversion of urine after radical cystectomy for bladder cancer, or for urinary diversion (with or without simple cystectomy) for bladder dysfunction due to end-stage bladder pain syndrome, radiation cystitis, TB, neuropathic bladder, intractable urinary incontinence, vesico-vaginal fistula, severe urethral stricture or fistula disease and ketamine bladder. The most common reasons for simple cystectomy and ileal conduit formation are a neuropathic bladder (due to SCI, multiple sclerosis and spina bifida), radiation damage to the bladder, and severe incontinence [82]. An ileal conduit is a better option for patients with poor manual dexterity, who would be unable to perform CISC of a Mitrofanoff channel or neobladder. It has the benefit of requiring a shorter length of ileum, as compared to a neobladder which can require up to 60 cm of bowel. Around 15–20 cm of ileum are required for an ileal conduit, however an individualised approach should be adopted taking into account the patient's body habitus. Once isolated, the distal ureteric ends are spatulated and either anastomosed to the segment of ileum for the conduit individually using the Bricker technique, or joined to make a ureteric plate and then anastomosed to bowel, known as the Wallace technique. The ureteroileal anastomosis is stented for 10 days with an 8 Fr single J stent. The distal part of bowel segment is brought up through the rectus muscles (to reduce the risk of hernia), secured with interrupted sutures to the rectus sheath, and a spout created on the skin of the lower abdomen (urostomy). The most convenient site for the stoma is marked prior to surgery by the stoma team, with training in stoma care and application of bags.

Complications of Using Ileum in Urinary Tract Reconstruction

- Nutritional problems due to vitamin B_{12} malabsorption (causing anaemia and neurological sequelae), deficiency in bile salt reabsorption (causing diarrhoea) and fat malabsorption (causing fat soluble vitamin deficiencies and osteomalacia). These are most common if terminal ileum is used, or the ileocaecal valve is compromised
- Ileal mesentery can be short, limiting mobilisation of the segment
- Mesenteric fat can be thickened, making both visualisation of arcades difficult, and creation of a skin stoma challenging
- Post-operative bowel obstruction or ileus is reported in around 20 % [82]

Complications of an Ileal Conduit

Metabolic Acidosis

This occurs to a mild degree in the majority of patients, but is clinically significant in fewer patients, with around 10 % having a metabolic acidosis requiring treatment [83]. The mechanism of hyperchloraemic metabolic acidosis is due to ammonium chloride in the urine being absorbed across the lumen of the bowel and into the blood in exchange for carbonic acid, with the additional loss of bicarbonate, which is exchanged for chloride. It is manifest clinically as fatigue, anorexia, lethargy, and weakness. When treatment is clinically necessary, options include the prescription of alkalinising agents (oral bicarbonate) or blockers of chloride transport (chlorpromazine).

Infection

An increased incidence of bacteriuria is reported, with UTI and acute pyelonephritis in 23 % of ileal conduits, 12 % being described as acute or recurrent pyelonephritis [84]. Although most patients remain systemically well, around three quarters of ileal conduit urine specimens are infected. Deterioration of the upper tracts is more likely to occur when pure cultures of *Proteus* or *Pseudomonas* are cultured, and these infections should be treated.

Stones

The incidence of complications relating to urolithiasis is around 15 % [85], with upper tract stones

constituting 9–13 % [83, 84], and conduit stones in 5 % (at a median follow-up of 3 years) [83]. Urolithiasis is attributed to altered urinary excretory products from the bowel segment and the alkaline nature of the urine. The risk is higher with urea-splitting organisms (such as *Proteus mirabilis*), and the stones are commonly composed of calcium, magnesium, and ammonium phosphate.

Anatomical and Stoma Problems

Parastomal hernia is reported to occur in approximately 10–29 % of patients [82–84, 86], and can cause pain, partial or complete bowel obstruction or strangulation, requiring surgical repair in around 45 % of those patients with a hernia [86]. Stenosis of the stoma is seen in 2–6 % [82–84], and stomal prolapse in 1.5–8 % [82, 87]. Most stomal complications occur within 5 years of surgery [84]. These complications make the application of containment devices (stoma bags) problematic. The bowel segments used can also bleed at the skin edge and cause irritation in 5 % of cases [84]. Excoriation and dermatitis of the skin around the stoma is common.

Quality of Life (QoL)

There is conflicting evidence in the literature regarding health-related QoL scores between continent (neobladder) and incontinent (ileal conduit) urinary diversion after radical cystectomy. A recent systematic review of 21 non-randomised studies included 2285 patients [88]. Sixteen studies could not demonstrate a difference in QoL between the two types of urinary diversion; 4 studies reported a better QoL with orthotopic neobladder, although it should be noted that 2 of the 4 studies had younger and fitter patients. One study reported a better QoL in ileal conduit patients, mirrored in other contemporary series [89]. The most important element is careful patient selection and counselling prior to deciding on the urinary diversion technique.

Appliances for Urine Collection

Urostomy pouches are prosthetic devices which have a round adhesive baseplate with a central hole designed to firmly fit and stick to the skin around the stoma and allow free drainage of urine into a collection bag. Single-systems consist of a collection bag with an integrated adhesive baseplate, which can be cut to size for best fit around the urostomy, and can last for up to 2–3 days. In the two-piece device, the collecting pouch has its own attachment mechanism (adhesive flange or round clip) and is separate from the adhesive baseplate. The two components can be clipped or sealed together, with the benefit that the adhesive baseplate can last for around 5 days and does not need to be removed every time the bag is changed (see Fig. 8.8). The base of the pouch has a tap which allows the bag to be directly drained or attached to a catheter bag. Ostomy support belts and girdles are available to help manage urostomies complicated by parastomal hernia.

Double Barrelled Wet Colostomy

'Wet' colostomies' were originally introduced for patients undergoing pelvic exenteration, where combined urinary and faecal diversion was required. This was achieved by implantation of freely refluxing ureters into an end colostomy [90], producing high volume offensive watery diarrhoea. Increased risks of pyelonephritis and electrolyte abnormalities were reported, and therefore the operation was abandoned. Most commonly, a separate ileal conduit and colostomy are now fashioned, however, managing two stomas is challenging, and so the double barrelled wet colostomy was developed [91]. A loop colostomy is made and brought to the skin surface as a double stoma. From the proximal end (and upper stoma), semi-formed faeces are intermittently evacuated. The distal segment of colon is used to create a separate colonic conduit for urinary diversion. The ureters are implanted into the distal colonic segment which is sealed at its lower end, allowing drainage of urine into the lower stoma. Both stomas can be covered with one appliance. Studies with longer-term follow-up report a risk of pyelonephritis in 10 %, ureterocolonic anastomotic stricture in 2 %, stone in the urinary reservoir in 7 %, hydronephrosis in 2 %, fistula in 29 %, and urine leak in 10 % [92].

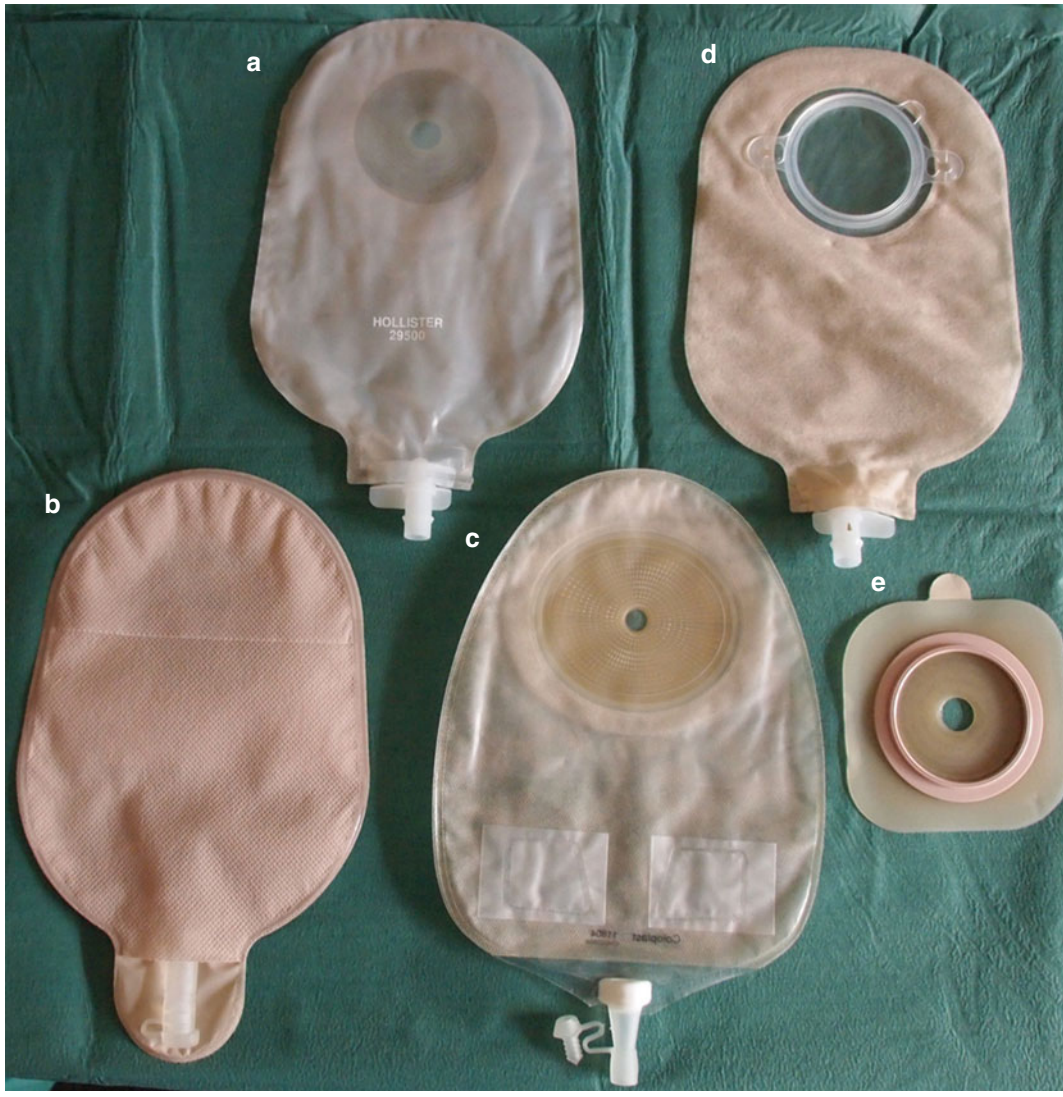

Fig. 8.8 Ileal conduit urostomy stoma bags. (**a**) Single piece opaque urostomy pouch with tap. (**b**) Single piece split film urostomy pouch with bung. (**c**) Single piece clear chambered urostomy pouch with bung. (**d**) Two piece clear urostomy pouch with tap. (**e**) Hydrocolloid baseplate for two piece urostomy pouch

Mitrofanoff

This is a continent catheterisable conduit from the skin to the bladder which was first described by Mitrofanoff in 1980 [93], originally using the appendix (appendicovesicostomy), although the use of ureter, ileum, stomach and Fallopian tube are also reported. It is constructed for patients who require catheterisation of either a native or neobladder, but find it difficult to access the urethra, are unable to tolerate urethral instrumentation, or where the urethra has been excised or the bladder neck closed. It is used in neuropathic bladder dysfunction (spina bifida), after paediatric lower urinary tract reconstruction (bladder exstrophy-epispadias complex, Prune-Belly syndrome, posterior urethral valves), for Fowler's Syndrome (hypercontractile, poorly-relaxing external urethral sphincter associated with urinary retention in women), and for antegrade continence enema (ACE) procedures.

It is essential that the reservoir (bladder) is a low pressure system, and the Mitrofanoff can be combined with ileocystoplasty formation. The appendix is harvested on its mesoappendix, with or without mobilisation of the caecum. The continence mechanism is an anti reflux tunnel at the vesical end, made by either creating a tunnel under the bladder mucosa (intravesical technique) or by bringing a coat of detrusor muscle over it (Lich-Gregoire extravesical approach). In order to prevent reflux, the principle of Paquin's Law [94] is followed, with the aim of making the tunnel length to width ratio around 5:1 (generally aiming to create a tunnel 2–3 cm in length). As the bladder fills, this is compressed with a higher resistance (compared to the bladder pressure) to prevent urinary leak. A bladder hitch to the anterior abdominal wall can be performed to reduce the tension and maintain a straight channel. The other end of the appendix segment (caecal end) is brought out to the umbilicus or right lower quadrant at skin level. It is essential to create a skin flap to reduce the risk of stenosis at the skin level. This can be in the form of a V flap, whereby a triangle of skin is brought down into a spatulated end of appendix, or reconstruction of the abdominal wall skin to create a tunnel of skin which is anastomosed onto the end of the appendix (tubular skin flap [95], VQ [96] or VQZ plasty [97]). Some report a reduced risk of stomal skin stenosis using the umbilical site as compared to the iliac fossa (21 % versus 38 %, although not statistically significant), and with skin reconstruction versus the V flap technique (25 % versus 41 %) [98]. One study reports superiority of the VQZ plasty over the tubular skin flap and umbilical stoma site, with rates of stomal stenosis being 0 %, 45 % and 24 % respectively [99]. The placement of an ACE stopper (Medicina, Adlington, UK) into the channel between catheterisations can reduce the risk of stomal stenosis [100].

Complications

These include stomal stenosis (7–45 %) [101, 102], strictures (4–7 %) [101, 103], urinary leak/incontinence (0–25 %) [102], associated urolithiasis (5–32 %) [101, 104], difficulty catheterising the channel (due to kinking), and a need for revision (in up to 50 %) [102].

Yang-Monti

Where the appendix is not available, ileum is most commonly utilised for a continent catheterisable channel (Yang-Monti). Initially described by Yang in 1993 [105], it was later adapted by Monti, as a single or double tubular channel of ileum [106]. A short segment of ileum is harvested on its mesentery and detubularised longitudinally on the antimesenteric border to create a flat plate. This is then re-tubularised over a catheter by suturing the longer edges together. A 2 cm segment of ileum will create a 14 F calibre channel, whereas 3 cm will produce an 18 F tunnel. The Mitrofanoff technique is used to anastomose the conduit to the skin, and then tunnel the other end into the bladder. If more length is required, a double Monti tube can be created from adjacent segments of ileum. Alternatively, a spiral Monti technique can be utilised, whereby a 4 cm segment of ileum is opened on the antimesenteric border in the middle 2 cm, leaving longer 1 cm strips of bowel at the ends to facilitate reconstruction of a longer channel, with mesentery lying in the middle portion [107]. Overall complication rates of the Mitrofanoff and Yang-Monti channel appears to be similar (21 % versus 23 % at 4 years follow-up) [108].

Vesicostomy

This is considered a temporary form of urinary diversion. A cutaneous vesicostomy involves suturing a small part of the anterior bladder wall directly onto the lower abdominal wall to produce a small, (non-continent) stoma. Urine can be collected into a stoma bag or allowed to drain freely into a nappy or pads. It is used predominantly in infants and children with bladder outlet obstruction or bladder dysfunction, including disorders such as Prune-Belly Syndrome and posterior urethral valves (PUV), until formal reconstruction or ablation of the

PUV is possible. A continent vesicostomy (requiring CISC) can be achieved by taking a flap of bladder wall, which is then tubularised and brought out to skin level as a stoma, with an anti-refluxing valve created at the bladder-end using bladder mucosa (Casale continent catheterisable stoma) [109]. The disadvantages include loss of bladder capacity, and a high risk of stomal stenosis (in up to 45 %) [109]. An alternative continent technique is the button vesicostomy. This uses a short silicone gastrostomy tube such as the Mic-Key button or Mini balloon button, more commonly used for long-term enteral feeding. It is inserted into the bladder via a 2 cm skin suprapubic skin incision. It has a flat button which sits flush on the skin surface, a valve to prevent urinary leakage, and a self-retaining balloon which is inflated and lies on the internal bladder surface. The button is replaced initially every 6 weeks, going to 3 monthly. Again, it is considered a short- to medium-term solution, and has reported complications including urinary leak, UTI and device failure [110].

Ureterostomy

Cutaneous ureterostomy is a technique where the ureter is disconnected from the bladder, mobilised, the distal end spatulated and then directly anastomosed onto the skin (as a spout or with a skin flap) to drain urine freely. Where both ureters require diversion, they can be reconstructed as separate ureteric stomas, however this arrangement can be difficult for patients to manage. The alternatives are to join the ureters as a double barrelled ureterostomy, or to first join the ureters to create a transureteroureterostomy (TUU), with a single ureter being brought out to the skin. Cutaneous ureterostomies are not considered a good option for long-term urinary diversion due to the risks of stomal stenosis (overall risk 8–22 %) [111] and pyelonephritis (0–14 %) [112, 113]. They can be used in the elderly frail population after radical cystectomy as an alternative to an ileal conduit [114], with the benefits of avoiding bowel complications, and reducing the operative times and lengths of hospital stay. The risk of stomal problems (stenosis, hernia, dermitis) have been reported in upto 7 % in this group. In the paediatric population, a temporising role for ureterostomy is described for patients with hydronephrosis and a megaureter, until formal ureteric re-implantation is possible [111].

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Ureteric Stents

9

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Abstract

The ureteric stent is one of the most common urological prosthesis and is used in the management of ureteric obstruction along with reconstructive procedures involving the kidney, ureter and bladder. Stents are composed of synthetic polymeric biomaterials that must remain stable in an unstable chemical environment within the urinary tract. Although there have been many improvements in the design and functionality of stents, the search for an ideal stent continues.

Keywords

Ureteric stent • Urological prosthesis • Ureteric obstruction

Introduction

The ureteric stent is the commonest prosthesis used to manage ureteric obstruction secondary to both benign or malignant causes. It is also used in reconstructive surgery to maintain the patency of an anastomosis either between the two segments of the ureter or between ureter and other viscera such as bowel and bladder. Despite the evolution in design and biomaterials over the years, the ideal ureteric stent has yet to be developed. This chapter will provide an overview of the history and development of the ureteric stent and the different types of stents available for urological procedures.

History of the Ureteric Stent

The widely used double 'J' stent was first introduced by Finney in 1978. However, different types of ureteric stents have been described prior to this, with some dating back to the 1800s. Dr Gustav Simon is credited with performing the first ureteric stenting during open bladder surgery.

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The early stents dating back to the 1900s, were made from fabric coated in lacquer varnish. It was in 1967 that endoscopic insertion was introduced by Dr Paul Zimkind who placed a straight silicone prosthesis as a ureteric splint. McCullough devised the 'shepherd's crook' stent in 1974 with the aim of ensuring that the stent remained in a better position within the urinary tract [1]. Recently, modifications have focused on composition, patients' comfort and the longevity of the stents.

Stent Function and Physiology

The ideal ureteric stent should relieve intra/extra-luminal obstruction, be easily inserted, be radiopaque, resist encrustation or infection, avoid migration, be affordable and cause minimal discomfort to the patient [2]. Hollow ureteric stents are intended to allow drainage of urine through and around the stent [2]. The normal flow rate of urine in an unobstructed ureter is 0.5 ml/min, although it may be as high as 4 ml/min in patients with diabetes insipidus [3]. The presence of a stent reduces the urine flow rate by inhibiting ureteric peristalsis which results in a paralytic effect [4]. This loss of active propulsion also results in impaired transit of stones or stone fragments. Thus any movement within the ureter predominantly occurs due to a combination of ureteric dilatation and the effect of gravity [5]. This is highlighted by a study comparing the effects of stenting on the stone free rate after extra corporeal shock-wave lithotripsy (ESWL) for ureteric stones. In this particular study the authors concluded that there was a significantly higher stone free rate in patients without a stent compared to those with a stent. (89.9 % versus 81.3 %) [6].

Whilst some investigators have shown no difference in urine flow rates, with urine outputs of up to 100 ml/h achieved between commercially available stents, the composition of the stent does appear to be important [7]. A softer stent is easily kinked resulting in a slower flow and high pressures within the ureter regardless of the stent diameter. A harder stent has better drainage with less risk of kinking, but is found to be more uncomfortable for the patient and has the additional risk of ureteric ischaemia and erosion [8]. Stoller et al. reported an *in vitro* study proposing that urine flow and stone propulsion is greater with the use of a helically ridged stent when compared to a smooth stent. As most fragments of stone pass in the space between the stent and the ureteric wall, a spiral ridged stent not only optimises this but also allows most of the urine to travel around the stent. In instances of external compression, the helical stent is not as easily compressed and also allows urine to flow through the lumen [5]. It is important to remember that the rate of urine flow is also affected by additional patient related factors other than those mentioned above. These include the intra-renal pressure, intra-vesical pressure and urine density amongst others.

Indications for Stent Insertion

The main indications and contraindications to ureteric stenting are shown in Table 9.1.

Since its inception, ureteric stenting has played an adjunctive role to endoscopic stone surgery. This is to prevent post-operative mucosal oedema and residual stone fragments obstructing the ureteric lumen and causing renal colic. Due to the potential morbidity related to the ureteric stents themselves, the risk-benefit question 'to stent or not to stent?' should be considered.

Rane et al. studied 42 patients following elective ureteroscopy combined with lithoclast fragmentation for 6–10 mm ureteric stones. Follow-up at 24 h and 1 week showed that 55 % of patients had no post-operative discomfort, 38 % had some discomfort, and 7 % required parenteral analgesia. Only 1 patient had to be re-admitted with loin pain and 2 patients experienced discomfort at 1 week. The study concluded that routine stenting following elective stone treatment was not necessary in this subset of patients [9].

Another prospective randomised control trial by Denstedt et al. in 2001 included 58 comparable patients following routine ureteroscopy and laser fragmentation. They were randomised after stone fragmentation to a stent versus no stent

Table 9.1 Indications and contraindications to ureteric stenting [8]

Indications:
Intrinsic ureteric obstruction
Benign – stones, stricture, congenital obstruction, PUJ obstruction
Malignant – transitional cell carcinoma
External ureteric obstruction
Benign – retroperitoneal fibrosis, aortic aneurysm, endometriosis
Malignant – Colorectal/gynaecological/lymphoma/bladder and prostate cancer
Prophylactic
Post ureteroscopy with or without stone fragmentation
Protect ureteric anastomosis – renal transplant/pyeloplasty/ureteric injury
Intraoperative ureter identification – complex abdominal/pelvic surgery
Prior to chemotherapy/radiotherapy
Contraindications:
Infected, obstructed kidney in an unstable patient
Relative contraindication: Urine production <400 ml/day – high risk of encrustation

group. Those in the stent group had the stent removed at 1 week post-operatively. Follow-up was at 1, 6 and 12 weeks. Their results showed that at 1 week, the symptoms of flank pain, abdominal pain, dysuria and frequency were greater in the stented group. At 6 and 12 weeks no difference in the pain or analgesic requirements were seen. Only 1 patient was admitted with urinary sepsis in the stented group and 1 patient was admitted with vomiting in the non-stented group. The stone free rate was still 100 %. They concluded that patients with stents have significantly greater symptoms with no difference in complications or stone free rates and suggested that routine stenting is not recommended after uncomplicated surgery [10].

Types of Ureteric Stents

Ureteric stents are available in many shapes, sizes and biomaterials. Classically the double 'J' stent is used routinely but not all stents are either coiled or hollow. Stents without side holes have been shown to drain 40–50 % less efficiently than those with side holes [4].

Stents can be broadly classified into:

(a) Non-metallic stents
(b) Metallic stents

Non-metallic Stents

Stent Properties and Biomaterials

Ureteric stents are composed of synthetic polymeric biomaterials that must remain stable in the unstable chemical environment within the urinary tract [11]. Additionally the design must follow certain basic principles that provide the parameters for optimal stent function. Some of these parameters are summarised in Table 9.2 below [12–14].

Non-metallic stents can be either synthetic or biodegradable. The most common synthetic polymer currently used is polyurethane. Whilst silicone is more chemically inert, the inherent rigidity results in more patient discomfort. The alternative biodegradable stents must maintain integrity for at least 48 h before beginning to disintegrate spontaneously. They do not require a second procedure to be removed from the ureter and can only be used for short term purposes [15]. Lingeman et al. describe a biodegradable temporary ureteral drainage stent (TUDS). The safety and effectiveness of the stent was defined as adequate intervention-free drainage for 48 h without stent migration. The stent was effective in 78.2 % of the 88 patients in the study population with a satisfaction rate of 89 % [16]. Research into long term biodegradable ureteric prostheses is still underway.

Table 9.2 Stent properties influencing stent design & function [12–14]

Stent property	Comment
Biodurable	The resilience of a stent to disintegrating in the urine's chemical environment.
	The latest generation of biodegradable stents however, are designed to be less resilient. They biodegrade within the urinary tract after a specific length of time so that they do not require removal as a separate procedure.
Biocompatible	The effect of the stent on its environment. Stents should be chemically 'inert' and elicit a minimal inflammatory reaction.
Encrustation	Despite stent coatings designed to resist encrustation, this can be a significant problem particularly in stone patients. Silicone coated stents are particularly prone to encrustation.
Coefficient of friction	The ease with which a stent can be inserted into the urinary tract without friction.
Memory	Refers to the ability of a JJ stent to spontaneously curl when deployed and remain as that shape. A coil strength memory of 20 g prevents stent migration [12].
Radiopaque	Stent walls contain metal salts which allow radiological visualisation
Diameter	The ratio between the inner and outer diameter of the stent determines the urine flow as well as the tensile strength. The larger the internal diameter the greater the potential for flow.
Cost	As a widely used prosthesis requiring frequent changes, stents must be cost-effective

Metallic Stents

Due to their rigidity and discomfort, metallic stents are usually reserved for upper tract extrinsic obstruction in cases of advanced malignancy. Their use in stone disease is not recommended and they appear less effective for intrinsic obstruction. They are thought to have a longer lifespan and thus can be left *in-situ* for a longer time period. In general, the metallic stent provides an alternative to the use of two simultaneous double J stents in patients with extrinsic compression and frequent stent blockages [17]. Dual ureteric stents have also been successfully described and are more appropriate in selective patients [18].

Kulkarni and Bellamy described a 4 year follow-up study of their experience with a self expanding nickel-titanium Memokath ureteric stent. This stent has a thermal memory for shape and is used for both benign and malignant ureteric strictures. The expanded proximal fluted end holds the stent in position across the stricture (See Fig. 9.1). As the stent softens at low temperatures, it must be cooled to below 10 °C by irrigating cold water in order to allow stent removal. Of the 37 stents inserted since 1996, all bar 2 achieved upper tract decompression. The unsuccessful cases underwent replacement using stents which had a better length. Stent migration occurred in three patients after treatment of the underlying malignancy. Although upper tract decompression was maintained, the stents were replaced to relieve irritative urinary symptoms from malpositioning of the stent. There were no reports of stent encrustation or hospital attendance due to stent symptoms, sepsis or haematuria [19].

Ureteric Stent Design

A number of stents are currently available. The common ureteric stent designs are summarised in Fig. 9.1 [20–29].

Symptoms Related to Ureteric Stents

The morbidity associated with stent insertion is all too familiar. Patients often complain of general loin discomfort and experience irritative lower urinary tract symptoms (LUTS). Loin pain has often been attributed to reflux of urine the ureteric stent and has been documented in 79 % of stents [30]. Pressure flow studies have shown equal pressure transmission from the bladder to the renal pelvis in all phases of bladder filling and emptying which partly accounts for the loin pain [31]. This *in vivo* study concluded that stent insertion should be for the minimum duration required within

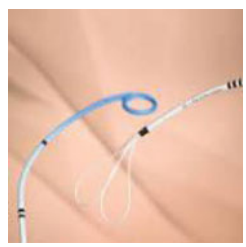
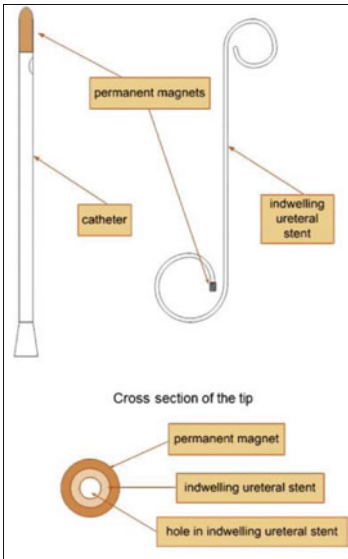
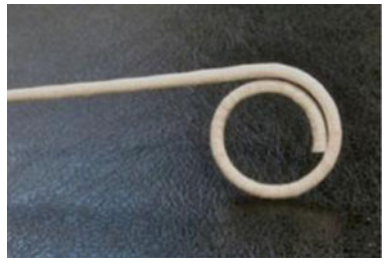
Non-metallic stents	
	**Double J stent** Standard ureteric stent.
	**Multi length stent [22]** Multiple curls allow accommodation of stent within ureters and is 22–30 cm in length.
	**Grooved stent [23]** Made of Tecoflex® material, softens at body temperature to minimise patient discomfort. Aims to encourage urine drainage around stent.
	**Spiral stent [4]** Developed for increased extraluminal drainage in particular for chronic external ureteric compression.
	**Dual durometer stent [24]** Dual Durometer Percuflex™ Stent with HydroPlus™ coating featuring a novel bladder loop design. Made up of two biomaterials. A firm material is used at the renal end and a softer one at the bladder end in order to reduce stent symptoms.

Fig. 9.1 Common ureteric stent designs



Magnetic tip stent [25,26]

Ureteric stent retrieval without the need for cystoscopy.



Biodegradable stents [27]

Uriprene™

Radiopaque, glycolic-lactic acid
Degrades starting distally and degradation continues proximally which prevents ureteric obstruction from the degraded fragments and also minimises bladder irritation.

Metallic stents

Fig. 9.1 (continued)

	**Double J stent [28]** **Resonance®** Nickel-cobalt-chromium-molybdenium alloy. Tightly coiled metal wire. Firm and ideal for external ureteric compression.
	**Double J stent [29]** **Passage™** Gold plated metal (Snake stent) Spiral windings along tubular coil structure and flexible pigtails
	**Double J stent [30]** **Silhouette®** Polyurethane and metal wire coil reinforcement

	**Self expanding** **mesh stent [31]** Large bore stents, 24Fr–30Fr, made of a super elastic alloy covered by a polymeric material for preventing tissue in growth. Useful in chronic ureteric strictures.
	**Self expanding** **Memokath® 051 [18,20]** Self expandable nickel-titanium stent.

Fig. 9.1 (continued)

sterile urine which prevents long-term renal parenchymal damage and avoids the morbidity associated with urosepsis [32].

Joshi et al. presented the first validated symptom assessment tool for patients with a ureteric stent by using the ureteral stent symptom questionnaire (USSQ) and EuroQol as assessment tools. The USSQ is a validated psychometric measure of stent symptoms and quality of life (QoL). The various domains include urinary symptoms, pain, general health, work performance and sexual health. Patients were subdivided into those with stents from healthy controls and those with a stone but no stent. The EuroQol is a QoL questionnaire with a visual analogue score which looks at holistic physical, emotional and social health of the patient. The results from studies using the EuroQol showed a cumulative effect of symptoms and a significant negative impact on health related QoL in those patients with a stent. The authors conclude the need for an improvement in stent design together with preoperative patient counselling. However, the limitations of this study included the use of only one type of stent, limited/unequal patient group numbers and the use of a relatively complex questionnaire [33].

A further meta-analysis has looked at the possible beneficial effects of alpha blockers on stent related discomfort and symptoms [34]. From a total of five studies, 461 patients were identified for inclusion into the meta-analysis having received the alpha blockers, tamsulosin or alfuzosin or placebo and the results suggest, that alpha blockers can help relieve stent symptoms and discomfort [34].

A randomised controlled trial by Dellis et al. also confirmed the above findings in 150 consecutive patients undergoing insertion of a double 'J' stent who were randomised to either tamsulosin, alfuzosin or placebo. The USSQ was completed at week 1 and 4 after insertion of the stent and again 4 weeks after stent removal. There was less pain, LUTS and impairment to general/sexual health in those taking the alpha-blockers with no difference between tamsulosin or alfuzosin [35].

Complications

The most common ureteric stent complications are summarised below (Table 9.3).

The Forgotten Stent

Despite the increasing use of stent registers, the system is by no means robust and stents are still left within the urinary tract for prolonged periods of time. The potential morbidity, mortality and legal implications as a result of these forgotten stents is well documented [36, 37]. Unfortunately it is often the non-compliant patient or those with no fixed abode that are at greatest risk. Stent encrustation and stone formation is not only one of the most serious complications but its management can also pose the greatest challenge. A further study has stated that stents need not be left in for very long durations for their encrustation burden to become problematic. This retrospective study reviewed 49 encrusted stents which required intervention. Of these 75.5% were encrusted within 6 months and 42.8% within 4 months of insertion. All, except one, were successfully treated using a multimodal approach using ESWL, ureteroscopy or PCNL. Only one patient required an open procedure to have the stent removed [38].

Future Developments

Currently biodegradable stents are an attractive option as they are designed to serve a purpose for a short period of time, after which they disintegrate. Hence, there is no need for removal with a second procedure. Another potential benefit of such a stent is decreased bacterial adherence and encrustation as the stent surface is constantly changing as it degrades. This may make the stent softer and more comfortable for patients. Materials currently under development include polyglycolic acid, polylactic acid, poly(lactic-co-glycolic acid) and alginate-based materials [39–41]. The most promising is the Uriprene™ stent and clinical trials are still ongoing [13].

Table 9.3 Complications with ureteric stents [11, 13, 14, 20, 32, 36]

Complication	Summary
Stent symptoms (pain, haematuria, urgency, frequency)	80 % of patients.
Reflux	79 % of stents- causing loin pain.
Stent induced UTI	Bacterial colonisation rates of 40–90 %
	A small subset suffer urinary tract infections.
Stent encrustation	Worse at proximal and distal ends of the stent.
	High risk in patients with urolithiasis or pregnancy
	Dependant on stent duration
	<6 weeks – 9.2 %
	>6 weeks – 47.5 %
	>12 weeks – 76.3 %
Malposition	Incorrect initial placement of ureteric stents
Stent migration	Displacement of the ureteric stent from the correct position
Inadequate relief of obstruction	Incorrect type of stent or the stent is blocked
Stent fracture	Seen with polyethylene stents in the past. These are brittle therefore fractured most commonly at fenestration sites.
Ureteric erosion or fistulisation	Rare complication. Erosion into surrounding structures e.g. vasculature may result in intermittent haematuria.
The forgotten stent	The forgotten stent still occurs despite the advent of stent registries.

Drug eluting stents have an established role in cardiovascular disease. Their use in urology however, has thus far been limited. In 2009, Kotsar et al. described a biodegradable urethral prostatic stent that eluted 5 alpha-reductase inhibitor directly into the prostate of patients with benign prostatic hyperplasia (BPH). The idea was that local inhibition of dihydrotestosterone would help reduce the prostate volume. Unfortunately over half of the patients developed urinary retention in under a month and required supra-pubic catheterisation [42]. Future developments may combine drug eluting prosthetic materials within the urinary tract in order to reduce the incidence of urinary tract infections, target cancer therapy, hormone replacement or deliver chronic pain therapies.

Tissue engineering with the use of autologous chondrocytes seeded onto a tubular biodegradable mesh may also have a role in future stent technology. Along with biodegradability, this stent would be flexible and biocompatible to its host's environment [43, 44].

Conclusion

The ureteric stent is still the most common prosthesis used in urological practice and has evolved significantly since the 1800s. The associated morbidity however, remains a problem. The expanding armamentarium of biomaterials and designs aim to achieve a balance between stent function and comfort. Whilst the perfect stent has yet to be discovered, much hope lies in a future with an ideal biodegradable, tissue engineered, drug-eluting stent.

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Prosthetics and the Prostate

10

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Abstract

The management of bladder outflow obstruction has progressed since the early management using catheters and drainage tubes to empty the bladder. Surgical interventions initially involved open retropubic prostatectomies but with the advancement of endoscopy, a number of techniques to resect the prostate are now common place. This chapter covers prosthetic devices used in the management of bladder outflow obstruction.

Keywords

Lower urinary tract symptoms • Bladder outflow obstruction • Urethral stents • Prostatic lift implant • Urolift

Introduction

Lower urinary tract symptoms (LUTS) become a common urological problem as men get older. The number of men requiring medical or surgical interventions for the management of LUTS thought to be due to bladder outflow obstruction has progressively increased as the life expectancy amongst the population has increased. The need for medical or surgical intervention will depend on the degree of bother that the patient suffers as a result of LUTS as well as the impact on renal function and whether complications such as renal or bladder calculi and recurrent urinary tract infections develop. Initially, lifestyle modifications and bladder retraining, for example pelvic floor exercises, double voiding, oral fluid modifications are suggested for LUTS as often the symptoms are a result of both obstructive voiding

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symptoms and bladder storage abnormalities. In young men the common causes of bladder outflow obstruction include urethral stricture disease, meatal stenosis or phimosis. In older men with and without lower urinary tract symptoms careful community based studies have shown that approximately half of symptomatic men have measurable benign prostatic enlargement (BPE) [1].

Following lifestyle modifications, pharmacological treatment options use selective alpha blockers (e.g. Tamsulosin, Terazosin, Alfuzosin). Alpha blockers were initially developed as a treatment for systemic hypertension but also showed an improvement in LUTS. The mechanism of action is by relaxing the smooth muscle within the prostate by antagonising α-1a adrenergic receptors within the prostate and bladder neck. This decreases the voiding pressure required to pass urine urethrally and can improve bladder emptying. However, α blockers are not likely to be tolerated in patients suffering from syncope or postural hypotension. Apart from symptomatic hypotension, male orgasmic dysfunction is another undesirable side effect reported in a proportion of men taking alpha blocker drugs [2]. Alternative drugs used for BPH include 5 α reductase inhibitors, such as Finasteride or Dutasteride, which inhibit the conversion of testosterone to dihydrotestosterone leading to a gradual decrease in the size of the prostate. However, 5 α reductase inhibitors can take up to 6 months to be effective as well as having side effects such as erectile dysfunction, reduced libido and reduced ejaculatory volume [3].

Failed medical treatment or patients developing acute urinary retention may undergo surgery in the form of a trans-urethral resection of the prostate (TURP) using a conventional loop resection of the prostate adenoma. However, novel methods of ablating the prostatic tissue and/or enucleation of the adenoma include green light laser or Holmium laser enucleation (HOLEP). These endoscopic procedures require either a general anaesthetic or spinal anaesthesia such that patients with significant comorbidity may not choose or be offered surgical intervention therefore leaving only less invasive alternative options such as intermittent self catheterisation or a long term indwelling catheter.

Urethral Devices

Minimally invasive techniques are available which use prosthetic devices to overcome or reduce bladder outflow obstruction and so allow urine to flow through the prostatic urethra. These devices include both permanent and temporary prostatic stents or a urethral lift device.

Temporary Urethral Stents

First Generation

Non-epithelialising temporary urethral stents have undergone several stages of development. Different designs have been trialled and the long-term outcomes have been variable with each generation. The first generation included both the Urospiral® stent (Porges, Paris, France) and the Prostakath® stent (Engineers and Doctors, Copenhagen, Denmark). The Urospiral stent was designed as a non-expandable coiled, rust proof, stainless steel stent. The stent is deployed cystocopically and initial studies suggested that most patients managed to void. The Prostakath stent was a later model and a modified non-expandable coiled stent that is gold plated for improved biocompatibility.

One study which has reviewed the outcomes of 110 men having undergone insertion of either the Urospiral or Prostakath stent demonstrated a 65 % success rate although this was only based on subjective symptoms and satisfaction [4]. After a minimum follow up of 3 years (mean 53 months, range 36–80 months), removal of the stent was required in a total of 35 patients and a further 41 patients demonstrated late complications which included stent migration, encrustation, failure to void and recurrent urinary tract infections. There was no significant difference in complications between Urospiral and Prostakath stents with the gold coating having little impact on outcomes. Urethral injury was more common during insertion of such stents as they are of fixed calibre.

The non-deformable design also posed a urethral injury risk at the time of removal. Both stents required regular cystoscopic surveillance in order to confirm the position and check for narrowing of the lumen due to early encrustation.

Second Generation

Following the experiences with the first generation of stents, the Prostacoil® stent (Instent, Eden Praire, MN) was developed as a second-generation stent. The Prostacoil stent was made from a Nitinol alloy and expands following insertion. The stent had a larger calibre than previous stents and allowed catheterisation and endoscopic examinations whilst still in-situ. In 1996 a comparative study by Yachia and Aridogan examined the differences between the Prostakath (first generation) and Prostacoil stents (second generation) [5]. The study reviewed 117 patients between the ages of 52 and 94. A Prostakath stent was inserted in 49 patients and the Prostacoil stent in 68 patients. The end-points in this study-included ease of insertion, need for repositioning, rate of migration (proximal or distal migration), infection, encrustation and length of time in situ. A tenth of the Prostakath insertion procedures were abandoned as the stent was found to be unstable and correct positioning was impossible. Correct positioning was achieved in 83 % of patients initially. The Prostacoil's large calibre allowed 100 % of the stents to be positioned correctly with no migration noted on follow up. However, the size of these stents did lead to a significant increase in irritative urinary symptoms. The rate of infection was the same for both stents at approximately 10 %. Encrustation was noted in 40 % of Prostakath stents at 1 year and 30 % of Prostacoil stents at 2 years and the overall maximum indwelling time for Prostakath stents was 12 months and 36 months for Prostacoil stents. The study confirmed the advantages of using second-generation stents and paved the way for future designs [6] (Figs. 10.1, 10.2, 10.3 and 10.4).

Third Generation

The third generation of stents were introduced in the early 1990s, these stents demonstrated thermo-expandable properties that reduced the rate of stent migration and decreased the risks of stent removal. The first example of the third generation stents was the Memokath® stent (Doctors & Engineers, Kvistjaard, Denmark) which were made from a nickel-titanium alloy with a floppy consistency that was thermosensitive and provided "shape memory". The stent could be deployed using a trans-rectal ultrasound and fluoroscopy to confirm positioning. The initial stent size was 24 F and expanded to 42 F when flushed with heated saline or water at a temperature of 55–65 °C. The stent could easily be removed by flushing the urethra with cold saline, which would in turn soften the stent and allow easy extraction. This resolved the previous issue of urethral injury on removal, which was noted in previous stent

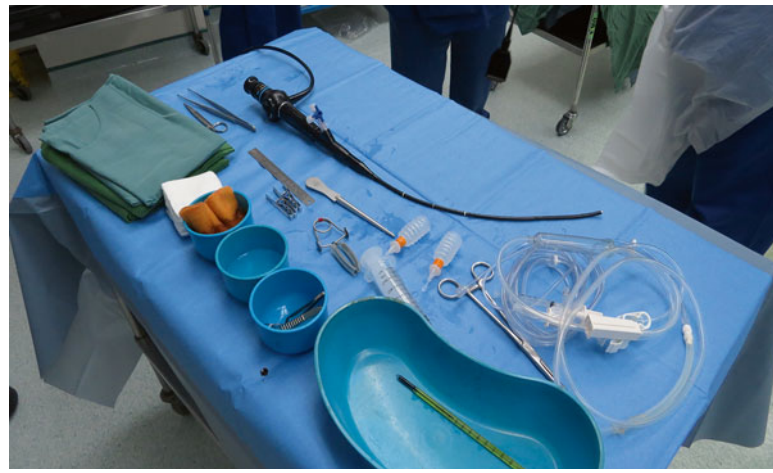

Fig. 10.1 STORZ® flexible cystoscope and Memokath stent insertion kit

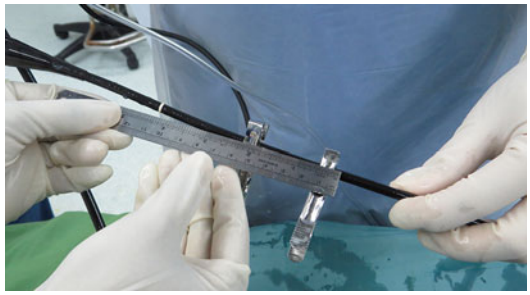

Fig. 10.2 Flexible cystoscope used to measure the length of the prostatic urethra to help plan insertion of the Memokath stent

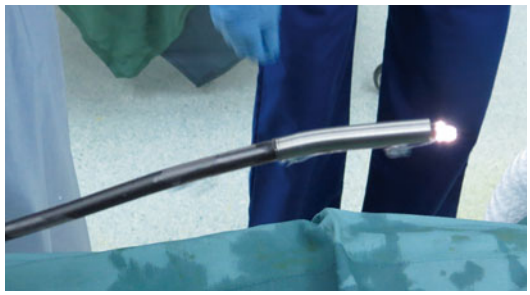

Fig. 10.3 Memokath stent sheathed over flexible cystoscope prior to insertion in the patient

Fig. 10.4 Irrigation delivery system in the Memokath stent insertion device

designs. The initial version of the Memokath stent expanded throughout its whole length but this still led to a high incidence of stent migration. In 1992, the Memokath stent was redesigned to expand in a cone shape where the distal end would only expand and this subsequently decreased the incidence of migration. The Memokath stent is available in different lengths between 30 and 70 mm, and therefore limits the range of patients that could benefit from the procedure to those with appropriate prostatic urethral lengths.

In 2006 Armitage et al. published a systematic review of the Memokath stents [7]. This study examined 14 case series previously published on Memokath stents after 1992. Less than 50 patients participated in each of the 11 series and all of the patients were deemed too high risk for traditional bladder outflow surgery. A total of 839 patients were examined and the outcomes of each study compared. A failure rate between 0 and 48 % was reported, although follow up was inconsistent in many studies. Immediate failure was reported in 4 % of the patients. The most common cause of failure or dysfunction was stent migration. Five of the studies reported an improvement in International Prostate Symptom Score (IPSS) of between 11 and 19 points. Seven of the studies demonstrated improvement in the urinary peak flow rate and a further four studies reported a decrease in post void residual volume. This systematic review concluded that the Memokath stent is a viable alternative to bladder outflow surgery in high-risk patients. Stent durability still remains uncertain, as the length of follow up was inconsistent throughout the studies and inadequate to provide definitive conclusions.

The Z-stent was another third generation stent (Wilson-Cook medical, Winston Salem, NC). This 0.3 mm stent was made of a stainless steel cylindrical shape with a zig-zag configuration of ten bends. Each bend was 10 mm in diameter and 10 mm in length. Each bend or segment was connected in tandem and coated with 24 carat gold in order to improve the biocompatibility. Clinical experience using the Z-stent was limited and it failed to gain widespread use. Further changes to the shape by changing to an hourglass or bell shape were made to improve the rate of stent migration. However, the rate of migration on long-term follow up rendered these stents clinically ineffective [6].

Fourth Generation

Further improvements in stent design were seen in the fourth generation of stents when, Markovic

et al. developed the Allium stent which was a triangular cross sectional stent that matches the contours of the prostatic urethra [8]. The stent's design allows for high radial force within the body of the stent that decreases in the region of the external sphincter complex. This was intended to reduce the risk of stent migration without any impact on continence. The stent also had a special plastic coating intended to reduce the risk of stent encrustation. The stent's large calibre at 45 Fr also allowed future cystoscopic procedures through the stent if necessary.

More recently the outcomes of the Allium TPS stent has been reported in a series of 51 patients [9]. This stent is a coiled and highly flexible stent made from a combination of nitinol and fully covered with a copolymer, which prevents tissue ingrowth, encrustation and stone formation. After at least 12 months follow up the mean IPSS reduced from 26.4 to 7.7 with an increase in the mean Q_{max} from 5.5 to 16 mL/s. Therefore the early published reports from this two centre study have shown that the Allium TPS provides a good option for those men who are not suitable for more invasive BPH surgery.

Permanent Epithelialising Stents

Permanent epithelializing stents have been designed to promote epithelialisation over the structure of the stent and so effectively embedding the stent within the urethral mucosa. The Urolume Wallstent (American Medical Systems, MN) consisted of a stainless steel alloy wire woven in a tubular mesh. This stent maintained a lumen of 42 Fr that allowed further cystoscopic procedures and even passage of a resectoscope. The stent is progressively covered by urothelium over approximately 4–6 months. De Vocht et al. published a series observing 10 years follow up of 15 patients with the Urolume Wallstent inserted for urethral strictures [10]. Two patients had their stent removed because of extensive and obstructive mucosal tissue proliferation. Two patients did not tolerate the Wallstent and required removal after complaining of symptoms of discomfort and pain. Two patients developed stenosis of the stent after 7 and 9 years. Half of the patients reported having occasional incontinence. Patients with the Wallstent generally still complained of lower urinary tract symptoms, stress incontinence, urge incontinence, and discomfort following ejaculation. Only two of the patients from this series felt satisfied with its function and the improvement in symptoms.

The ASI Titan stent was another expandable titanium intraprostatic stent. In a series of 30 patients published by Kirby et al. with BPH related infravesical obstruction, effective micturition was achieved in 25 patients [11]. After a 1-year follow-up in 21 of these men, the average Q_{max} was 10.8 mL/s. However, these stents developed excessive epithelialisation and also stone formation resulting in abandonment of this particular device.

Fundamentally, removal of these stents may have to be considered for severe symptoms due to obstructive mucosal proliferation or stone

Fig. 10.5 ASI prostatic stent with a stone requiring complex surgery to remove (Courtesy of Prof McNicholas)

formation due to failure of epithelialisation and yet may be extremely challenging, as their "permanent" description implies (Fig. 10.5). Ironically, a man undergoing insertion of such a stent because he is unfit for a standard procedure may therefore face a much more challenging procedure later when he is older and often even less fit. As a result these stents have largely fallen into disuse.

Urolift Implant System

The Urolift implant system (NeoTract, Pleasanton, California) is the latest device designed as an alternative to urethral stents. The aim of its design is to minimise foreign body exposure and reduce the risk of encrustation, calcification and recurrent urinary tract infections. The device is deployed cystoscopically and the procedure can be performed under intravenous sedation or by local, spinal or rarely under general anaesthetic if necessary. Initially, the cystoscope is placed at the level of the prostatic urethra. The prostatic fossa is opened with lateral traction from the cystoscope to the surgeon's satisfaction and a fine 19-gauge needle is deployed through the compressed lateral prostatic lobes and anchors to the fibromuscular prostatic capsule. The procedure is repeated on both lateral lobes and multiple implants can be used on each side, depending on the size of the prostate. The implants are small and retract into the prostatic adenoma and readily epithelialise. The tethering of prostatic tissue opens the prostatic urethra and subsequently reduces the level of obstruction.

A multicentre prospective study was published comparing the Urolift procedure to a "sham" procedure [12]. A total of 206 men were randomised with 140 patients having the urethral prostatic lift. Each patient was 50 years old or over with an AUASI (American Urological Association Symptom Index) score of 13 or more, maximum flow rate of 12 mL per second or less, and prostate sizes between 30 and 80 g. Patients undergoing "sham" procedures were visually obscured from the surgeon and underwent cystoscopy with noises mimicking deployment of the implant. Prostatic urethral lift patients showed a reduction AUASI of 22.1 at baseline to 11.0 and 11.1 at 3 months and 12 months respectively. Patients also experienced an improvement in the maximum flow rate of up

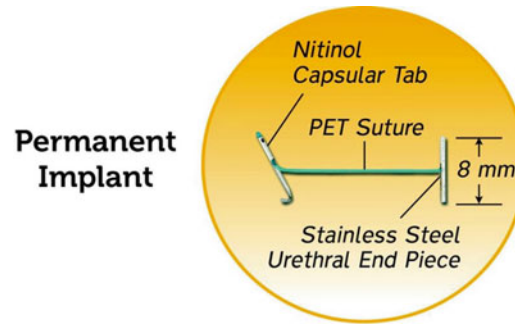

Fig. 10.7 Urolift permanent implant

Fig. 10.6 Urolift delivery device

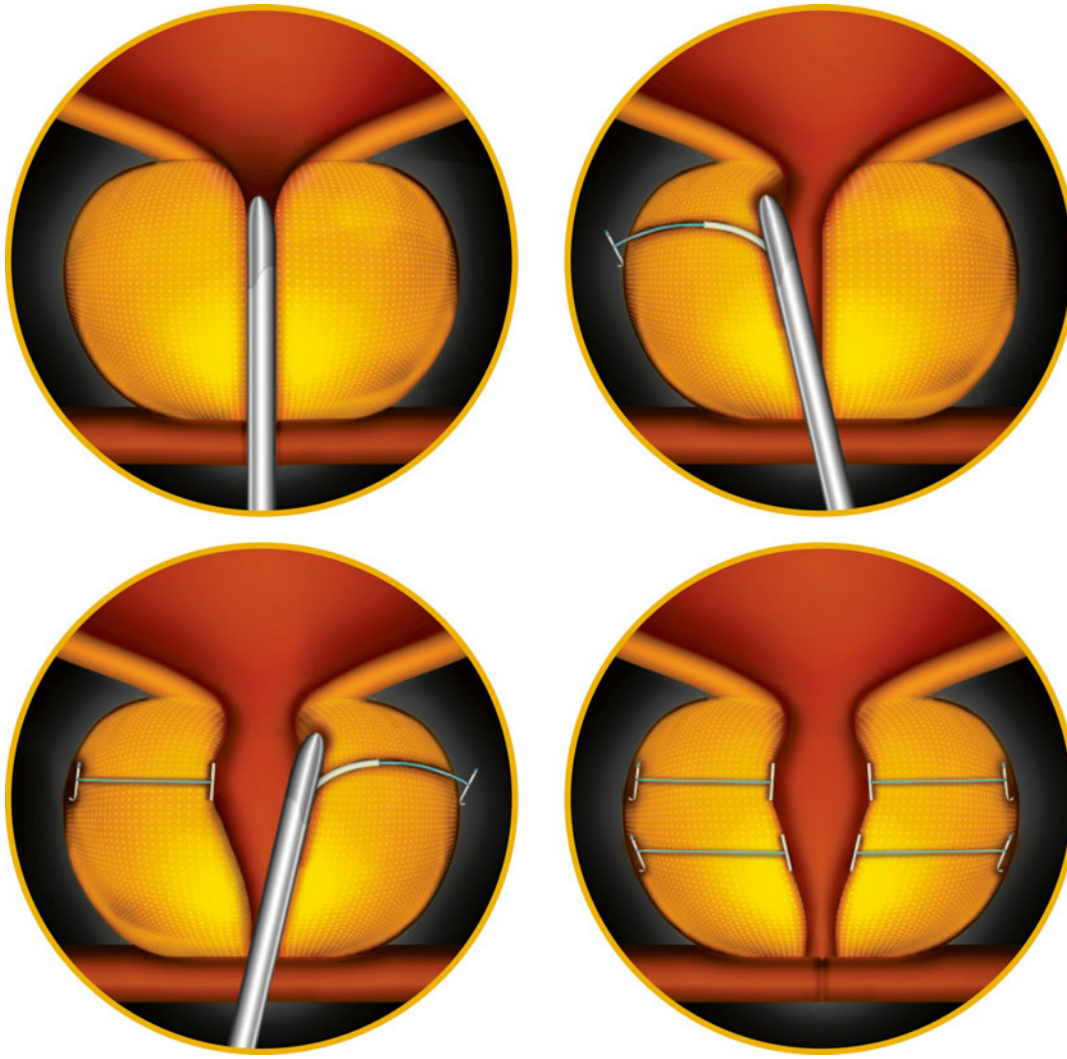

Fig. 10.8 Illustration showing the positioning of the Urolift permanent implant in the prostate gland

to 4.4 mL per second at 3 months and 4.0 mL per second at 12 months i.e., greater than seen with drug therapy. None of the patients reported any disturbance of ejaculation or sexual dysfunction. Three year data from the same study showing similar positive outcomes was reported by Roehrborn [13]. In particular stone formation has been rare if the devices are properly positioned.

Another international multicentre study described the Urolift technique and described 102 patients treated across seven centres. This study reported no failure in implant insertion and only 6.5 % of patients failed and underwent a subsequent TURP [14]. Overall, the Urolift implant has been shown to be a promising alternative to bladder outflow surgery and has been approved by the UK National Institute of Health and Care Excellence (NICE) as both safe and cost effective if performed in the day case scenario – as most are [15]. However, longer term follow up with this device have yet to be published (Figs. 10.5, 10.6, 10.7, 10.8, 10.9 and 10.10).

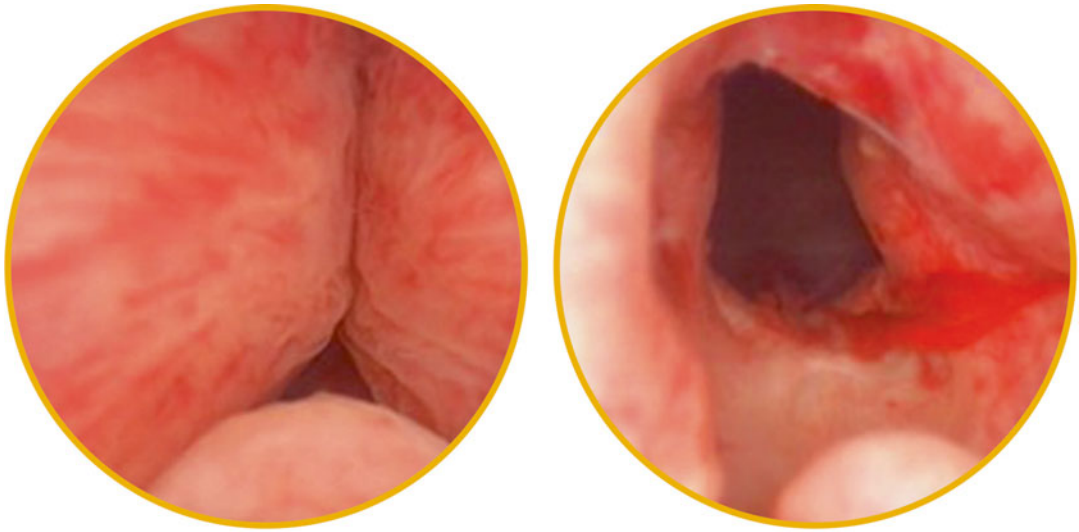

Fig. 10.9 Endoscopic views of the prostate cavity before and after the Urolift procedure demonstrating the open prostatic channel following placement (Images courtesy of Dr. Peter Chin, Wollongong, NSW, Australia)

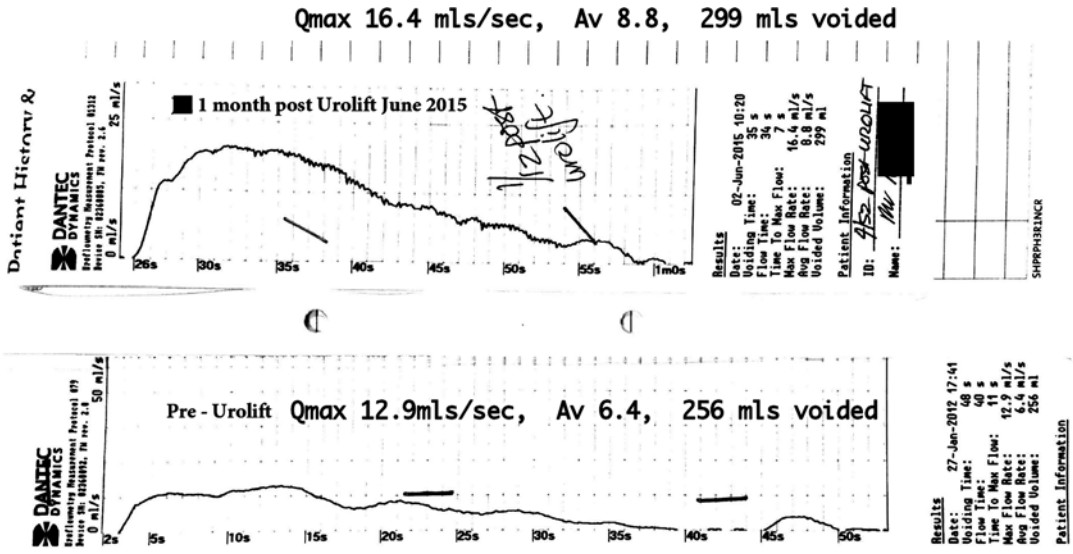

Fig. 10.10 Original flow rates demonstrating the change in the Q_{max} before and after the Urolift procedure

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Testicular Prosthesis

11

Francesco De Luca, Amr Abdel Raheem, and Giulio Garaffa

Abstract

Testicular prostheses or implants have been in use for more than 70 years to guarantee an acceptable scrotal cosmesis in patients who have an empty scrotal sac or an atrophic testis and also when scrotal reconstruction is contemplated. Although various materials have been used in the production of testicular implants, silicone still remains the most popular option. The overall patient satisfaction can be as high as 91 %, with an overall improvement of self-esteem and body image.

Keywords

Implants • Testis • Silicone • Testicular prosthesis

Introduction

The main indication for implanting a testicular prosthesis is the restoration of the normal scrotal symmetry in patients who present with an empty hemi-scrotum or have an atrophic testis. The scrotal sac may be empty due to a number of causes which are listed in Tables 11.1 and 11.2.

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For some patients, an empty scrotum can be associated with body dysmorphic disorder, psychological distress and concerns about masculinity. For this group of patients a testicular prosthesis can be extremely helpful.

The ideal prosthesis should resemble a normal testicle in shape, size and consistency and should be made of an inert material, which resists trauma and does not start an immune response or deteriorate with time.

A testicular prosthesis can be also used as a "spacer" between the inferior aspect of the pubic bone and the dorsal aspect of the penis after suspensory ligament division. This is to prevent the risk of reattachment of the penis to the pubic bone and helps to push the shaft forward and downward [1].

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Table 11.1 Benign aetiology of missing testicle

Testicular agenesis
Testicular atrophy
Cryptorchidism
Torsion
Trauma
Infection
Female to male transsexualism

Table 11.2 Malignant aetiology of missing testicle

Testicular cancer
Orchidectomy for paratesticular lesions
Castration for prostate cancer

History

Testicular implants have been used for more than 70 years and the history of their development is covered in Chap. 2. Girdansky and Newman described testicular prosthesis implantation in two patients in 1941 [2]. The operation was successful, but the patients were unhappy with the texture of the implants, which were made of Vitallium, an inert alloy of cobalt, chromium, and molybdenum used in dentistry and orthopedic surgery. Since then a variety of different materials have been used, including lucite [3], glass [4], methacrylate and gelfoam [5], rubber silicone [6], plastic [7], silastic gel, plexiglass and dacron [6]. Silicone testis implants became available in 1973, and were manufactured with a design similar to the one used for breast implants. This type of prosthesis became very popular between 1973 and 1992 [8]. Despite the lack of official reports of patients with silicone testicular prosthesis developing systemic diseases, the manufacture of the silicone gel filled testis prosthesis in the US was discontinued in 1992 because of concerns regarding the risk of connective tissue disease, autoimmune disorders and carcinogenic potential. This was as a result of legal cases initiated by patients claiming that leaking breast implants caused autoimmune disorders or even cancer.

Robinson et al. analyzed silicone breast implants removed from 300 consecutive patients and found that 64 % had some form of device disruption and most of the breast implants lose the integrity of the silicone shell approximately 8–14 years after implantation [9]. Another study that analyzes the draining lymph node and the reactive capsule surrounding the implant in patients who have undergone revision of genitourinary prosthesis, including penile prostheses and artificial urinary sphincters, found silicone particles in 18 of 25 tissue specimens and in all lymph nodes biopsied. The results of this study demonstrated that leakage of small amounts of silicone from the prosthesis into the surrounding tissues can occur, a phenomenon now known as gel bleed [10].

Despite the risk of gel bleed, to date there has been no study that confirms a connection between testicular prostheses and connective tissue disease and there are no reported cases in the literature of any malignancy associated with the use of silicone testicular prostheses in humans. Although, based on this evidence, the association between prostheses and autoimmune disorders or cancer has been disproved, testicular prostheses manufacturers were reluctant to put devices back into the market as the FDA requested proof that the devices were safe and effective.

Turek et al. conducted a multicentre study of a newly developed saline filled prosthesis. A total of 149 adult and pediatric patients from 18 Institutions were enrolled in a 5-year study between 1998 and 2003. Patients were followed up for a minimum of 1 year after placement of the prosthesis. The new, saline filled testis prosthesis appeared to be safe and well tolerated in all patients and a validated self-esteem questionnaire confirmed an improvement in the quality of life after prosthesis placement. By the end of the follow up period, none of the patients had developed connective tissue disease based on clinical findings and by using a detailed rheumatological questionnaire [11].

Current Testicular Prostheses

The testicular prostheses currently available in the US, UK and Europe are listed in Table 11.3.

The Coloplast Torosa® Saline-Filled (available in the US), comes in four sizes, which are

Table 11.3 Available types of testicular implants in US, UK and Europe

Coloplast torosa® Saline-Filled
The Coloplast KiWee®
The Coloplast® (formally Mentor®) soft-solid testicular prosthesis
Silimed®
Nagor® gel filled and elastomer
Polytech®
Osmed® ellipsoid self-inflating tissue expander

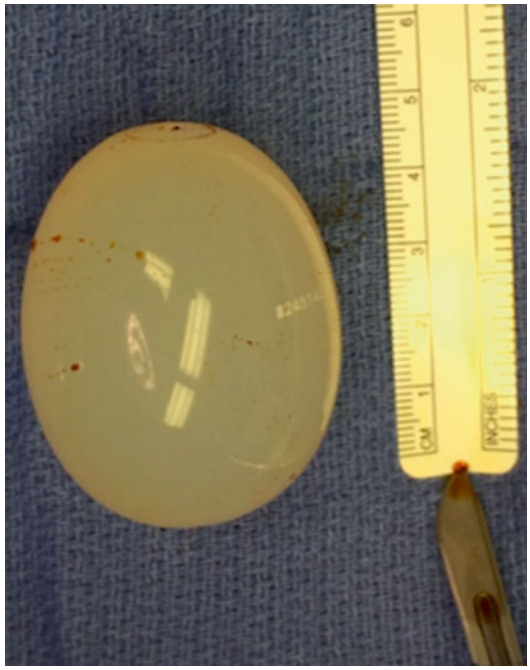

Fig. 11.1 The Coloplast Torosa® (size large) explanted

extra-small, small, medium and large. The implant is made of a moulded silicone elastomer shell, which is approximately 0.035 in. thick and not visible on X-ray. The device is filled with saline at the time of surgery just prior to implantation, though a self-sealing injection site at one end of the testicular prosthesis. On the opposite pole of the implant is a silicone elastomer tab that enables suturing and securing the implant to the dartos muscle in the scrotum (Fig. 11.1).

The Coloplast KiWee® (available in the UK and Europe) is made of a thin and soft silicone elastomer envelope filled in with a high performance, transparent, highly resilient silicone gel. It comes in five different sizes (Extra-small, Small, Medium, Large, and Extra-large) (Figs. 11.2, 11.3, and 11.4). The Coloplast® (formally Mentor®) Soft-Solid Testicular Prosthesis (SSTP) has not received FDA approval and it is therefore not yet available in the United States. The SSTP is available in five different sizes:

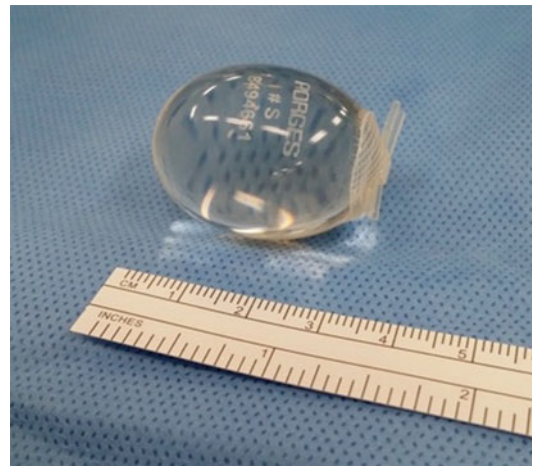

Fig. 11.2 The Coloplast KiWee® (size small)

Fig. 11.3 The Coloplast KiWee® (size medium)

extra-small, small, medium, large, and extra-large. The device consists of a moulded silicone elastomer shell, ranging between 0.012 and 0.018 in. in thickness, filled with cured silicone elastomer. A silicone elastomer Dacron reinforced patch for anchoring the prosthesis to the dartos muscle is located at one pole of the device shell.

Silimed® supplies five standard testicular prosthesis sizes, available in softer gel filled testicular prostheses and silicone elastomer. Silimed® also manufactures customized prostheses according to the surgeon's specifications.

Nagor® testicular prostheses are gel filled or elastomer prostheses and are available in three sizes, small medium and large. These feature a low profile reinforced suture loop closely aligned to the shell for ligature fixation or to remain flat and unobtrusive if not used to fix to the dartos muscle.

Polytech® are silicone gel-filled or elastomer implants with or without suture loops. The silicone-gel filled prostheses are fitted with a short piece of removable teflon to guide the needle when anchoring the prosthesis to the dartos layer to protect the implant and thereby preventing inadvertent puncture of the prosthesis. The prostheses are filled with soft silicone elastomer with a reinforced cap that allows anchoring of the prosthesis by placing a suture through the cap. Both types of prosthesis are available in five different sizes.

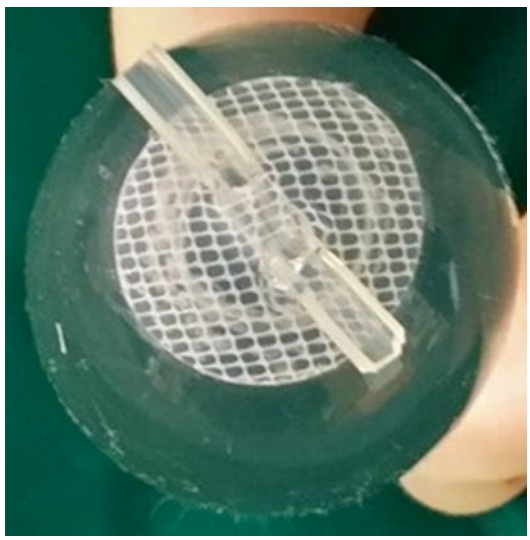

Fig. 11.4 The Coloplast KiWee® (size medium) with suture loop and short piece of removable guide for the needle in case the surgeon wishes to fix the prosthesis in place

Osmed® ellipsoid self-inflating tissue expanders are self-filling devices consisting of an osmotic active hydrogel (vinylpyrrolidone and methylmethacrylate), a material also currently used to manufacture contact lenses. The material has been tested and confirmed to be non-toxic as well as using the osmotic principle to gain volume. Before expansion, Osmed® hydrogel expanders are small, hard and easy to handle. After implantation, Osmed® hydrogel expanders absorb bodily fluids and expand consistently to reach their predefined form and size.

To date, there are no studies comparing the different type of prostheses and the choice is made both by the implanting surgeon and the patient according to the shape, consistency, and size of the prostheses as the volumes are slightly different between the various manufacturing companies. As a common rule, the choice should fall on the prosthesis that matches best for shape, size and texture to the contralateral testicle. In female to male transsexuals, the size is dictated by the room available in the neoscrotum and by the size of the phallus. In particular, patients undergoing metoidioplasty, should be offered a smaller prosthesis, as larger implants would make the neophallus appear too small (Fig. 11.5).

Preoperative Assessment of Patients

Testis prosthesis implantation is contraindicated if the patient has one or more of the following conditions:

- Untreated local or systemic infection
- Open wound in the groin or scrotal area
- Chronic scrotal pain (risk of worsening of the pain)
- History of sensitivity to foreign materials (silicone allergy)

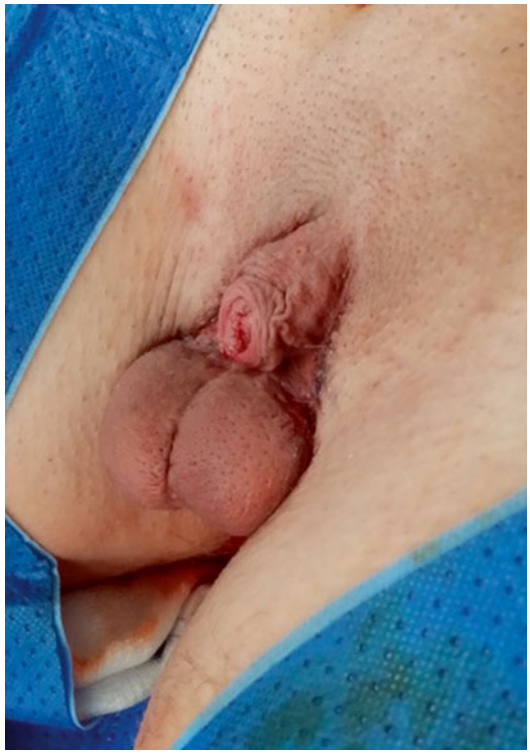

Fig. 11.5 Bilateral small testicular implants inserted in a FTM metoidioplasty patient

Relative Contra-Indications

Relative contra-indications to testicular prosthesis implantation are:

- Severe scrotal tissue contracture
- Previous irradiation of the scrotum
- Psychologically unsuitable patient

Surgical Approach

The approach is similar for both children and adults. As proposed by Lattimer in 1973, the prosthesis should be placed in a dartos pouch to allow a certain degree of movement.

Preferably, the implant should be placed though a subinguinal approach, to guarantee adequate distance between the implant and the skin incision, as the skin is a well-recognized source of infection.

A 3–4 cm long transverse subinguinal incision is used and the external oblique's fascia is exposed and the scrotal neck identified and a dartos pouch created with blunt dissection. The prosthesis is preventively soaked in iodine or antibiotic solution and inserted into the space. At this stage an anchoring suture can be placed to maintain the testis in place, although some surgeons prefer not to anchor the prosthesis in order to allow it to find a more natural position within the scrotum. The majority of testicular prostheses are inserted at the time of radical orchidectomy for testicular cancer. The incision is performed as for a standard radical orchidectomy and meticulous haemostasis ensured in the scrotum. The prosthesis is inserted into the same space as the original testicle.

In female to male transsexuals the prosthesis is inserted through a subinguinal approach and a pouch is created in the lax areolar tissue of the labia majora, which has been previously fused along the midline to form a neoscrotum.

The site of the skin incision can significantly affect the outcome of surgery. The main rule is that the skin incision must not overlie the prosthesis in order to minimize the risk of postoperative infection of the implant. Another precaution relates to patients who have had a previous orchidopexy and are undergoing an orchidectomy. Caution should be exercised as the scrotal skin is thin and can lead to ischaemia and skin necrosis if a prosthesis is inserted at the same sitting.

Most common alternative approaches include prosthesis insertion through an inguinal, inguinoscrotal, or infrapubic incision. The infrapubic approach is a good option for bilateral testicular prosthesis insertion. In 1972 *Abbassian* described the insertion of a testicular prosthesis in a dartos pouch, through a contralateral scrotal incision [12].

This type of approach is associated with a high risk of erosion but may be indicated in patients presenting with diffuse scrotal scarring or contracture when a subinguinal approach would not allow the creation of an adequate dartos pouch [8, 13]. Libman et al. introduced a suprascrotal approach. This approach uses a 2-cm long semilunar incision just above the scro-

tum 2–3 cm lateral to the penis and allows better scar concealment under the pubic hairs. It also avoids dissecting through dense scar tissue in patients who have undergone previous inguinal surgery [14].

The creation of the dartos pouch can be achieved with scissors, sponge-holding forceps, Hegar dilators, 30-mL catheter balloons or nasal/vaginal speculums [15–18].

Once the testicular prosthesis has been placed in the correct position the dartos, dermis and skin are closed in layers using absorbable sutures.

For patients undergoing subcapsular orchidectomy for prostate cancer, an alternative technique involves placing a small prosthesis within the tunica albuginea once all of the testicular parenchymal tissue has been excised and cauterised. A running suture can then be used to close over the prosthesis.

Timing of Insertion

In children, the timing of insertion of a testicular prosthesis should be carefully planned. The psychological impact of an absent testicle in a child or adolescent is a good enough reason to consider early prosthesis placement. However, the prosthesis size represents the main limitation, as the contralateral testis will eventually grow in volume and the patient will necessitate further surgery to replace the prosthesis with a larger one as they go through pubertal development. An alternative option is to delay the placement of the definitive prosthesis until the child has reached adolescence. However, prosthesis placement at a later age, apart from the psychological trauma of having an empty hemi-scrotum, may be challenging due to scrotal hypoplasia, which may prevent the surgeon from placing a reasonable sized prosthesis.

For the above reasons it is now accepted that a testicular prosthesis should be placed as early as possible and replaced with a larger one at a later stage, if required. To obviate the need for further surgery, some surgeons prefer inserting a prosthesis slightly larger than the contralateral testicle.

Robinson et al. have compared the complication rate of simultaneous radical orchidectomy and prosthesis insertion with orchidectomy alone.

In their series, 904 men underwent radical orchidectomy for testis cancer during the study period. There was no significant difference in terms of length of hospital stay (LOS), hospital re-admission rates or return to theatre rate, between the 229 patients who underwent simultaneous implantation of testicular prosthesis and those who underwent radical orchidectomy alone. Prosthesis insertion at the time of orchidectomy for testis cancer is now considered safe and not associated with significant additional morbidity [19].

Complications

According to a survey of the members of the Western Section of the American Urological Association regarding testicular prostheses inserted within the previous 10 years, overall complication rates for this procedure are low. Generally, the scrotal cavity distends easily to a size adequate to accommodate the prosthesis. However, in cases of delayed secondary scrotal surgery, or when a previous inflammatory process had produced dense scrotal scarring, the limited scrotal distensibility may lead to an increase in complication rates. In a 10-year long single institution experience of 45 implantations in 43 patients, Teo et al. noticed that pain was the most common complication as it occurred in 8 (18.6 %) patients. Two patients had their prosthesis removed due to infection and pain [20]. No spontaneous erosion was reported. Marshall et al. reviewed the records of 2533 testicular prosthetic implantations to establish a list of postoperative complications. In their series prosthesis erosion was the commonest complication (3–8 %), and mainly occurred in patients who had previously undergone orchidectomy for epididymo-orchitis, especially if a scrotal approach

had been used to implant the device. The other common complications included scrotal contracture (3–5 %), pain (1–3 %), hematoma (0.3–3 %) and prosthesis infection (0.6–2 %) [21]. They also noted that previous scrotal surgery and a prolonged time interval between the orchidectomy and the insertion of the prosthesis were associated with an increased risk of complications. There has been a case report of spontaneous rupture of a silicone testicular prosthesis 11 years after its insertion [22]. Turek et al. also reviewed the complication rate in his multicentric study of a total 149 patients at 1 year. The most common complications in his series were erosion (2 %), scrotal contracture (2 %), chronic pain (9 %), hematoma (1 %) and infection (1 %). In current practice, the most common postoperative complaints concern body image, when the patient is unhappy with size, texture and position of the implant [11].

Alternative Uses of Testicular Prostheses

Ugarte y Romano described a case of a 45-year-old man with body dysmorphic disorder concerned about his testicular volume. The authors described a new surgical technique for testicular augmentation. Via a lower groin incision, a solid silicone chin implant (Invotec International Inc.®, Jacksonville, FL, USA) was placed on the front of the left testicle using a 3–0 polypropylene suture. The prosthesis was fixed to the tunica vaginalis with full thickness sutures. This technique provided testicular augmentation preserving testicular function and providing a favorable aesthetic outcome in this particular patient [23].

Wu et al. developed a tissue engineered testicular prosthesis with high-density polyethylene (HDPE, trade name: Medpor) and polyglycolic acid (PGA). After isolating the chondrocytes from swine cartilage, they were seeded onto Medpor-PGA scaffold and cultured for 2 weeks. The cell-scaffold construct was implanted into subcutaneous pockets on the back of nude mice and left to grow. Ultimately, the newly formed complex of Medpor-PGA and cells was very similar to the testicle with regards to texture and macroscopic appearance and to normal cartilage from a histological point of view [24].

Raya-Rivera et al. explored the possibility of creating a hormone releasing testicular prostheses that could continuously supply and maintain physiologic levels of testosterone *in vivo* over time using chondrocytes, harvested from bovine articular cartilage, and seeded on testicular shaped polymer scaffolds. The scaffolds were maintained in a bioreactor for 4 weeks to form cartilage tissue. Subsequently, testosterone enanthate (100 mg) was injected into the central hollow space of each testicular prosthesis, and maintained for 40 weeks in culture. Engineered testicular prostheses were then implanted into the scrotal space of castrated athymic mice.

Engineered cartilage testes can be created in bioreactors and implanted in vivo, and can release testosterone for a prolonged period. Furthermore, the levels of testosterone release can be maintained within the physiologic range. Periodic reinjection may potentially provide permanent physiologic hormonal replacement. This novel technology may be beneficial for patients who require testicular prostheses and chronic hormone supplementation [25].

Satisfaction Rates Following Testicular Prosthesis Insertion

Despite the procedure being relatively straightforward with minimal complications, there is still a reluctance to offer the procedure at the time of radical orchidectomy despite studies showing that there is no increased risk of complications [19].

A study by Adshead et al. found that 91 % of patients who replied to a questionnaire felt it was extremely important for them to be offered an implant at the time of an orchidectomy [26]. They also demonstrated that 73 % of those who had a prosthesis inserted felt that they either had an excellent or good result but 23 % were dissat-

isfied because of the shape or the position of the prosthesis. In another study published by Incrocci et al. 68 % of their patients reported a significant improvement in body appearance following the insertion of a testicular prosthesis with only one patient (5 %) dissatisfied [27].

Conclusions

Although there are a number of different testicular prostheses available, only a few are currently FDA approved. Testicular prosthesis surgery is a straightforward and safe procedure, with satisfactory functional and cosmetic results in the vast majority of patients.

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Surgery for Female Urinary Incontinence

12

Tina Rashid and Ian Pearce

Abstract

Urinary incontinence, the complaint of involuntary leakage of urine, may affect up to 50% of women at some point in their lifetime. Incontinence negatively impacts psychological health and women who live with incontinence have a significantly lower quality of life compared to continent women. The surgical options available to treat urinary incontinence are extensive and have evolved significantly over the years. This chapter focuses on those techniques used to treat incontinence that involve the use of prosthetics.

Keywords

Pubovaginal sling • Mid-urethral sling • Adjustable sling • Single-incision sling • Hybrid sling • Artificial urinary sphincter in women

Introduction

Urinary incontinence (UI) is defined by the International Continence Society (ICS) as the complaint of any involuntary leakage of urine. Whilst it is estimated that up to 50% of women will experience UI at some point in their lifetime, embarrassment coupled with the fear of stigmatization mean that UI remains under-reported to healthcare professionals [1].

UI has a negative impact on the psychological health of women as well as causing sexual dysfunction, relationship issues, withdrawal from sports and hobbies, restrictions in travelling and increased time off work. The negative impact stems not only from the distress of the actual leakage, but from fear and anxiety related to being incontinent in public and the possibility that others may find out [2]. It is not surprising then that women living with UI have a significantly lower quality of life compared with continent counterparts [3, 4].

UI can be subdivided into two main subtypes: stress incontinence and urge incontinence. The type of incontinence determines symptoms experienced and the treatments offered. The role of

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surgery in UI has evolved such that minimally invasive options are favoured where possible. Stress incontinence may be treated with bulking agents, pubovaginal or mid-urethral slings, bladder neck suspension procedures, bladder neck closure with Mitrofanoff formation and artificial urinary sphincter implantation. Figure 12.1 demonstrates videocystometrogram images of different types of stress incontinence according to the Blaivas classification.

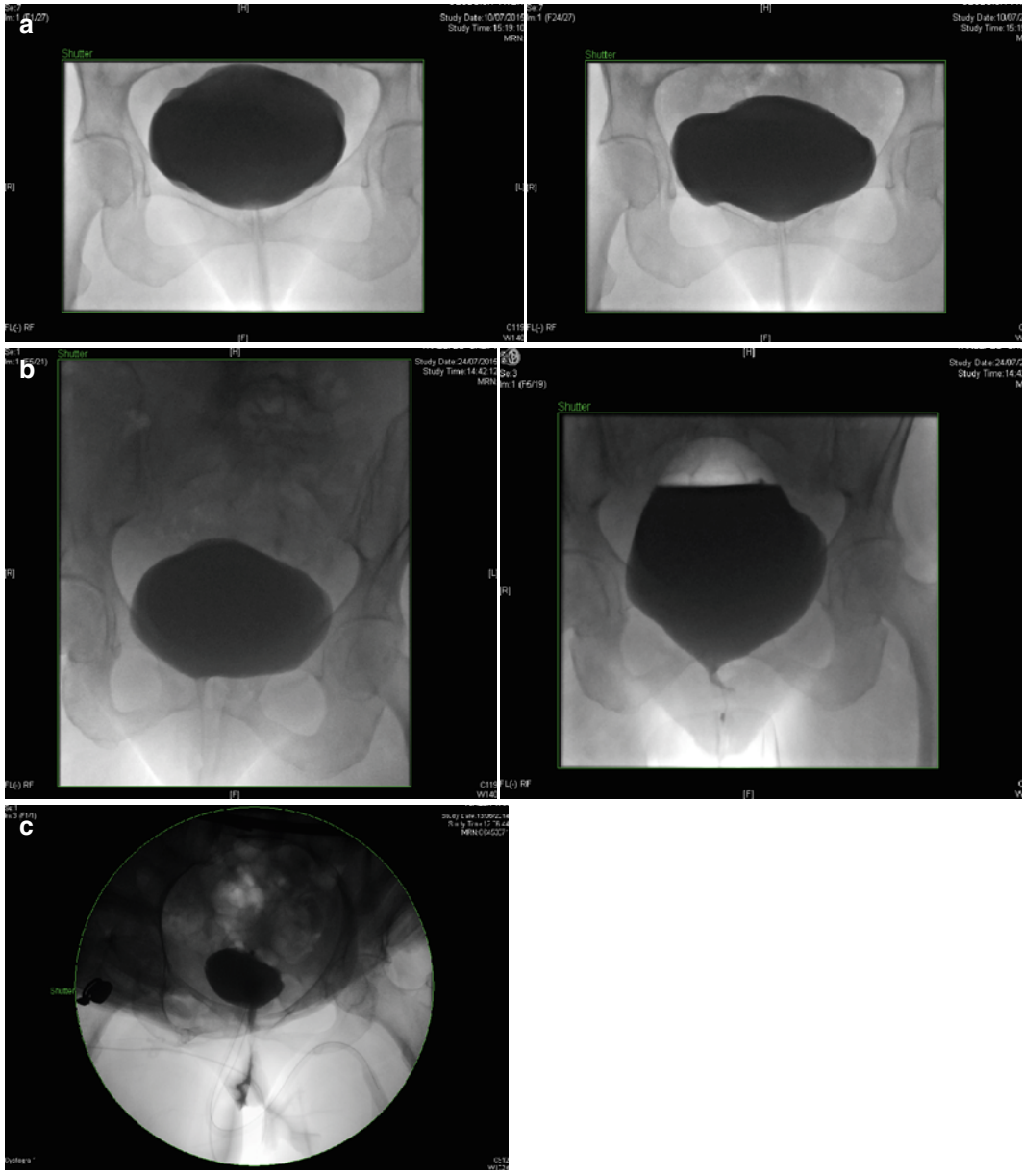

Fig. 12.1 Videocystometrogram images demonstrating stress incontinence (Blaivas classification). (**a**) type 1 SUI: the bladder neck at rest is well-supported at or above the inferior margin of the pubic symphysis. On coughing, there is less than 1 cm descent of the bladder neck. Leaking is not visualised on this image. (**b**) type 2b SUI: the bladder neck at rest is below the inferior margin of the pubic syphysis. On coughing, leakage is demonstrated. (**c**) type 3 SUI: the bladder neck and urethra are open

Urge incontinence may be treated surgically with intravesical botulinum injections, posterior tibial nerve stimulation, sacral nerve stimulation, detrusor myomectomy and bladder augmentation. In refractory cases, ileal conduit diversion may be offered in either type of UI.

This chapter is focused on those surgical options for UI in women that involve the use of prosthetics: pubovaginal slings, mid-urethral slings and artificial urinary sphincter implantation. Whilst urethral bulking agents and sacral nerve stimulation fall within this category, they have been discussed in detail elsewhere in the book.

Pubovaginal Slings

A pubovaginal sling (PVS) describes a sling placed suburethrally within the vagina and passes retropubically. The aim is to support the proximal urethra and bladder neck by reinforcing the 'hammock' against which the urethra is compressed during the transmission of increased abdominal pressure, thus providing continence. The technique may utilise synthetic material (monofilament, large-pore or 'type 1' mesh), allogenic material (cadaveric fascia lata), xenogenic tissue (porcine or bovine dermis and porcine small-intestine submucosa), autologous fascia (rectus fascia and fascia lata being the most commonly employed tissue) or a 'hybrid' of synthetic and non-synthetic material [5].

Although McGuire was not the first to perform a PVS, it was he who popularized their use. In 1978, he published his case series of 52 women with stress urinary incontinence (SUI) associated with poor urethral sphincter function and a urethral pressure of less than 10 cm H_2O, treated with autologous fascial pubovaginal sling (AF-PVS). Despite 42 of these patients having undergone previous SUI surgery, 50/52 had 'good urinary control' [6].

Indications

Originally established for the treatment of intrinsic sphincter deficiency (ISD), the PVS has subsequently been described as a primary treatment for UI secondary to urethral hypermobility, neurogenic SUI [7], a salvage procedure for recurrent or persistent incontinence after one or more failed synthetic mid-urethral slings [8] with or without vaginal tape extrusion, sling lysis or excision [9], as an adjunct to urethral and bladder reconstruction and as a mechanism to functionally close the urethra when urethral access to the bladder is obsolete. In addition, the PVS is favoured when prior radiotherapy has been given, in those who have concurrent urethral injuries, or in simultaneous or previous repair of urethrovaginal fistula or diverticulum.

Surgical Technique

In some centres, patients are taught to perform self-catheterisation prior to surgery.

1. The operation is performed with the patient under general (or spinal) anaesthesia. Full-patient paralysis may facilitate closure of the rectus fascia (step 7).
2. Perioperative antibiotics are administered providing cover for skin and vaginal flora.
3. The patient is placed in a low lithotomy position. Preparation of the abdomen and perineum provides access to both the vagina and lower abdomen.
4. A Foley catheter is inserted into the bladder – **the bladder must be allowed to empty**.
5. A weighted vaginal speculum (Ovard speculum) is placed inside the vagina. Exposure may be further improved by using labial retraction sutures, a 'Lone-star' or 'Scott' retractor or a self-retaining retractor system.
6. An 8–10-cm Pfannenstiel incision is performed approximately 3–5 cm above the symphysis pubis. The dissection is continued to the rectus fascia, using electrocautery and blunt dissection to ensure the fat and subcutaneous tissue is cleared off the rectus sheath.
7. When autologous fascia is being used, a fascial segment at least 8 cm in length and 1.5–2 cm in width is required. *TIP*: *mark the required graft with a surgical marking pen*

or electrocautery. The segment is then incised using a scalpel, scissors, or electrocautery. It is recommended to leave a rim of at least 0.5–1.0 cm of fascia from the pubic symphysis , which coupled with muscle relaxation and paralysis will facilitate closure of the defect, which is performed using a heavy absorbable suture (e.g. 0 or 1/0 polydiaxonone as a continuous suture). If synthetic material is being used, this step is not required.

8. To prepare the fascial sling, mark the midline of the fascial sling or synthetic material with a pen and gently grasp it using a hemostat. Suture a single 1.0 non-absorbable suture (for example, polypropylene or polyester) to each end of the fascial segment by passing the needle through the undersurface of the sling and then back through the top of the sling or by passing a suture through each of the upper and lower aspect of each lateral margins of the harvested facial strip. In either case a clip is attached to the sutures
9. Hydrodissection of the anterior vaginal wall may be performed by injecting saline or local anaesthetic, (with 1 in 200,000 epinephrine) into the subepithelial tissues over the urethra. A midline inverted "U" incision is made in the anterior vaginal wall allowing the tissue flap to fall away from the field of vision revealing the sub-epithelial tissues. The dissection is continued superolaterally and anteriorly until the endopelvic fascia is reached. The endopelvic fascia is incised and dissected from the posterior surface of the pubis to enter the retropubic space, often with the aid of sharp dissection with Mayo or Mcindo scissors in cases of recurrent stress incontinence and previous surgery.
10. Stamey needles are passed into the retropubic space from the open abdominal wound immediately posterior to the pubic bone, approximately 4 cm apart, advancing the tip of the needle as close to the posterior surface of the pubic bone as possible to avoid inadvertent bladder injury. Maintain distal control of the needles by direct finger guidance through the vaginal incision and ensure the bladder is empty.
11. Careful cystoscopic examination of the urethra and bladder using a 70° lens is mandatory after passing the needles to rule out inadvertent injury, which typically occurs at the 1 o'clock and 11 o'clock positions. It is recommended to fill the bladder completely and gently move the needles to visualize their position in relation to the bladder wall.
12. The free ends of the sutures are thread through the Stamey needle eyes and each suture is pulled up to the anterior abdominal wall through the retropubic space. The sling is kept centered and flat at the area of the bladder neck.
13. *Optional*: the sling may be fixed in the midline to the underlying periurethral tissue using delayed absorbable sutures.
14. To ensure adequate "looseness," the sutures are tied across the midline while holding a right-angled clamp between the sling material and the posterior urethral surface. The goal is for the sling to prevent the descent of the proximal urethra during increases in abdominal pressure without creating any outlet obstruction to the normal flow of urine.
15. The rectus fascia is closed using 0 PDS. The abdominal skin incision is closed using either 3-0 and 4-0 absorbable sutures or skin clips. 3-0 absorbable sutures are used to close the vaginal mucosa. The vagina may be closed either before or after tensioning.
16. A urethral catheter and a gauze pack are placed within the bladder and in the vagina respectively for 24 h.

Variations in Technique

A half-length sling may be used which extends into the retropubic space above the perineal membrane, suspended by sutures applied to the ends. The third method employs a patch of sling, the ends of which are attached by sutures that extend through the retropubic space to the attachment site. The harvested facial sling may remain

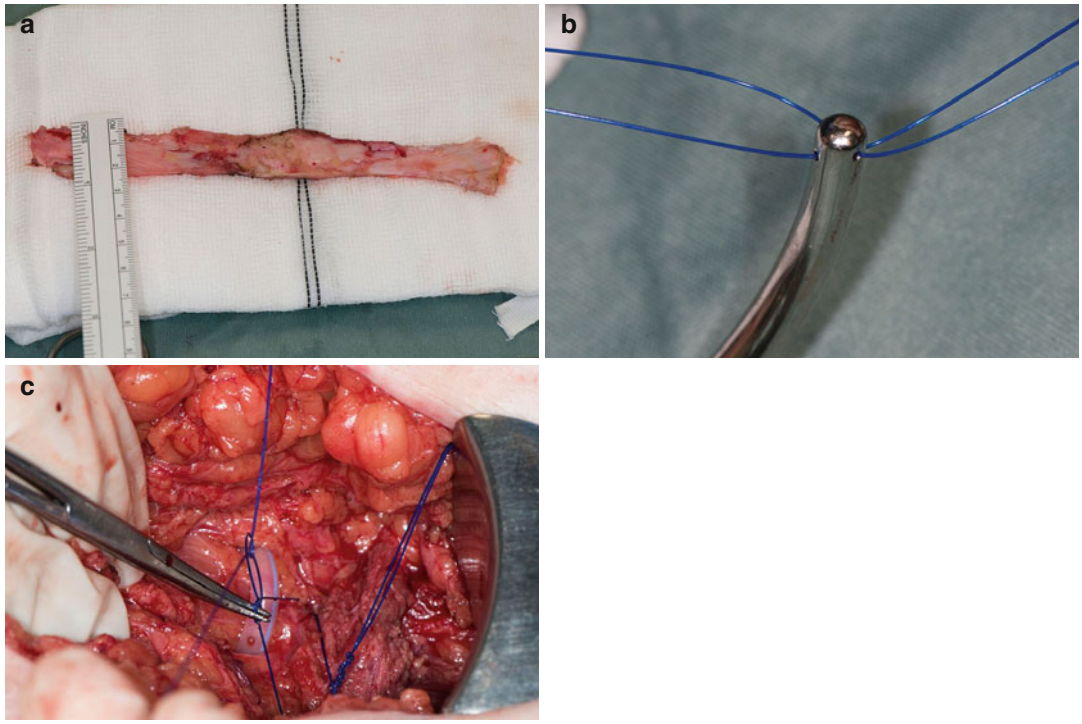

Fig. 12.2 Placement of a pubovaginal sling. (**a**) Recturs fascia has been harvested. (**b**) Non-absorbable sutures threaded through the end of the Stamey needle (or similar device). (**c**) Loose tensioning of the sling (Courtesy of Mr Hashim Hashim, Consultant Urological Surgeon, Bristol Urological Institute)

attached to the midline (approx 2 cm) and the lateral ends passed on either side of the urethra and closed without tension beneath the urethra. Alternatively, bone screws may be used to hold the sutures in place and anchor the sling to the pubis (Fig. 12.2).

Complications

Recognised complications of PVS include bladder perforation, persistent incontinence, outlet obstruction requiring transient or permanent intermittent self catheterization and urethral erosion [10, 11].

Outcomes

The technique has stood the test of time. A 2011 Cochrane review [12] described 26 RCTs, including 2284 women undergoing AF-PVS compared to other operations including coloposuspension and mid-urethral slings (MUS). Most trials were of variable quality. Within these, the SISTEr trial [13], demonstrated that fascial sling and colposuspension had a similar cure rate at 1 year, patients having had fascial sling surgery experienced a higher risk of voiding difficulty and urinary tract infections compared to colposuspension but a lower risk of bladder perforation. AF-PVS also demonstrated similar efficacy to MUS, but the latter resulted in shorter operating times and lower rates of complications, including voiding difficulty. Six trials compared autologous fascial slings with other materials of different origins, with results favouring traditional autologous fascial slings.

Mid-Urethral Slings

In 1990, Ulmsten and Petros [14] introduced the 'integral theory' of urinary incontinence, describing how fixation of the mid-urethra to the pubic

bone via the pubourethral ligaments creates a physiological 'backboard' promoting continence. They described how loss of this backboard is responsible for inhibition of normal urethral coaptation during episodes of increased intra-abdominal pressure, with resultant loss of urine (Fig. 12.3).

This concept led to the introduction of the mid-urethral sling (MUS) into the market in 1995 [15]. The principle of the MUS was to allow a tension-free placement of synthetic mesh under the middle portion of the urethra (as opposed to the proximal urethra and bladder neck as in PVS), providing support during episodes of increased intra-abdominal pressure and thus recreating the missing backboard.

The technique of tension-free vaginal tape (TVT) insertion involves retropubic passage of a 1–2 cm wide strip of synthetic mesh via trocars from the vagina, to the suprapubic region. The ideal mesh is a non-absorbable monofilament fibre, macroporous in nature (relatively large pore size, typically >75 μm), typically polypropylene (Fig. 12.1). The TVT may be placed from top-down (i.e. skin to vagina) or from down-up (i.e. from vagina to skin). The down-up approach is favoured for retropubic tape insertion over the top-down approach, the latter being less effective, with associated higher rates of voiding dysfunction, bladder perforation and vaginal erosion [16].

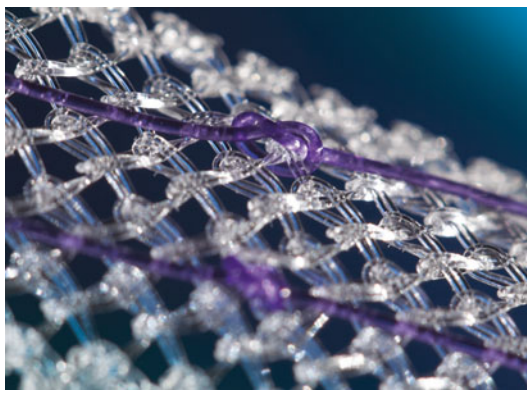

Fig. 12.3 Nonabsorbable monofilament macroporous mesh used in mid-urethral sling placement (Image reproduced with permission of American Medical Systems, copyright®.)

Anxieties related to blind trocar insertion into the retropubic pelvis and the need for routine cystoscopy to exclude bladder perforation led to the development of a MUS which could be placed via the obturator route [17], with reduced risk of bladder perforation and *theoretically* negating the need for cystoscopy. The transobturator tape may be placed from outside-in (i.e. from skin to vagina) or from inside-out (i.e. from vagina to skin). Both approaches are thought to be equally effective.

The introduction of the MUS to the armamentarium of the urologist and urogynaecologist has revolutionized the management of SUI. MUS are now the most frequently used surgical intervention in Europe for the treatment of women with SUI.

Indications

MUS are indicated in primary SUI secondary to urethral hypermobility or in intrinsic sphincter deficiency. In the latter, the MUS may need to be placed with tension and are therefore subject to higher risks of complications. A MUS may also be placed in recurrent or persistent SUI.

Technique

Many kits exist for MUS placement, each with variations in technique for insertion (Table 12.1). Below is described the most common technique for retropubic MUS placement (down-up) and transobturator MUS (outside-in) accepting that surgeon experience and technique may differ.*

Patient Preparation for Retropubic or Transobturator MUS

MUS placement may be performed under local anaesthesia (with or without sedation), regional or general anaesthesia.

Peri-operative antibiotics must be administered to cover skin and vaginal flora, according to local microbiological guidelines.

Table 12.1 Available kits for MUS placement

Name	Manufacturer	Technique approach
TVT	Ethicon	Retropubic, down-up
SPARC	AMS	Retropubic, top-down
Advantage	Boston scientific	Retropubic, down-up
Lynx	Boston scientific	Retropubic, top-down
TVT-O	Ethicon	Transobturator, inside-out
Monarc	AMS	Transobturator, outside-in
ObTryx	Boston scientific	Transobturator, outside-in
Aris	Coloplast	Transobturator, outside-in
TVT-Secur	Ethicon	Single incision
MiniArc	AMS	Single incision
Solyx	Boston scientific	Single incision
Ajust	Bard	Single incision (adjustable sling)
Remeex	Neomedic	Adjustable sling
Safyre	Promedon	Adjustble sling

The patient is placed in a dorsal lithotomy position (Fig. 12.4).

The vagina, perineum and suprapubic region (retropubic tape) or obturator region (transobturator tape) are prepared and draped.

A Foley catheter (18-French for retropubic MUS) is inserted and **the bladder emptied completely**. Catheter placement is important to reduce the risk of bladder perforation, and to accurately identify the bladder neck, urethra and the position of the mid-urethra.

Optional: exposure can be improved by placing labial retraction sutures and a weighted Ovard speculum within the vagina.

By pulling on the catheter and feeling for the balloon, the position of the bladder neck becomes obvious. This allows the position of the mid-urethra to be estimated, which will direct the vaginal incision. Two Allis forceps are placed on either side of the anticipated incision, which is at the same position for either technique (Fig. 12.5).

Optional: some surgeons choose to hydrodissect the anterior vaginal wall using saline or local anaesthesia (e.g. bupivacaine containing epinephrine) in order to reduce the risk of bleeding and facilitate dissection in the correct plane.

Retropubic MUS Insertion

1. If local anesthesia is used, it is injected into the skin just above the pubic tubercle, approximately 2–3 cm on either side of the midline. The injection is continued from the skin into the rectus fascia, the rectus abdominis muscles, and into the space of Retzius, staying as close to the inner surface of the pubic bone as possible. Apart from providing anaesthesia, this allows hydrodissection and may prevent inadvertent organ injury.
2. A small vertical incision (large enough to admit your forefinger) is made in the anterior vaginal wall at the level of the mid urethra. The Allis forceps are replaced onto the cut edges of the vaginal epithelium. The dissection is continued paraurethrally toward the endopelvic fascia. The direction of dissection is towards the suprapubic incision on the ipsilateral side (Fig. 12.6). It is important to dissect the correct plane to avoid subsequent tape extrusion or urethral perforation/erosion.
3. The rigid catheter guide is inserted into the Foley catheter.
4. For insertion of the TVT trocar on the patient's right side: the assistant pivots the handle of the catheter guide to the surgeon's right to move the bladder away from the anticipated needle tract and to expose the patient's right endopelvic fascia. The trocar is passed from the right vaginal incision through the dissected tract, to puncture the patient's right endopelvic fascia with the TVT trocar. The trocar is advanced through the space of Retzius and through the anterior abdominal wall incision. **The trocar must hug the posterior wall of pubic bone during this manouver** (Fig. 12.7).
5. The catheter guide and catheter are removed. A cystoscopy is performed using a 70° cystoscope, ensuring the bladder is completely

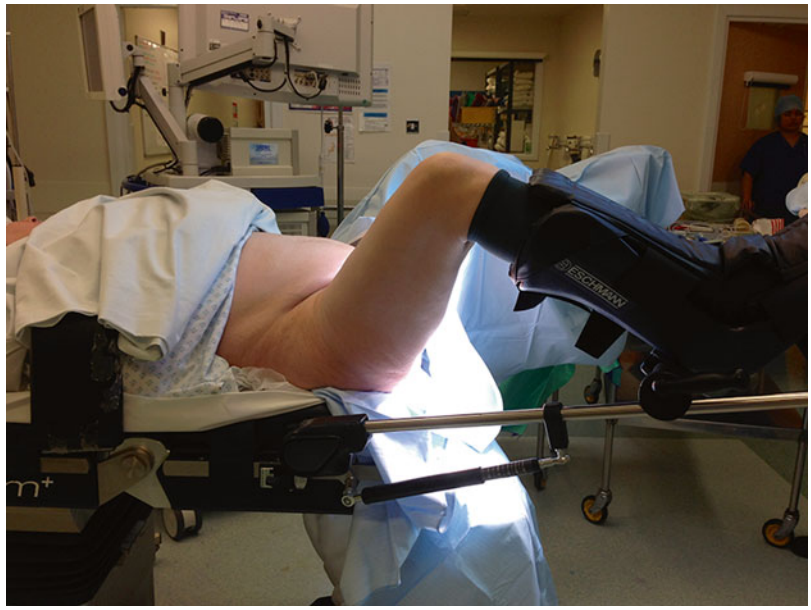

Fig. 12.4 patient positioning for MUS placement

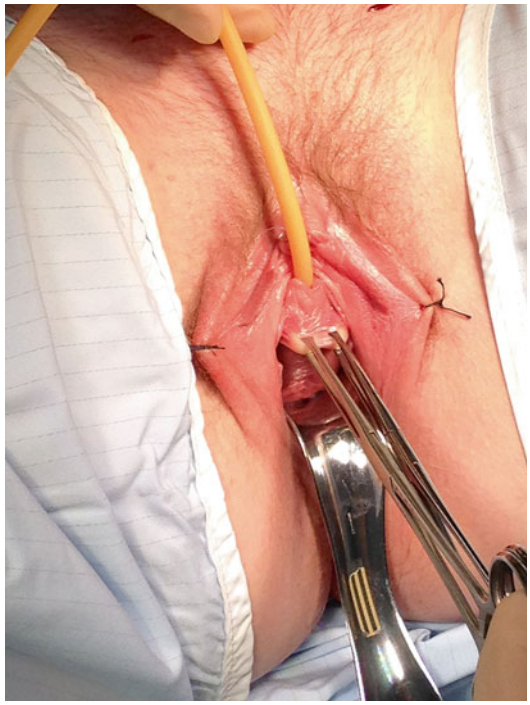

Fig. 12.5 Note the use of labial retraction sutures and weighted speculum to increase access. An 18-French catheter is in situ. Allis forceps have been placed at the anticipated site of the incision

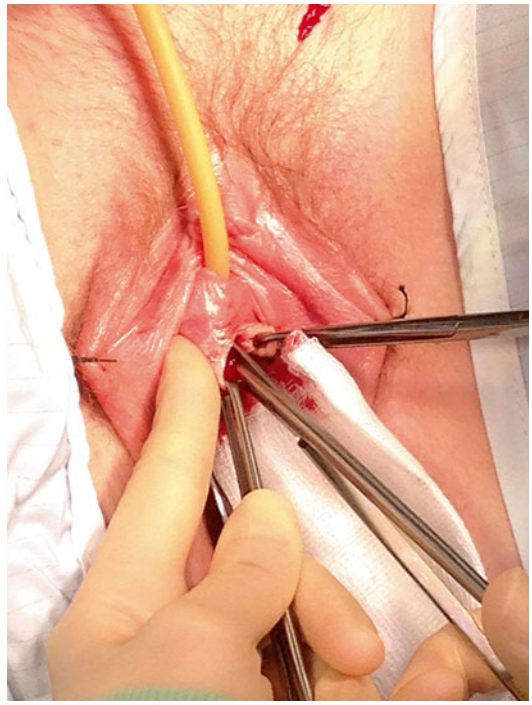

Fig. 12.6 Paraurethral dissection toward the endopelvic fascia

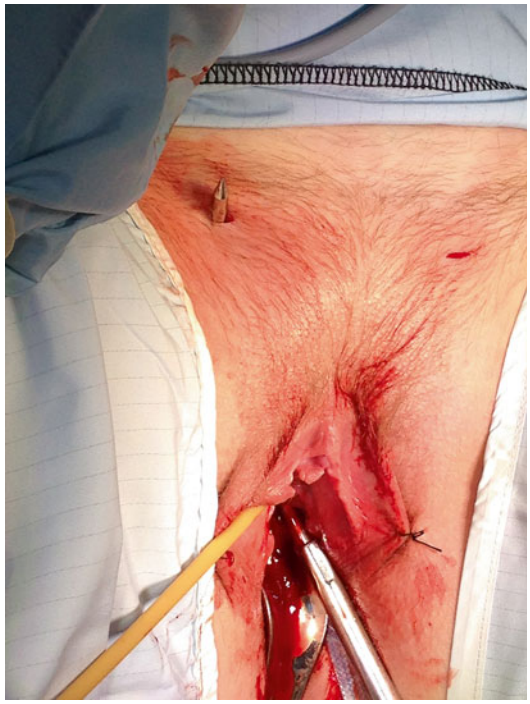

Fig. 12.7 Trocar passage on the patient's right side. The trocar must hug the posterior wall of the pubic bone during retropubic passage to avoid inadvertent bladder or bowel injury

filled, to ensure that there is no inadvertent bladder or urethral injury. The bladder is emptied using the cystoscope sheath (faster than allowing it to drain after placing the catheter).

6. The tape is attached to the trocar which is then advanced above the abdominal wall.
7. The same procedure is repeated on the contralateral side, with care being taken not to twist the tape during insertion. The tape is cut (leaving the plastic sheath in place) at both abdominal ends, and the needles removed.
8. Tensioning the tape: the weighted speculum (if used) is removed. A pair of Metzenbaum scissors or a small instrument is placed between the tape and urethra to prevent overtensioning of the tape (Fig. 12.8). The sheath and tape are gently pulled to tension the tape over the instrument and urethra. It should be easy to remove and re-insert the instrument in between the tape and urethra. To remove the plastic sheaths enclosing the mesh, the ends of the plastic sheaths are grasped with an artery clip. Whilst maintaining the instrument in between the tape and urethra, the sheath is pulled off one side and then the other. Once the plastic sheaths have been removed further adjustment is minimized.

   If the tape must be loosened, an instrument is placed between the tape and the urethra and pulled down, or away from the urethra, until optimal tension is achieved.

   If the tape needs to be tightened, the tape and tensioning suture exiting the skin incision on each side are grasped with a hemostat. The tape is rolled around the hemostat in order to improve the grip and pulled up or out until the proper tension is achieved.
9. Closure: the tape is trimmed flush with the skin at the exit site and the incisions are closed with skin glue or an interrupted absorbable suture. The vaginal incision is closed using 2-0 or 3-0 polydiaxonone sutures (interrupted or vertical mattress). To avoid tape extrusion, full thickness epithelial closure is encouraged and large gaps in between each suture should be avoided.
10. The catheter may be removed post-procedure.

Transobturator Sling

1. The first step involves palpating the tendon of the adductor longus in the groin crease. Just inferior to this and lateral to the bony edge, a 1 cm skin incision is made ensuring that the incision is in line with the clitoris. This is repeated on the contralateral side.
2. A small vertical incision (large enough to admit a finger) is made on the anterior vaginal wall at the level of the mid urethra. The Allis forceps are replaced onto the cut edges of vaginal epithelium. The dissection is continued paraurethrally toward the endopelvic fascia. The direction of dissection is lateral until the tips of the scissors touch the inferior portion

of the inferior pubic ramus. This is repeated on the contralateral side.

3. For the patient's right side, the trocar is grasped with the surgeon's left hand. The tip of the trocar is placed perpendicular to the skin with the tip in the incision. The right hand index finger is placed into the vaginal incision, advancing until the inferior pubic ramus is palpable. The thumb from the right hand is placed on the outside curve of the needle to control the needle movement as it perforates the obturator membrane and muscle. The obturator membrane is perforated and the needle pushed through the membrane and muscle until two 'pops' (usually after about 3–4 cm depending on the patient's anatomy) are felt.
4. The needle shaft and handle are placed at a 45° angle to the patient's vertical axis and close to the body. The needle handle is rotated by moving the tip and curve around the posterior surface of the ischial pubic ramus and toward the vaginal incision and index finger.

   The index finger meets the needle tip as it moves around the pubic ramus. If the needle tip cannot be located, the needle is withdrawn to just behind the pubic ramus and advanced again.
5. Cystoscopy using a 70° telescope is performed either at this point (or at the end of the procedure) to ensure no bladder perforation has occurred. The advantage of performing a cystoscopy at this point is that the trocars can be easily removed and therefore the tape has not been wasted. It is also imperative to check the vaginal fornices at this point to ensure there has been no perforation. If there is, the trocar is removed and reinserted. The vaginal epithelium at the point of perforation is closed using 3/0 polydiaxonone sutures.
6. The sheath's pre-attached connector containing the tape is attached to the trocar in the vaginal incision, with the blue markings on the plastic sheath facing outward, away from the urethra. It is important to ensure the tape lies flat and is not twisted prior to attaching the second connector. The connectors cannot be removed once they are snapped into place. Once the connector is attached to the needle end, the needle is reverse-rotated back through the skin incision, pulling the connector, associated plastic insertion sheath and tape into position. Some obturator tapes are fed through the lumen of the trocar without securing and the trocar is withdrawn taking with it the tape

   This maneuver is repeated on the contralateral side.
7. The sheath and tape are divided below the blue mark on the end portion of the plastic sheath on each side or removed from the trocar. The tape will now slide freely to enable tensioning. The tape is tensioned and the inci-

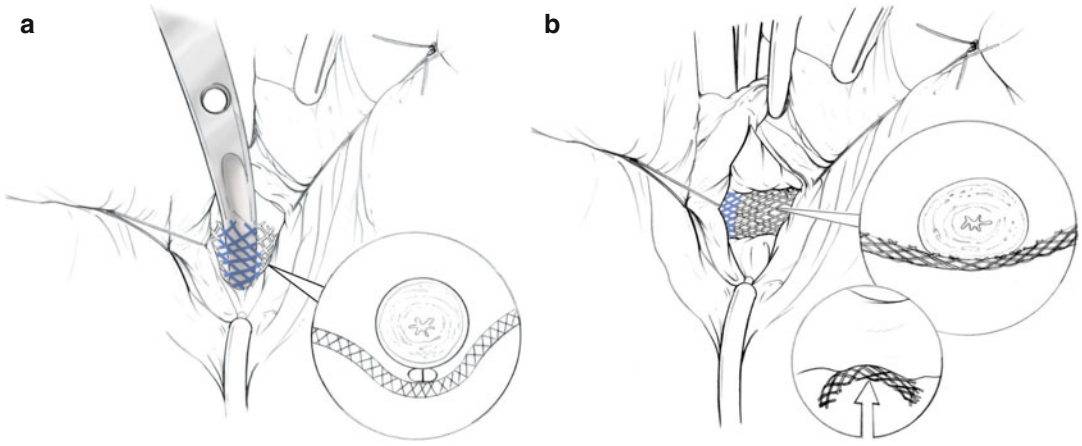

Fig. 12.8 Diagram demonstrating: (**a**) tape too loose; (**b**) tape too tight (Reproduced with permission from American Medical Systems, copyright®)

sions closed as in the retropubic tape method described above.

Outcomes

Although both retropubic and transobturator techniques provide mid-urethral support, the different exit sites of the slings result in a different anatomic relationship between the tape and the urethra. The sling axis of the obturator tape is much more horizontal than that of the retropubic tape which is roughly vertical in relation to the urethral axis (Fig. 12.9). It was suggested that these differences may result in decreased urethral compression by the obturator tape, with consequent lower continence rates and less success in intrinsic sphincter deficiency (ISD, type 3 incontinence), off-set by a lower rate of voiding dysfunction and irritative bladder symptoms post-operatively.

Early Outcomes

The TOMUS (Trial Of Mid-Urethral Slings) trial was a two-arm, blind, multi-centre randomised controlled trial (RCT) comparing retropubic and transobturator MUS designed to assess objective and subjective success rates for resolution of UI at 12 and 24 months. The study population included 597 women diagnosed with stress predominant UI by symptoms on questionnaire and a positive standardised stress test, treated with the TVT (down-up) or TVT-O (inside-out) or the TOT (outside-in). At 12-months, objective success was 80.8 % in the retropubic arm and 77.7 % in the transobturator arm. Subjective success was 62.2 % and 55.8 %. Voiding dysfunction was seen in 2.7 % in the retropubic arm but not seen in the obturator arm with no significant difference in urge incontinence, satisfaction or QoL [18]. One quarter of the women had concomitant procedures (most commonly vaginal prolapse repair).

A further meta-analysis performed by a European Association of Urology Panel reported no difference in cure rates at 12 months (77 % in retropubic tapes versus 85 % for transobturator tapes) [19]. The meta-analysis included 34 RCTs and 5786 women treated with MUS by either route.

Medium-to-Long Term Results

Seventeen-year data on retropubic tapes suggests that the TVT is durable with minimal long-term complications, with objective continence of 90 % in 70 women (87 % subjective cure or significant improvement) [20]. Medium-to-long term results of the obturator tapes suggest objective and subjective cure of 87.3 % and 65.9 % respectively in 126 women who underwent TOT for SUI and mixed UI at 5 years [21] and 81.5 % and 83.5 % in 124 women from TVT-O at a median of 7.5 years [22].

Sexual Function After Mid-Urethral Tape Surgery

Sexual dysfunction after MUS surgery is not generally addressed in many studies. However, a reduction in coital incontinence has been noted [23]. Although a recent RCT [24] and another

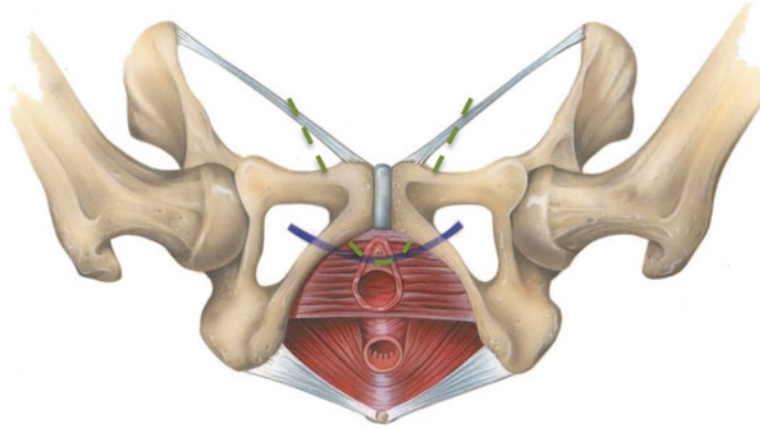

Fig. 12.9 Diagrammatic representation of the relationship of a retropubic MUS (*green dashed line*) and obturator MUS (*blue solid line*) with the urethra (Image adapted with permission from American Medical Systems, copyright®)

cohort study [25] have shown that overall sexual activity improves after sling surgery, this may be related to feelings around reduction in coital incontinence and cases do exist of anorgasmia following MUS insertion (*author experience*, *unpublished work*).

MUS Versus Other Surgical Techniques

MUS have stood the test of time and both 12 month and 5 year data suggest no difference in cure rates when compared to the old gold standard treatment for SUI, colposuspension, although the latter was associated with higher rates of voiding dysfunction (15 % versus 9 %) whilst bladder perforation was higher for the MUS (7 % versus 2 %) [26].

MUS and AF-PVS have also been shown to be similarly efficacious, the advantage of the MUS being shorter operating times and lower rates of complications and voiding dysfunction [12].

Complications

Retropubic tapes have been reported to be associated with a 3–9 % bladder perforation rate and, on rare occasions, with bowel and major vascular injuries [27, 28]. The transobturator technique has been advocated because it avoids the blind retropubic passage of trocars and, therefore, is expected to reduce the risk of bladder, bowel, and iliac vessel injury. However, in experienced hands, this rate of bladder perforation with retropubic tapes may be as low as 0.3 % [19].

Obturator slings are associated with their own characteristic complications, mainly groin pain [29–31]. Chronic perineal pain at 12 months after surgery was reported in the EAU Panel meta-analysis to be 7 % with transobturator tapes compared to 3 % with retropubic tapes [19].

However, both approaches are associated with voiding dysfunction which is quoted as 4 % following transobturator tape insertion compared to 7 % with retropubic tape insertion [19]. Other risks include urethral perforation, *de novo* urgency and vaginal perforation.

The use of synthetic MUS has introduced risks that are unique to the use of mesh: mesh erosion (also known as extrusion or exposure) is reported in ≤5.8 % [32]. In 2011, the US Food and Drug Administration (FDA) held a panel meeting of scientific experts (Obstetrics and Gynaecology Devices Panel of the Medical Device Advisory Committee) and sanctioned a systematic review of the relevant literature relating to mesh use from 1996 to 2011. In March 2013, a statement was released outlining concerns regarding mesh used in the treatment of pelvic organ prolapse (POP) [33]. Although much of the FDA notification dealt with mesh used for transvaginal POP, mesh used for stress incontinence was implicated by association.

Vaginal tape extrusion may be asymptomatic [34, 35]. Alternatively, women may present with persistent vaginal discharge [34–36], partner discomfort during sexual intercourse [34, 35], vaginal bleeding [36] and pain [36]. The time to erosion may occur as late as 10 years after MUS insertion [37].

The optimal management of tape erosion remains undefined and our evidence-base is derived from individual case reports and small case series only. Rashid et al. [38] analysed 23 retropubic MUS erosions. Nine were managed with tape excision as the primary procedure; 14 erosions were treated with epithelial closure. Epithelial closure was successful in only 5 cases (4 after 1 closure, 1 after 2 attempts at closure). The remainder required excision after 1, 2 or 3 failed attempts at closure. Of 16 patients who had tape excision (either as a primary procedure or after closure), eight patients developed recurrent SUI. Managing this complication represents the next conundrum to the surgeon treating SUI.

The FDA has encouraged patients to question the need for the use of mesh anti-incontinence surgery over non-mesh alternatives and to enquire about surgeon experience. In a study where 201 women were given the option between a PVS and a MUS, 45 % chose PVS and 55 % chose MUS [39]. Whilst National organisations such as National Institute for Health and Care Excellence (NICE, UK) have specified that MUS should not be inserted by surgeons who do relatively few procedures a year, whether a decline in the actual number of MUS being used in favour of non-mesh alternatives is yet to be seen.

Single-Incision Slings

The single-incision sling (SIS) was developed to provide mid-urethral support as with the traditional MUS, also to shorten the length of macroporous polypropylene tape required and to avoid the risks associated with retropubic or transobturator passage of trocars and tape (Fig. 12.10). The first SIS (TVT-Secur®, Gynecare, Ethicon, Somerville, NJ, USA) was approved by the FDA in 2006 but countless kits have been subsequently brought into the market.

Data on SIS is still in consideration. There is a significant variation in kit design and whether they should be considered as one class of device is debatable. In addition, some devices, e.g. TVT Secur and the Minitape, have been withdrawn from the market, but data relating to their use is sometimes included in SIS outcomes.

The most recent meta-analysis [40] (excluding TVT Secur data) have shown no difference in efficacy between SIS and traditional MUS. However, not all SIS devices have been subjected to RCT evaluation.

Although SIS were brought into the market to reduce complications associated with conventional MUS, vaginal perforation, mesh erosion and urinary retention have still been reported and longer-term data in RCTs are required to make any accurate recommendations.

The Adjustable Sling

Adjustable slings were designed to address voiding dysfunction seen in both retropubic and transobturator slings. The premise was to allow the tension of the newly implanted sling to be increased or decreased, either during or shortly after implantation.

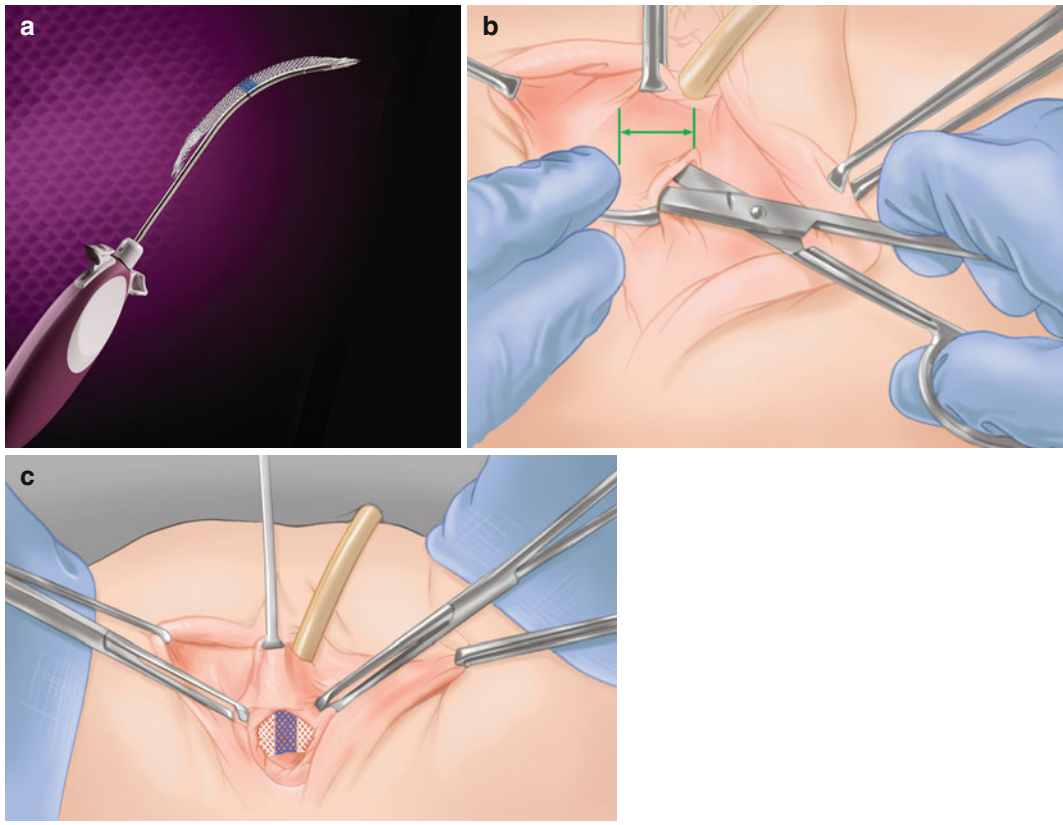

Fig. 12.10 Single-incision mini-sling (SIS): (**a**) shorter mesh compared to traditional MUS; (**b**) single incision; (**c**) SIS once positioned (Reproduced with permission from American Medical Systems, copyright®)

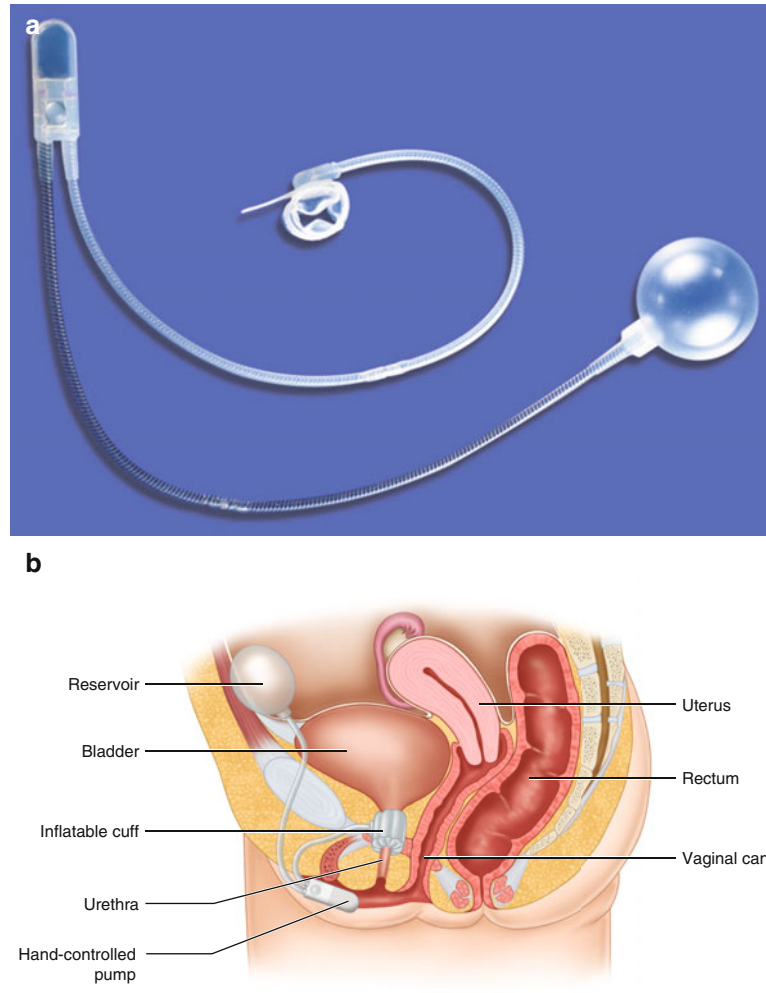

Fig. 12.11 (**a**) The AMS 800 (**b**) Illustration demonstrating the position of the artificial urinary sphincter (Reproduced with permission from American Medical Systems, copyright®)

However, no RCT comparing adjustable slings to conventional MUS exist and studies which have been published tend to be poorly designed and include small numbers of patients. In addition, the existing devices vary considerably, making it difficult to compare them.

The Artificial Urinary Sphincter in Women

The artificial urinary sphincter (AUS) is an established treatment modality for incontinence secondary to sphincter weakness in men and is described in detail in Chap. 14. Its use in women, however, is more selective, being reserved as a salvage option in many cases following one or more failed incontinence operations.

The AUS in its most common form comprises three silicone elastomer components: a urethral cuff placed around the bladder neck, a pressure-regulating reservoir inserted in the retropubic space, and a control-pump situated in the labia majora (Fig. 12.11). The prosthesis is filled with saline or contrast. Pressure on the pump allows passage of liquid from the cuff towards the balloon and allows micturition. After 3–4 min, the liquid is automatically transferred from the balloon to the cuff to restore continence.

As originally described in 1988, AUS insertion in women may be performed vaginally, requiring exposure of the bladder neck and urethra anteriorly, providing easier accessibility for dissection of the vagina from the posterior wall of the vesical neck and upper urethra [41]. However, a combined abdominal-vaginal approach is often favoured due to the risks of concomitant bladder and bowel injury when patients have had multiple previous operations. Some centres are also placing the AUS laparoscopically or robotically.

After initial introduction of the technique, AUS use increased worldwide, but whilst the number of AUS implanted in men increases (likely to be a reflection of the increased uptake of radical prostatectomies), the annual implant rates in women are much lower compared to men and decreasing: in 1990, 298 procedures reduced to only 67 in 2008 [42].

Outcomes

The AUS is indicated in women with severe SUI secondary to intrinsic sphincter deficiency, usually in a salvage setting. Due to this, studies looking at outcomes of surgery involve only small numbers (n = 8–367, Table 12.2) with variable lengths of follow-up. In addition, case series are confounded by a variable selection criteria, with a proportion of women having neurological dysfunction or one or more previous anti-incontinence procedures.

Table 12.2 shows the available literature on outcomes after implantation of an AUS in women. Most patients achieved an improvement in SUI, with reported subjective cures in 59–88 %. Common side effects included mechanical failure requiring revision (up to 42 % at 10 years) and explantation (5.9–15 %) secondary to infection or erosion.

Risk factors for failure included older age, previous Burch colposuspension, pelvic radiotherapy [43] and peri-operative injury to the urethra, bladder or rectum [44].

Whilst laparoscopic and robotic-assisted techniques are thought to be feasible, larger studies are required to accurately assess the place of minimally-invasive approaches in AUS implantation [45–47].

It follows that AUS implantation in women should be centralized to high-volume specialist centres only.

Adjustable Compression Therapy

The ACT uses specially designed introducers to insert two small silicone balloons filled with contrast on either side of the urethra, close to the bladder neck, via a percutaneous perineal approach and using radiological guidance. The procedure can be performed under local, regional or general anaesthesia. Each balloon is attached to a subcutaneous port placed in the labia majora. These ports act as conduits to add or remove fluid to the balloon postoperatively, thereby achieving the best balance between controlled leakage and voiding.

Recognised complications of the procedure include urinary tract infection, balloon dislocation, port erosion, urethral pain and *de novo* urgency.

Evidence for the device is limited to small case series with variable follow-up (5–84 months). Whilst UI is seen to improve, the device requires adjustment in most patients to achieve continence and explantation rates are high.

Post-operative Precautions and Care

Traumatic catheterisation may encourage sling erosion at the level of the urethra. Therefore, it is important for patients to be informed that if they need catheterization, this should be done using the smallest available catheter and preferably by medical staff familiar with the surgery they have had. In addition, catheterization in a patient with an artificial urinary sphincter requires prior deactivation of the AUS.

Following surgery, sexual intercourse may resume any time from 6 weeks. Patients must be warned about the risk of dyspareunia if there has

Table 12.2 Published studies of AUS for SUI women

Author, year	N=	Continence	Infection	Erosion	Explanation	Notes
Light and Scott (1985) [48]	39	92 %				Severe, persistent urinary incontinence following surgical correction of the anatomical deformity
Diokno et al. (1987) [49]	32	Nineteen-one (dry without pads)				Recurrent urinary incontinence after failed bladder suspension procedures. Mean follow-up 2.5 years
Webster et al. (1992) [50]	25	100 %	0	0	0	Severe intrinsic urethral weakness in most patients with multiple prior failed cystourethropexies. One death – CVA
Karram et al. (1993) [51]	7 (8 implants)	100 %				Six to twenty-four months follow-up Severe and/or recurrent SUI
Chatelain et al. (1995) [52]	45	78 %			13 % Revision rate for technical failure of 24 %.	Recurrent incontinence after surgery, due to sphincter insufficiency
Heitz et al. (1997) [53]	144 70 – type III SUI after 208 previous unsuccessful incontinence procedures; 54 neuropathic bladder dysfunction; 20 – congenital or acquired internal sphincter weakness	86 %				Four patients went on to urinary diversion
Marques Queimadelos et al. (1999) [54]	18	88 %	1 (5.5 %) – explanted			
Costa et al. (2001) [55]	207 (179 non-neurogenic, 27 neurogenic) mean FU 3.9 years	88.7 % non-neurogenic; 81.8 % neurogenic	12 (5.9 %) explanations due to prosthesis erosion, extrusion or both			

Chung and Cartmill, 2010 [55]	47	59 % with AUS only; this figure increased to 85 % when concurrent clean intermittent self-catheterization was performed.	(17 %) AUS removed due to AUS erosion or infection. There were 20 AUS revisions			25-year follow-up
Chung et al. (2011) [56]	29	The continence rate with no pad use was 70 % and this increases to 83 % in patients wearing one precautionary pad.	Five (17 %) AUS devices were explanted due to AUS erosion or infection. Thirteen AUS revisions were made and device malfunction accounted for 95 % of the cases.			Following failed anti-incontinence surgeries.
Vayleux et al. (2011) [43]	215	158 patients (73.5 %) were continent			7 %	Mean follow-up 6 years
Vayleux et al. (2012) [57]	215 (Group 1 = 206, no previous radiotherapy) Group 2 = 9 previous pelvic radiotherapy)	Group 1 = 78 % <50 % group 2		26 % group 1 60 % group 2	Group 2 (all eroded)	Mean follow-up 6 years
Costa et al. (2013) [58]	344 (367 implants)	85.6 %				Mean follow-up 9.6 years The 3-, 5-, and 10-year device survival rates were 92.0 %, 88.6 %, and 69.2 %, respectively. The mean mechanical survival was 176 months (14.7 years)
Phe et al. (2014) [59]	34	61 %			26 %	Mean follow-up 17 years The 10-, 15- and 20-year device survival rates without explanation were 80 %, 80 % and 74 %, respectively. The 10-, 15- and 20-year survival rates of the device without revision were 79 %, 65 % and 40 %, respectively.

been a vaginal incision and dissection. In addition, partners may experience persistent discomfort or pain during intercourse, usually signaling tape or sling extrusion into the vagina.

The artificial urinary sphincter is activated 6 weeks after the initial surgery and this is an opportune time to assess healing of the incision and position of the labial pump. Follow-up after 3 months for all operations discussed is important to evaluate the outcome of the surgery as well as any side-effects. It is recommended that a vaginal examination be performed at the follow-up appointment to exclude a small (often asymptomatic) tape extrusion in the case of mid-urethral slings. Subsequent follow-up is individualized to patients and according to clinician preference. Patients must be warned that recurrent urinary tract infections, persistent pain or dyspareunia and return of incontinence are a sign that they should seek help from their clinician earlier than planned.

Conclusions

Surgery to treat incontinence has evolved to include the use of a number of prosthetic devices and therefore urologists managing patients with female incontinence should be familiar with the principles involved in the implantation of prostheses. Early recognition of complications is essential in order to avoid extensive surgery to remove the prosthesis and to avoid more complex procedures such as AUS insertion around the bladder neck.

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Sacral Neuromodulation

13

Simon C.W. Harrison

Abstract

Neuromodulation of the central nervous system (CNS) reflexes that control lower urinary tract (LUT) function, using electrical stimulation of sacral nerves has become established as an effective treatment option for a range of LUT dysfunctions. The treatment has opened up a whole new field of surgical research and provides a much-needed new approach to treating LUT symptoms that are having a devastating effect on a person's quality of life. Sacral nerve stimulation (SNS) offers patients with severe bladder overactivity and women with urinary retention the possibility of a substantial improvement in their urinary symptoms; other patient groups, such as those with bladder pain or neurogenic bladder dysfunction, may also be potential candidates for treatment. While the surgical procedures are minimally invasive, complications remain problematic. At least 30 % of patients will require unplanned reoperations for problems such as loss of clinical benefit, stimulator-associated pain and cable breakages. The expense of the hardware itself and the costs of follow up mean that there are unanswered questions regarding the cost-effectiveness of SNS. The treatment has the potential to be used in a large cohort of patients given the prevalence of the conditions being treated but cost-containment may lead to its use being restricted to patients with very severe symptoms.

Keywords

Sacral nerve stimulation • Neuromodulation • Urinary incontinence • Urinary retention • Bladder pain syndrome • Neurogenic bladder

Introduction

A wide range of electrical stimulation techniques have been used in attempts to influence lower urinary tract function; the history of these efforts dates back to the late 19th century [1]. Electrical stimulation can be used to alter LUT

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function through a variety of mechanisms. These include direct stimulation of smooth or striated muscle, inhibition of pain pathways and modulation of reflex activity [2]. External stimulation, using transcutaneous and transvaginal systems, have been widely incorporated into clinical practice but the use of implanted devices has been more limited until recent years. The Brindley sacral anterior root stimulation device was developed to drive bladder contractions in patients with complete spinal cord injuries but has no role in other patient groups [3]. In contrast, sacral nerve stimulation (SNS) using the InterStim® (Medtronic, Inc.) implanted neuromodulation system is used in several different patient groups and the device has now been used in tens of thousands of patients.

The introduction of SNS as an effective therapy for LUT dysfunction followed the pioneering work of Tanagho and Schmidt [4]. Following the initial development work, multicentre, prospective controlled clinical trials were carried out and provided an evidence base which has led to the incorporation of SNS into clinical guidelines and pathways. For example, the National Institute for Health and Care Excellence, (NICE), has placed SNS in their management algorithm for female urinary incontinence [5]. Although there is strong evidence to support the use of SNS in patients with LUT dysfunction, there are important issues that have yet to be satisfactorily addressed. These include the imperfect methodology for selecting patients for treatment with a minority of patients who receive implants failing to maintain long-term clinical benefit. Questions also remain regarding the cost-effectiveness of the treatment, the equipment is expensive and there are additional surgical costs from the test procedure and surgical implantation. In addition approximately one third of patients undergo re-operation for complications. This chapter examines the theoretical basis for neuromodulation using the InterStim system, the procedures involved, the benefits of treatment, its potential risks and questions about cost-effectiveness.

Neural Mechanisms Underlying Neuromodulation

It is generally accepted that SNS influences LUT function through a modulating effect on reflex pathways, rather than by direct stimulation of motor nerves or retrograde activation of sensory nerves. Evidence that afferent nerve stimulation underpins neuromodulation effects comes from several observations. Neuromodulation effects can be seen during stimulation of the dorsal nerve of the penis, which is a pure sensory nerve that does not carry any fibres to or from the urinary tract [6]. Furthermore, treatment effects are seen with electrical stimulation intensities that are below those that activate motor nerves and produce reflex contractions of the anal sphincter with long latencies that indicate that stimulation is activating the anal sphincter via a polysynaptic pathway [7]. However, efferent nerve stimulation cannot be completely excluded as a component of the neuromodulation therapeutic mechanism as activation of motor nerves has been reported to be associated with enhanced clinical outcomes [8].

The question arises as to where in the central nervous system (CNS) do the fundamental alterations in neuronal activity that trigger the therapeutic effect of SNS take place. It is possible that the key changes are occurring in the spinal cord, in the brain or in both structures. Functional brain scanning has shown that an SNS influences activity in many different areas of the brain with such changes being seen both in patients with overactive bladders [9] and in women with urinary retention [10]. However, these studies do not disentangle cause from effect; a region of the brain may become either more or less active during SNS but this does not mean that the change in neurological function is key to the therapeutic effect that is sought.

There are limits to the scope of clinical studies, whether imaging-based or electrophysiological. Animal models have the potential to offer further insights into the neuro-physiological processes that underpin SNS. For example, acute studies in the cat have been used to look at the neurotransmitters that might be central to neuromodulation processes [11].

Indications

The two established urological indications for SNS are urinary retention in women, in the absence of either urethral stenosis or a neurogenic cause, and idiopathic detrusor overactivity (IDO). However, there are a number of additional indications for which there is at least some evidence to support a potential role for SNS. These include male bladder outflow obstruction, bladder pain syndrome and neurogenic lower urinary tract dysfunction (NLUTD).

The use of SNS in the treatment of IDO is supported by both randomised trials and case series which describe improvements in symptoms of frequency, urgency and urge incontinence [12–16]. Patients are considered for SNS when symptoms persist despite conservative management with lifestyle advise, bladder training and pharmacotherapy. In general, authors have reported results of treatment in patients who have had urodynamic proof of detrusor overactivity [17] but equally good results have been reported in patients with symptoms of bladder overactivity whether or not they have proven IDO on urodynamic studies [18].

Women with spontaneous onset of severe voiding difficulty or urinary retention have also been shown to be candidates for SNS, with a strong evidence base supporting its use in this context [19–23]. A sub-group of women with this condition have been shown to have electrophysiological and structural changes in the striated urethral sphincter and are categorised as having Fowler's syndrome. There is limited evidence that suggests that such patients might respond particularly well to SNS [24] although the large majority of publications do not separate out Fowler's syndrome patients specifically. Urodynamic investigations of women who have a return of voiding following an SNS implant demonstrate that stimulation does not restore a normal pattern of voiding but appears to alter reflex behaviour sufficiently to allow, albeit abnormal, bladder emptying to be restored [25].

Less well established indications for SNS include the bladder pain syndrome and NLUTD. Although it might be expected that control of pain pathways might necessitate modulation of all of the pain carrying pathways, and therefore more widespread stimulation than is provided by the standard SNS implant, encouraging results have been published for patients with bladder-related pain. Success rates have mirrored those achieved for patients with bladder overactivity or urinary retention [26–29].

There are many reports describing the use of SNS for NLUTD. However, there is a lack of information from randomised trials which is not altogether surprising, given the difficulties presented by carrying out trials on this heterogeneous patient population. Benefit has been demonstrated in patients with bladder overactivity or urinary retention after incomplete spinal cord injury [30] and multiple sclerosis [31, 32]. Although most studies have described outcomes of SNS which are similar to those seen in non-neuropathic patients [33], disappointing long-term results have also been described [34].

SNS has been used to treat patients in all age groups. In the paediatric age group, children with LUT dysfunction, often due to a neurogenic cause, have been treated using neuromodulation [35–37]. At the other end of the age spectrum, successful use of the technique in the elderly has also been reported [38–40].

Severe lower urinary tract symptoms (LUTS) inevitably have an impact on a person's psychological well-being. In addition, psychiatric disease can coexist with urinary symptoms either as a simple coincidence or through a process of somatisation which can lead to psychological disturbance manifesting itself in the form of urinary symptomatology. For these reasons, a number of patients with intractable LUTS who are being considered for SNS will have co-existing psychiatric symptoms. The question has been raised as to whether SNS may be less successful in patients with a combination of LUTS and psychological disturbance [41], however, the very limited information that is available suggests that psychological factors do not correlate with success rates [42]. It is also relevant to consider the impact of SNS on psychiatric symptoms. The treatment has been shown to induce, not only an improvement in general quality of life measures,

but also a reduction in symptoms of depression following treatment of LUTS [43].

Surgical Procedures

It is widely accepted that it is appropriate to undertake a preliminary test procedure before committing to implanting a permanent neurostimulator. The primary driver for this approach has been the high cost of the stimulator but it is also desirable to avoid carrying out an implant which is not effective and might be associated with complications such as infection, pain and MRI incompatibility. However, the ability of the test procedures that are in use to reliably predict which patients will benefit from SNS in the long-term has not been subject to rigorous scientific scrutiny in a controlled trial.

Two approaches to preliminary testing, using an external stimulator generator, are available: the peripheral nerve evaluation (PNE) test and the two-stage implant. The former involves threading a wire, with a single stimulating electrode, into a sacral foramen through a test needle. The latter requires a more formal surgical procedure to implant a four-electrode stimulation lead into position; if the test stimulation period is successful, the stimulation lead is retained and connected to the definitive implanted stimulation generator.

The PNE test can be carried out either under local or general anaesthetic. The patient is positioned prone with the legs supported on a pillow, so that movement of the toes can be seen (Fig. 13.1). The perianal area is exposed using tape applied to the buttocks. Surface markings are used to identify the approximate positions of the relevant sacral foramina. These typically lie 2 cm lateral to the midline with the S3 foramen lying on a transverse line that runs between the upper margins of the greater sciatic notches. The test needle is introduced at an angle of approximately 30° from the vertical, so that the tip passes through the tissues in an antero-inferior direction (Fig. 13.2). Typically the needle tip will encounter the bone of the sacral ala with the correct sensation being one of encountering hard bone. If the needle tip is advanced through "gristle", then the needle tip is often either too far medially or laterally. The tip of the needle is used to probe the sacral ala until the needle tip drops into one of the sacral foramina.

The test needle is completely insulated other than for a few millimetres at the tip and a short length of needle near the hub. Once a foramen has been entered, the external pulse generator is connected using a spring clip electrode attached to the non-insulated segment of the needle near its hub. The circuit is completed with an adhesive patch electrode on the patient's skin. The needle tip acts as the cathode. It is now necessary to

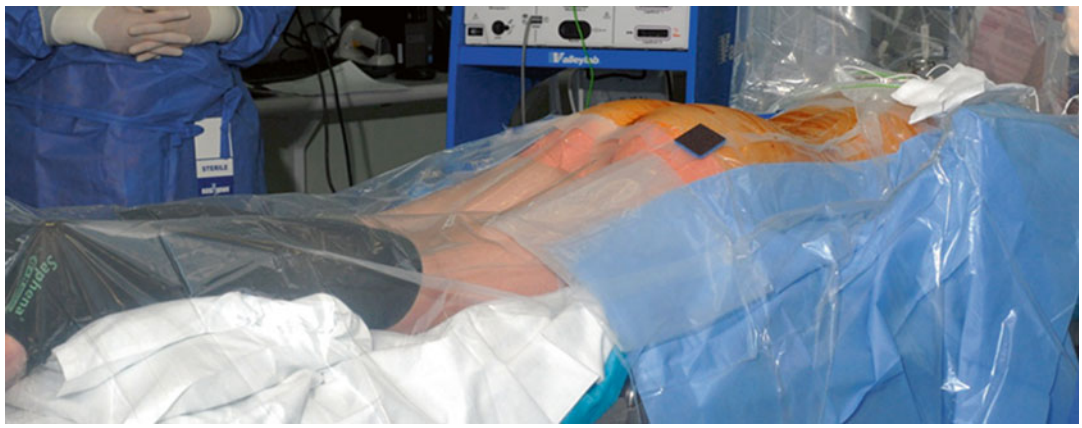

Fig. 13.1 The patient positioned prone and covered with a transparent isolation drape to allow visualisation of the operation site, peri-anal region and legs

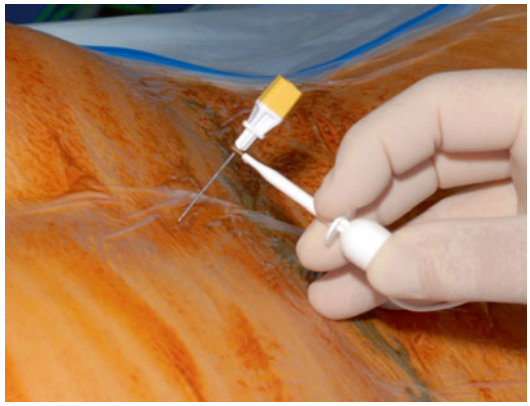

Fig. 13.2 An insulated test needle is inserted into a sacral foramen and muscle responses to electrical stimulation are assessed

identify which foramen has been entered. If the subject is awake, then stimulation is gradually introduced until the patient can localise where stimulation is being sensed. If the needle is in either S3 or S4, they will typically feel a tapping or bubbling sensation in the immediate perianal area. In women, this may drift forward into the vagina. S2 will typically give a sensation several centimetres away from the anal canal. Stimulation is then increased to the point where muscle responses can be detected. If the patient is under general anaesthetic, then muscle responses alone are used to identify the foramen level. S2 stimulation will produce contraction of the gluteal muscles and rotation of the leg. S3 will produce a pelvic floor contraction (bellow's response), coupled with flexion of the toes. S4 will only produce a pelvic floor and anal contraction. The depth of the needle in the foramen is then adjusted to give optimal responses. The temporary implanted electrode is threaded down the needle and the needle withdrawn. The electrode itself is made of a wire helix which allows it to stretch without the tip becoming displaced from its position in the foramen. An adhesive dressing is used to secure the electrode to the skin and an external pulse generator is attached to the electrode with the circuit being completed with an adhesive patch, as during the PNE procedure itself.

A PNE test is carried out for between 1 and 2 weeks, and extended for longer if necessary. During that period of time, the patient maintains contact with the clinical team to ensure that there are no technical difficulties. A technical problem is suspected if the patient loses the classical sensory response to stimulation or if the stimulation voltage has to be increased to high levels. The patient maintains a careful frequency/volume chart for the duration of the test period. If their problem is urinary retention, then volumes retrieved by self-catheterisation are also recorded. At the end of the test period, a global clinical assessment of the effectiveness of the intervention is made and the urine frequency volume charts from both before and after implantation are scrutinised to look for evidence of a clear improvement in lower urinary tract function.

If a two stage implant is being carried out, the first stage involves implanting a definitive tined lead electrode into position. The tined lead has four individual electrodes sited over the distal 3 cm. Proximal to the electrode array are several plastic tines which spring out from the lead during deployment, thereby anchoring the lead in position. The introduction of the tined lead has enabled a minimally invasive procedure to replace the original open surgical placement of the permanent stimulating electrode [44, 45].

Some centres carry out insertion of the tined lead under local anaesthetic but in others a general anaesthetic is used. A meticulous approach to sterility is required. A large plastic isolation drape can be used to cover the operative area while still allowing clear views of the perianal area and legs. The test needle is used to locate an appropriate sacral foramen as in the PNE test. Once the needle is positioned, a 2.0 cm transverse incision is made, which incorporates the site of needle entry through the skin. The incision is deepened through subcutaneous fat to the deep fascia. The needle core is removed and a stiff guidewire inserted (Fig. 13.3). The depth of its tip is then checked using lateral sacral X-ray screening. The needle is removed and a dilator passed over the guidewire to dilate a track into the foramen (Fig. 13.4). Once again, X-ray screening is utilised to verify the position of the dilator. The dilator and guidewire are then removed, leaving the sheath in place, through

which can be threaded the definitive tined lead (Fig. 13.5) The depth of the tined lead is checked again with lateral screening of the sacrum and the sheath removed, so that the plastic tines deploy into the tissues, thereby fixing the electrode in place (Fig. 13.6). The preference is to have the most proximal stimulation point within the sacrum with the adjacent stimulation point positioned on the anterior periosteum of the sacrum with the two distal electrodes lying within the pelvis.

With the lead in position, each of the four stimulating electrodes is checked to evaluate their responses aiming for at least two electrodes to be producing clear pelvic floor muscle contractions in response to a stimulation level of less than three volts (Fig. 13.7). The tined lead can be pulled out and repositioned if necessary.

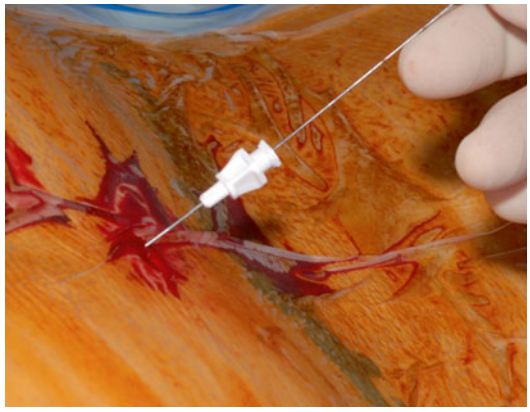

Fig. 13.3 Once an appropriate foramen is identified, a guidewire is passed down the needle and a small incision is made at the site of needle placement

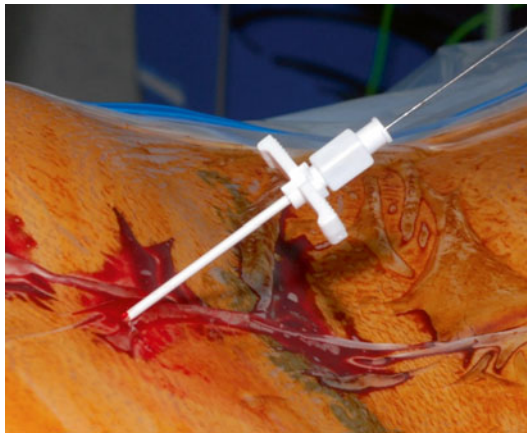

Fig. 13.4 The needle is exchanged for a dilator and sheath which is inserted under radiological control

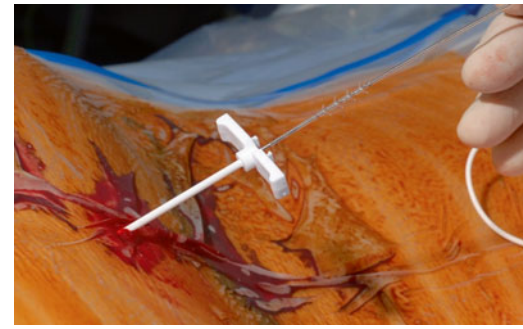

Fig. 13.5 After removal of the dilator, the external sheath is left in situ to allow the permanent tined stimulating electrode to be inserted and positioned under radiological control

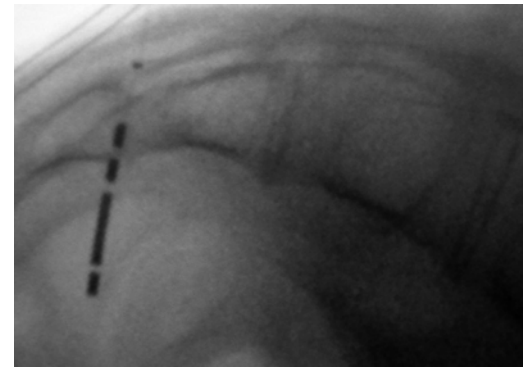

Fig. 13.6 The position of the tined lead stimulating electrodes with the most proximal of the four electrodes positioned in the sacral foramen and the distal three electrodes within the pelvis

Once the tined lead is positioned, a second incision is made in the ipsilateral upper outer gluteal area. This incision is approximately 5.0 cm long and is deepened into the subcutaneous tissue. A tunnelling trocar and sheath is passed from the tined lead incision to the gluteal incision. Withdrawal of the metal trocar leaves the plastic sheath *in situ*, along which the tined lead can be threaded. The sheath is withdrawn and the tined lead is connected to an extension cable, which passes from the gluteal pocket back towards the midline to exit well away from the tined lead incision. It is good practice to wash out the wounds with antibiotics before they are

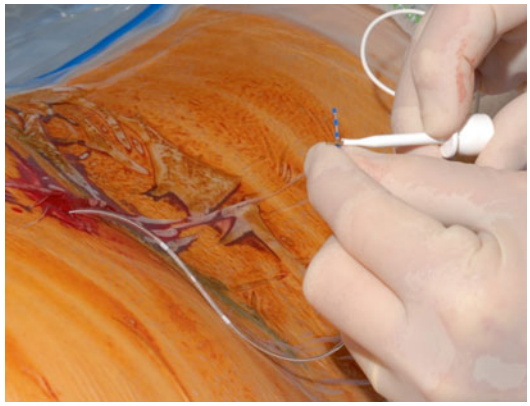

Fig. 13.7 Muscle responses are checked for each of the four tined lead electrodes. At least two electrodes should produce a pelvic floor/anal sphincter contraction at low voltage

closed and dressings applied. The cable emerging through the skin is then connected to the pulse generator for a period of at least 2 weeks. Urine frequency/volume charts are used to assess the response, as in the PNE test.

The patient returns after the test period for the second stage of the implantation procedure. An assessment is made as to whether the period of testing has demonstrated a clear improvement in lower urinary tract function. If no improvement has been seen, then the wounds are re-opened and the tined lead and extension cabling is removed. If, however, the test has been successful and clear benefit has been obtained, the gluteal incision is opened and the extension wire removed, leaving the tined lead in position. A slightly larger subcutaneous pocket is created and the definitive pulse generator is implanted (Fig. 13.8) The wounds are again washed out with antibiotics and closed (Fig. 13.9)

In patients where a PNE test has been carried out and shown to be successful, a single procedure is used to implant the generator, whereby the tined lead is positioned and tunnelled to a gluteal pocket, into which is implanted the pulse generator.

The majority of published reports refer to implantation of a single tined lead into one foramen. However, there is some evidence that a minority of patients will respond to stimulation delivered through bilateral tined leads [46]. Both

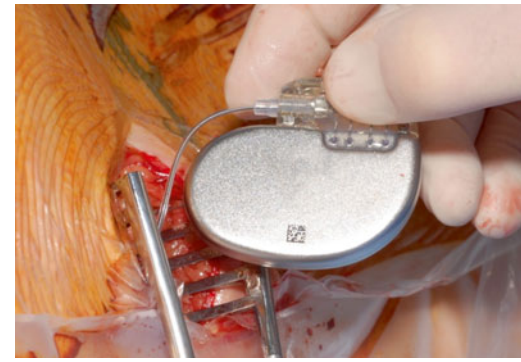

Fig. 13.8 The tined lead is tunnelled across to an ipsilateral incision in the upper, outer quadrant of the gluteal region and attached to the implanted pulse generator which is placed in a subcutaneous pocket

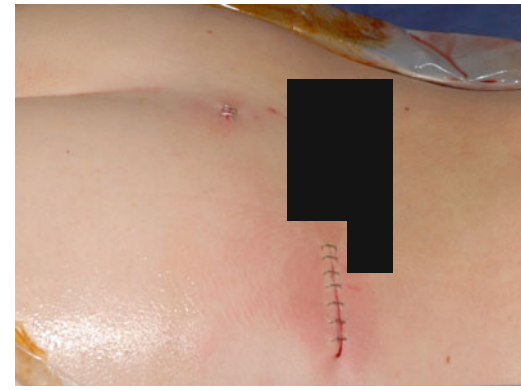

Fig. 13.9 The smaller incision is at the site of the tined lead implantation while the larger incision is used to implant the pulse generator

leads are implanted in the same way as for the unilateral procedure but are tunnelled to a single gluteal pocket where a dual pulse generator is implanted.

Programming

The implanted pulse generator is programmable from an external device which establishes a telemetry link to the implant. The system is extremely versatile, so that each of the four electrodes can be used as an anode or cathode. Alternatively, current can flow back to the pulse generator itself from one or more of the tined lead electrodes. The pulse frequency,

pulse width and pulse voltage can all be adjusted independently. Furthermore, stimulation can be delivered either continuously or in trains of pulses. The programmer therefore has a range of variables that can be used in an attempt to optimise the performance of the implant. The patient has a simpler telemetry device, which they can use to turn the implant on or off, and adjust the voltage of stimulation between set limits.

The technical aspects of programming have received little attention in the published literature despite the clinical benefits from stimulation being dependent on accurate programming. However, there has been some interest in using electrophysiological recording as an aid to programming [47]. Programming is important, not only for optimising clinical benefit, but also in the pursuit of the lowest possible battery usage. Once the battery is exhausted a new pulse generator has to be implanted; the new generator is an expensive piece of hardware and the replacement operation is accompanied by a risk of damage to the tined lead and the introduction of infection.

There is a lack of published data looking in detail at the correlation between the use of different programming criteria and the clinical outcome although it has been suggested that obtaining satisfactory motor responses might be a better predictor of a successful outcome than sensory responses alone [48].

Programming should follow a set procedure which involves using each of the four tined lead electrodes in turn as a single cathode with the anode being set as the generator box itself. The electrode or electrodes giving the strongest sensory and/or motor response is then set as the definitive cathode with the adjacent tined lead electrodes being used as anodes. This allows stimulation to be delivered using a minimum consumption of electrical power.

In situations where stimulation is ineffective or is associated with pain, stimulation parameters can be altered. For example, painful stimulation may be improved by adjusting pulse width, while a lack of benefit can sometimes be overcome by using intermittent stimulation.

Results

For patients with standard indications for sacral nerve stimulation, such as female urinary retention, bladder overactivity or painful bladder syndrome, there are similar proportions of patients who respond positively during a test PNE. However, implantation of the definitive electrode as the first part of a two stage implant has been advanced as providing a more reliable screening evaluation for SNS than the PNE [45]. The two stage approach is believed to produce a higher proportion of positive clinical responses, and therefore of permanent stimulator implantation, than does the PNE test [49]. One possible explanation for an excess of false-negative test procedures with the PNE test is that the single electrode stimulation point can migrate away from the relevant nerves, thereby leading to suboptimal stimulation. To counter this possibility, two PNE wires can be left *in situ* with close follow up of patients in order to pick up suboptimal stimulation or suboptimal sensory responses and allow a switch to the alternate electrode in order to maintain satisfactory stimulation if necessary.

The question arises as to what is the optimum period for the first stage screening process; longer tests may reduce the number of false negative tests but are inconvenient for patients and might be associated with higher implant infection rates due to bacterial invasion via the extension cable, which emerges from the skin. In circumstances where the outcome of testing is uncertain, there is some evidence that extending the testing period beyond 3 weeks may increase the proportion of patients who go on to definitive implantation without excessive infection rates [50, 51].

Despite the encouraging response rates to two stage implantation compared with PNE testing, there are some unresolved issues. Experience with the two stage implant has demonstrated a higher conversion rate to definitive implantation in patients with urinary retention. Those patients receiving implants maintained similar long term results from the definitive implant as those selected by PNE. In contrast, the increased conversion rate amongst patients with overactivity was accompanied by a deterio-

ration in long term outcomes for neuromodulators implanted for this indication. One possible explanation for this discrepancy is that clinicians respond to patient pressure to proceed to the second stage of the procedure, as opposed to removing the tined lead, when the patient returns at the end of the first test stage. For patients with urinary retention, a negative test result will be very obvious, as they will continue to be dependent on intermittent catheterisation; there is clarity as to whether the test has been successful or not. In contrast, patients with bladder overactivity have more subtle levels of benefit, which include alterations in the sense of urinary urgency in addition to more easily measured changes, such as urinary frequency or voided volumes. A patient with a potentially useful but incomplete response will often be very keen to proceed with implantation of the neuromodulator with the result that permanent implants may be carried out in patients with a relatively limited response to sacral nerve stimulation.

The results of permanent sacral nerve stimulation appear to be relatively consistent for the different indications. Multiple randomised controlled trials were carried out in the years immediately after the commercial development of the Medtronic Neuromodulation System [12, 13, 19, 22]. These trials were designed to answer the question as to whether neuromodulation was capable of delivering clinical benefit. Patients who had undergone a successful PNE test were randomised to either receive an immediate implant, or to have their implantation date delayed for 6 months. The latter group acted as a control group for the immediate implantation patients. The criteria for a successful implant consisted of a 50 % improvement in one of the main clinical variables, such as urinary incontinence or frequency of intermittent catheterisation. These studies successfully demonstrated that sacral nerve stimulation does produce a measureable change in lower urinary tract function in patients with bladder overactivity or urinary retention.

The next step was to look at the durability of responses. It had been feared that the neuromodulation effect would be short-lived, as neuroplasticity might lead to abnormal reflex pathways adjusting and overcoming the neuromodulation input. Follow up data from the multicentre studies [15, 19, 22] and single centre case series [14, 16, 21], demonstrated an element of decline in success rates over time but that stimulation could remain beneficial over the course of many years. The durability of the benefit comes into sharp focus when patients experienced a loss of battery power after a number of years of neuromodulation. The near universal experience is for such patients to become symptomatic within a short period of time once the generator battery is exhausted. A change of the pulse generator is accompanied by a restoration of clinical benefit in the large majority of patients.

While the original controlled trials provided scientific evidence for there being a neuromodulation effect, they provided less convincing evidence regarding the overall level of benefit provided to patients. The original trials did give some indication as to the proportion of patients whose symptoms were completely alleviated by treatment. The complete responders progressed to having no episodes of urinary incontinence in the urge urinary incontinence group, or were no longer practicing intermittent self-catheterisation in the group with urinary retention. However, it was difficult to determine whether patients with a greater than 50 % reduction in one of the main parameters being measured, would themselves equate that improvement to clinical success.

Calculating the number needed to treat in order to achieve substantial clinical benefit necessitates combining those patients showing a complete response with those in whom the response is sufficient to lead to a marked improvement in quality of life. Some authors have approached this problem by using more stringent criteria for success [14]. Data from such studies showed lower success rates, as would be expected, but did continue to demonstrate that a substantial proportion of patients had a durable benefit at 5 years and longer. Alternatively, a global clinical assessment can be made as to whether substantial benefit has been obtained. In general patients with urinary retention, bladder overactivity or a combination of symptoms have a 5 year success

rate of 55 % and a 10 year success rate of 45 % after implantation of a neuromodulator. However, the majority of patients with a successful outcome are not entirely symptom free. For example, they might have occasional episodes of urinary incontinence or continue to pass a catheter in order to check the residual volumes on an occasional basis.

Published results of sacral nerve stimulation using the Medtronic System have consistently shown that at least 30 % of patients will require an additional unplanned operation because of complications [52–54]. Complications include device infection, loss of benefit due to equipment failure, loss of benefit for non-technical reasons and chronic pain. In addition, pulse generator replacement will be needed as and when the generator battery is exhausted. This planned generator replacement will typically take place between 4 and 7 years after implantation, depending on the type of pulse generator used.

As with all surgical implants or prostheses, infection of the device is a serious complication that will almost always require remove of the entire neuromodulation system. Wounds will generally have to be left open and can take a number of weeks to heal. Once sepsis has been dealt with, then the option remains open to carry out a further implant in order to restore benefit. Published infection rates have varied but, given that the implantation is carried out into a clean site, this should be no more than 2–3 %.

Loss of benefit due to technical reasons is readily detected. A cable break or a problem with the pulse generator will be diagnosed using the programming telemetry equipment. For example, broken cables show as an "open circuit" when the impedance of an electrode's circuit is tested. This type of technical problem will be accompanied by a loss of the stimulation effects, which can be demonstrated by testing sensory and motor responses. Replacement of the damaged equipment will be very likely to restore clinical benefit. However, the majority of patients who lose clinical benefit will do so without there being a clear technical explanation for the loss of effect; displacement of the electrode out of the foramen is an extremely rare event. The implication is that the ability of the stimulation to produce a change in lower urinary tract reflex function has been lost through resetting of reflex function within the central nervous system. In this situation it is common practice to remove the tined lead and replace it with another tined lead, implanted into a different foramen. Almost invariably, per operative testing shows that the implanted electrode continues to produce satisfactory motor responses. An alternative to implanting a fresh tined lead electrode is to undertake a PNE test using an alternative foramen to the one which contains the implanted tined lead. If a favourable response is obtained, or if bilateral stimulation is effective, a revision procedure can then be performed.

Chronic pain is a well described complication of the Medtronic SNS system. Pain that is only perceived while the stimulator is switched on will often respond to re- programming or, failing that approach, re-positioning or replacement of the tined lead. Revision surgery will also be needed if there has been damage to the insulation of the cables. This will be apparent through impedance testing and the finding that stimulation is felt at a site other than the perianal region. In contrast, approximately 10 % of patients report pain in the region of the pulse generator. This pain is typically present even with the device switched off. It is unclear whether it arises as a result of an interaction between the metal of the implant and the local tissues. It would be interesting to know whether this type of pain continued to be seen in patients who have their pulse generator coated with silicone rubber or some other inert material. Relocating the generator within the gluteal subcutaneous pocket, or moving the generator to the contralateral side, is effective at resolving the pain problem in approximately 60 % of patients. However, investigating post-implant pain is hampered by the incompatibility of the InterStim device to MRI scanning, although there is evidence that scanning can be carried out in some circumstances [55].

One of the difficulties with evaluating both the benefit and complications of sacral nerve stimulation revolves around the cohort of patients in whom implantation may be appropriate. Many patients who have had disabling lower urinary

tract symptoms for many years will have secondary effects on their psychological wellbeing. Other patients have coincidental psychological co-morbidity, as is evidenced by the proportion of patients taking antidepressants. A surprising proportion of patients are also found to be taking strong analgesics. For these reasons, there is an acceptance that managing a large cohort of patients with sacral nerve stimulation will involve a need to manage patients' difficulties that extend beyond their lower urinary tract symptoms.

The hardware costs for the InterStim Neuromodulation System are significant. Furthermore, patients will undergo multiple procedures which will include test procedures, definitive implantation, subsequent pulse generator battery changes and any unplanned revision surgery. For these reasons, questions have been raised as to whether sacral nerve stimulation provides a cost effective way of managing severe lower urinary tract symptoms. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) has a cost effectiveness threshold, whereby a treatment will be funded only if it provides an Incremental Cost Effectiveness Ratio (ICER) of less than £20,000.00 per quality adjusted life year (QALY). In the case of sacral nerve stimulation, this approach creates some ethical dilemmas as alternative treatment options, such as augmentation cystoplasty for patients with urge urinary incontinence, will be associated with possible serious morbidity and even mortality. The methodology for constructing cost-effectiveness models involve the use of a series of estimates for key parameters that feed into the computer model; in view of this, such models are open to methodological challenge. As a result of this it is not surprising that estimates of the ICER for SNS vary and don't necessarily support the use of SNS on cost-effectiveness grounds [56, 57].

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The Artificial Urinary Sphincter

14

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Abstract

The artificial urinary sphincter (AUS) is the gold-standard treatment for male stress urinary incontinence. This chapter covers the history of AUS development and the technical modifications that have resulted in the most commonly used device worldwide, the AMS 800. The indications and contraindications to surgery are highlighted, followed by a discussion of the importance of accurate patient investigation and assessment prior to surgery. The surgical technique to insert an AUS is followed by a review of the outcomes of sphincter implantation. Finally the management of postoperative complications and device malfunction are discussed

Keywords

AUS • Artificial urinary sphincter • SUI • Stress urinary incontinence stress urinary incontinence stress urinary incontinence

Introduction

The implantation of an artificial urinary sphincter (AUS) is an effective surgical treatment for the management of stress urinary incontinence (SUI). The commonest reason for an AUS implantation in males is for the treatment of SUI following treatment for prostate cancer, whether this is following radical prostatectomy or following minimally invasive techniques such as cryotherapy or High Intensity Focal Ultrasound (HIFU).

History and Development of the AUS

The AUS was first described by Foley in 1947 [1] when he reported the use of an inflatable cuff placed under the anterior urethra and attached to a detachable external control pump that the patient carried in his pocket in order to treat urinary incontinence. However it was not until

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1972 that Scott, in collaboration with American Medical Systems, reported the first device which was successfully implanted into a female patient suffering from myelodysplasia and subsequently into both male and female patients suffering from urinary incontinence [2]. The first AUS (AS 721) (Fig. 14.1) device consisted of a cuff, two pumps (one for inflation and the other for deflation), a reservoir between the two pumps, and unidirectional valves that controlled the device. One of the problems with this system was indentified in the V4 valve that controlled the pressure in the device and was found to be related to high rates of urethral or bladder neck erosion. In order to control the pressure in the system, another modified AUS (AS 761) (Fig. 14.2) device was developed with an extra balloon between the cuff and the deflate pump. The issue with this modified device was mechanical malfunction due to the incorporation of multiple components. In 1978 a simplified model with fewer components was introduced (AMS 742) and consisted of a cuff, a pressure-regulating balloon and a single deflate pump [4].

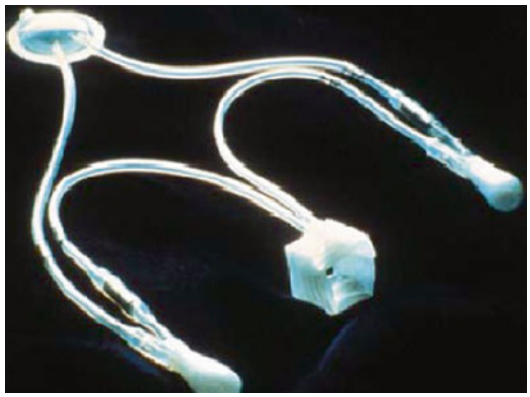

Fig. 14.1 The AS 721 (From Montague [3]; with permission)

The basic AUS design (AMS 800), which remains largely unchanged, was introduced in 1982. The new developments consisted of a deactivation button that was incorporated onto the pump, the belt design of the cuff and the combination of the control and deflate pump into one component. The first modification that took place on this model was in 1987 with the use of a narrow backing occlusive cuff, followed by kink resistant tubing and antibiotic coating of the device [5, 6].

The current AMS 800 comprises three parts: the inflatable cuff, the pressure-regulating balloon, and the pump (Fig. 14.3). The device functions by maintaining a pressure in the cuff to occlude the urethra. The pressure in the system is determined by the three different available pressure-regulating balloons (51–60, 61–70 and 71–80 cmH_2O). When the patient wants to void the pump is compressed thereby transferring fluid from the cuff into the pressure-regulating balloon. The occluded urethra is then decompressed allowing the patient to void. It takes approximately 2–3 min for the pressure-regulating balloon to refill the cuff and recompress the urethra through a resistor in the pump.

Indications for Implantation

The AUS is used to treat SUI that has occurred as a result of sphincteric weakness (intrinsic sphincter deficiency) in both men and women.

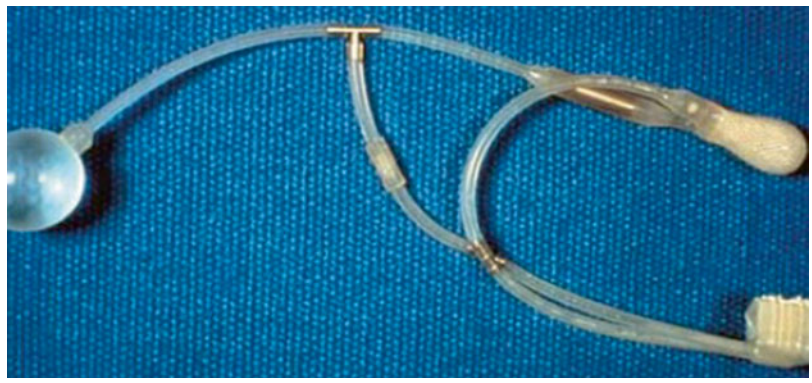

Fig. 14.2 The AS 761 (From Montague [3]; with permission)

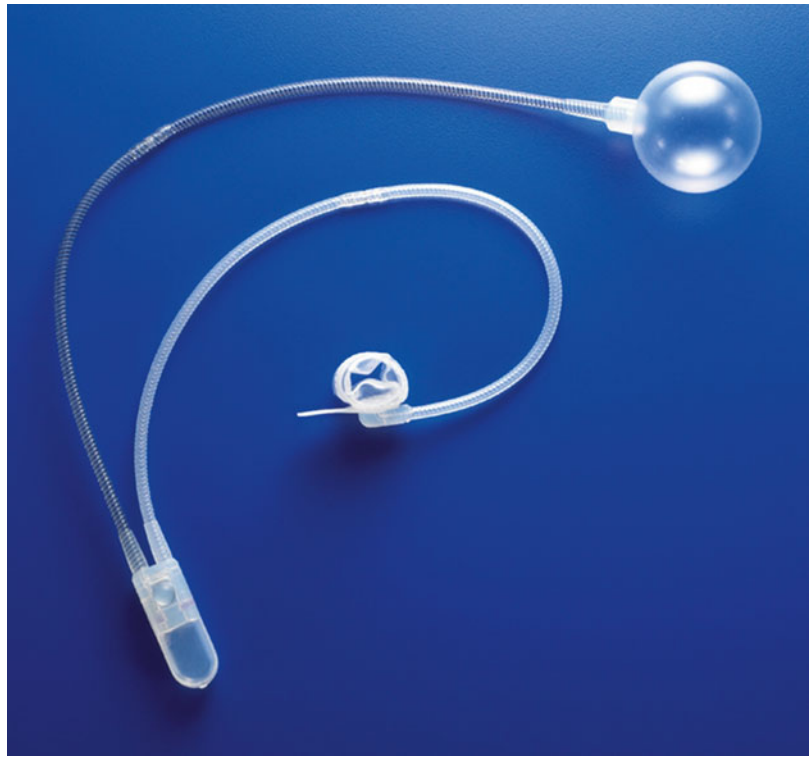

Fig. 14.3 AMS 800 artificial urinary sphincter

Intrinsic sphincter deficiency (ISD) is a condition in which the urethral sphincter loses its ability to coapt and generate enough resting urethral closing pressure in order to maintain urinary continence, and can result from:

1. Iatrogenic injury
   - Pelvic surgery, radiotherapy
   - Treatment for prostate cancer (surgery, minimally-invasive techniques)
2. Neurologic disease
3. Trauma (prostato-membranous urethral distraction injuries) or injuries following endoscopic surgery to the prostate
4. Congenital conditions (such as spina bifida or the exstrophy/epispadias complex)

Patient Evaluation

Overview

Patients with urinary incontinence who may be potentially suitable for AUS implantation should undergo a thorough evaluation in order to identify the cause of the incontinence, quantify its severity, assess its impact on the patient's quality of life and understand their desire for treatment. This should consist of a clinical history and physical examination, urinalysis, uroflowmetry and post-void residual measurement, together with a 24-h pad weight testing. Once these investigations are complete, all patients should also undergo a cystoscopy and urodynamic evaluation should take place.

These investigations will aid the differentiation of SUI from other causes of incontinence such as urge incontinence or overflow incontinence, for which the management is different. Assessment of the strength of the urinary flow and the need for straining may indicate an underlying bladder neck contracture or urethral stricture. Impact on the quality of life (QoL) should be assessed using a validated questionnaire such as the International Consultation on Incontinence Questionnaire- Short Form (ICIQ-SF), and a review of any medical comorbidities that may impact upon treatment decisions should be undertaken. Specifically, an assessment of the mental capacity and manual dexterity should be recorded.

Physical Examination

Clinical examination will detect chronic urinary retention, as well as identifying problematic surgical incisions or hernias that may impact upon the surgical placement of the reservoir. Scrotal examination should be performed in order to exclude any scrotal pathology (particularly the presence of a hydrocoele or extensive scrotal surgery) that will affect pump positioning, and it should be determined whether the patient is right or left handed in order to determine the location of the pump. This should be followed by a brief neurological examination to exclude an underlying neurogenic abnormality. Demonstration of incontinence on cough or Valsalva aids the diagnosis of ISD.

Pre operative Investigations

A urine culture should always be performed to ensure that a urinary tract infection is not present prior to surgery. Men who have had treatment for prostate cancer require an up to date serum prostate-specific antigen (PSA) in order to assess the cancer status, as adjuvant treatment may be indicated if the PSA is rising. A 24-h pad-weight measurement on a day that reflects the patients maximal desired activity is recommended to provide an objective measure of the degree of incontinence, and a bladder diary should be reviewed to assess the number and frequency of incontinence episodes as well as the voided volume and functional bladder capacity. The AUS is widely recommended as the first-choice surgical treatment for moderate or severe incontinence, or if a sling procedure is contraindicated (see Chap. 15) [7]. The definition of moderate and severe incontinence varies, but is most accurately described in terms of 24-h pad-weight measurements, with a pad weight of >400 g thought to represent severe incontinence for which the AUS would be most suitable [8]. The retroluminal sling has poorer outcomes for more severe degrees of incontinence, with one study showing a reduction in efficacy of 0.4 % for each 1 g increase in 24-h pad-weight [9], and some suggesting that a sling is only suitable for patients with <150 g leakage on a 24-h pad test [10]. However, the two have not undergone direct comparison and is currently the focus of a multicentre randomised controlled trial in the UK (MASTER trial) [11].

Table 14.1 Recommended investigations prior to AUS surgery

Pre-operative investigations
Bladder diary
24-h pad weight
Flow rate and post-void residual urine estimation
Mid-stream urine culture
Serum PSA
Flexible cystiurethroscopy
Urodynamics

Flexible cystourethroscopy is performed to ensure that a bladder neck contracture is not present and also assesses the voluntary sphincter contraction. Assessment of the degree and length of circumferential sphincteric coaptation with perineal pressure may help identify those patients who may be more suitable for a transobturator male sling instead of an AUS.

Finally urodynamic investigation is an essential component of the evaluation of SUI in order to confirm ISD, to evaluate bladder capacity and function (compliance, contractility), and to identify the presence of detrusor overactivity or underactivity (Table 14.1). These are important considerations that will influence the surgeon's decision on the best surgical treatment for a particular patient, and aids patient counselling. The prognostic value of adverse urodynamic parameters are discussed later in this chapter.

Timing of Surgery

Surgical treatment of bothersome SUI should be reserved for patients who have failed conservative measures which include lifestyle and fluid modification and pelvic floor muscle training as well as weight reduction [12]. Progressive improvement in the degree of incontinence has been reported up to 1–2 years post-prostatectomy and so surgical intervention is typically delayed, or until no fur-

ther improvement in incontinence can be achieved using conservative treatment options [13, 14]. Although a number of surgical procedures have been introduced for the treatment of SUI in recent years, the AUS continues to have the highest long-term success rates for men with moderate to severe incontinence and is therefore the benchmark against which all of the other procedures are compared. Despite this, a number of factors need to be considered before determining the optimal surgical procedure for an individual patient with SUI.

Patient Factors

AUS implantation should not be considered in the following groups of patients:

- Patients at high risk from surgery or anaesthesia due to significant medical comorbidities
- Patients with cognitive impairment that will affect their ability to use the AUS
- Patients with poor manual dexterity that will affect their ability to use the AUS
- Patients with conditions that require regular transurethral access for treatment (such as bladder cancer or refractory vesico-urethral anastomotic strictures) should be considered a relative contraindication due to the increased difficulty with transurethral surgery with an AUS *in situ*, and the potential risk of cuff erosion and infection with repeated instrumentation. The inside diameter of the smallest cuff (3.5 cm) when fully deflated is approximately 28Fr, although additional clearance is required to allow for the patients urethral tissue in between the cuff and the transurethral device.

Patient preference is also an important factor in the decision-making process, with a recent study showing that the majority of men would prefer treatment with a male sling compared to an AUS if given a choice, largely related to the desire to avoid a mechanical device [15].

Patients with a History of Radiotherapy Treatment

The outcomes of male slings in patients with prior radiotherapy are poor, with retrospective case series reporting success rates (improved or cured) of only 25–50 % [16, 17]. Consequently, the AUS remains the procedure of choice in these patients.

Prognostic Value of Urodynamics

The prognostic value of the presence of adverse urodynamic parameters (such as detrusor overactivity, poor compliance, or detrusor underactivity) in patients with SUI has been a source of debate. Up to 30–40 % of men with SUI undergoing urodynamic evaluation are found to have detrusor overactivity, with 5 % found to have reduced compliance, in addition to ISD [18] (Fig. 14.4). Some authors have suggested that the finding of bladder dysfunction in the presence of severe ISD is simply an artefact of supraphysiological filling rates used during urodynamic testing in men who's bladders are otherwise under-filled due to persistent leakage [8], and the outcome from AUS surgery is unaffected [19]. In patients where the predominant symptom is stress incontinence, and who have proven ISD, and who have a good capacity bladder, we recommend that the sphincteric-weakness is treated initially and then the remaining bladder dysfunction treated.

Surgical Procedure – Implantation of AUS

The patient is usually admitted to the hospital on the day of the operation, ensuring that the most recent urine culture is clear. Following regional or general anesthesia, intravenous broad-spectrum antibiotics (Aminoglycoside and Co-amoxiclav) are administered to the patient according to the European Association of Urology guidelines on antibacterial prophylaxis [20]. The patient is then placed in a lithotomy position and the genitalia are shaved and scrubbed for 10 min with either Hibiscrub® solution or iodine based preparations, followed by a skin preparation with chlorhexidine gluconate and isopropyl alcohol. A 16 Fr Foley catheter is inserted and the bladder is drained at the start of the procedure.

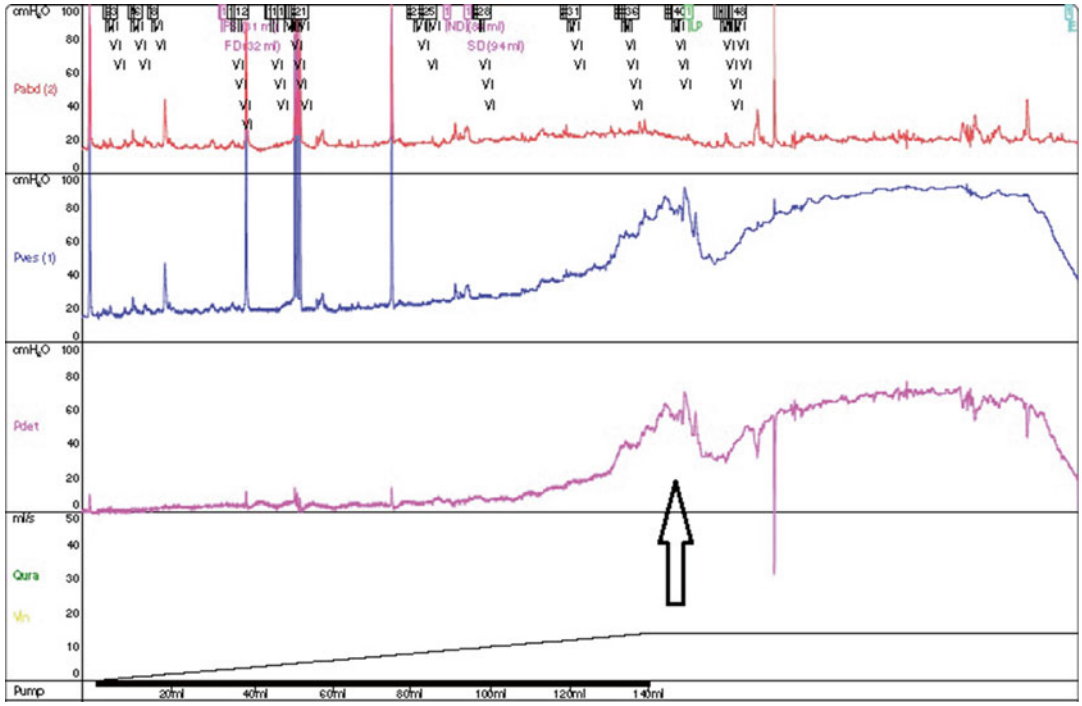

Fig. 14.4 Urodynamic trace of a 68 year-old man 3 years after radical prostatectomy showing detrusor overactivity (*arrow*) resulting in incontinence

Incision

A midline perineal incision is used for the placement of the cuff. Sharp dissection of the subcutaneous tissue and the perineal fat is carried out using diathermy up to the level of the bulbospongiosus muscle (Figs. 14.5 and 14.6). The muscle is divided in the midline in order to expose the mid or proximal bulbar urethra (Fig. 14.7). The bulbar urethra is dissected off the corpora until it is completely mobilized circumferentially for approximately 3–5 cm (Fig. 14.8). Once the space is created the cuff size should be selected by passing the cuff ruler through this urethral window and the urethral circumference is measured (Fig. 14.9). The actual cuff size is then placed in this mid bulbar urethral window.

A second inguinal incision is performed and dissection of the subcutaneous fat and Scarpa's fascia is performed until the external oblique aponeurosis is identified and incised. Blunt scissors are then used to perforate the internal and transversus muscles to expose the fascia transversalis (Fig. 14.10). Following an incision in the

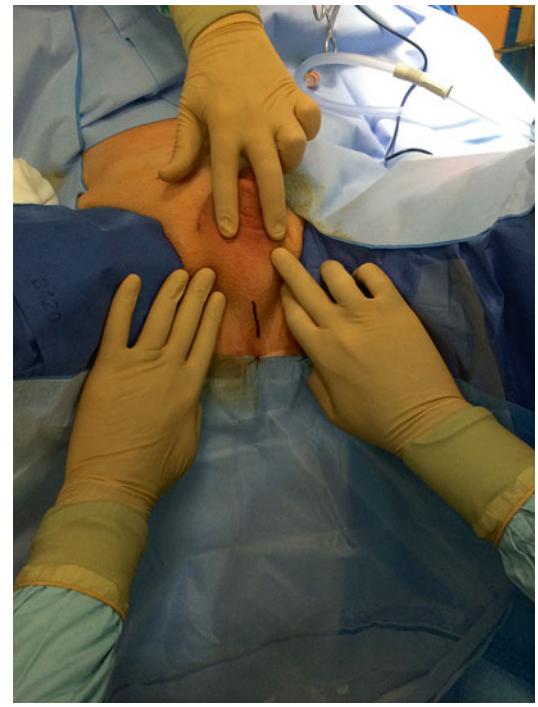

Fig. 14.5 Patient positioning and location of perineal incision

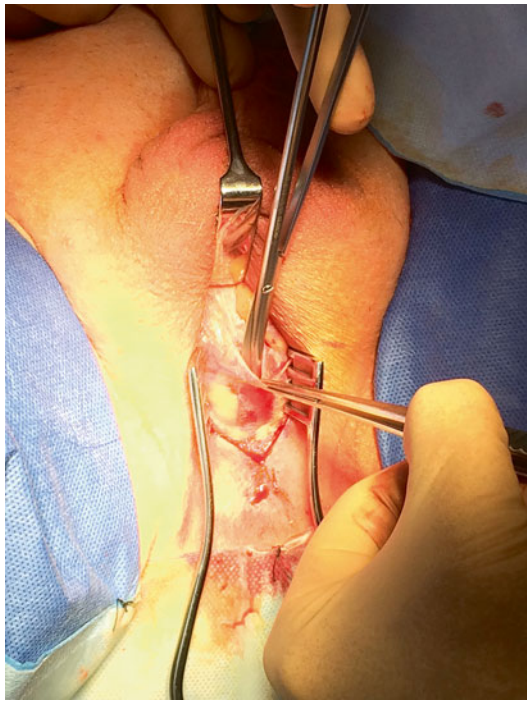

Fig. 14.6 Dissection of subcutaneous tissue and bulbospongiosus muscle

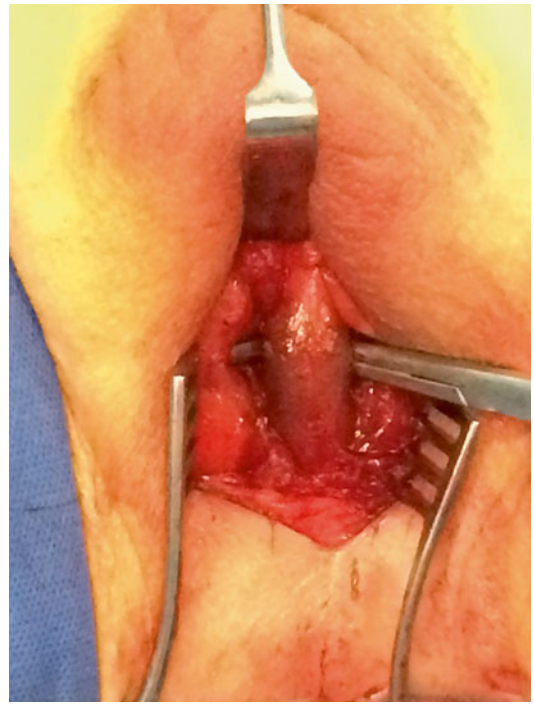

Fig. 14.8 Mobilisation of bulbar urethra for 3–5 cm

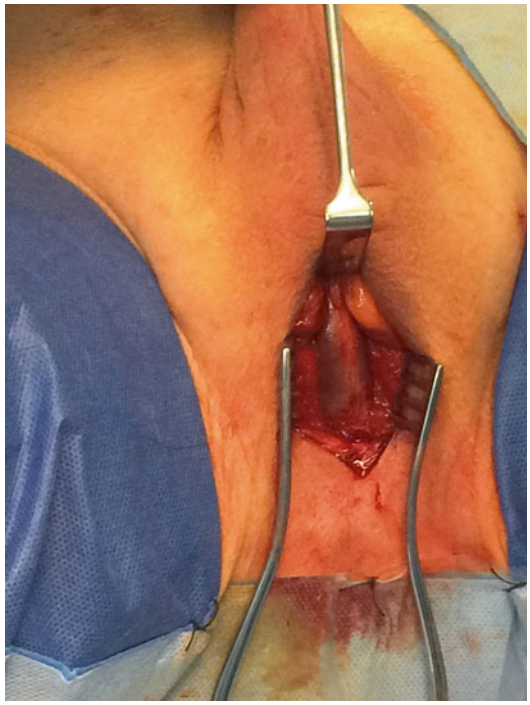

Fig. 14.7 Exposure of bulbar urethra

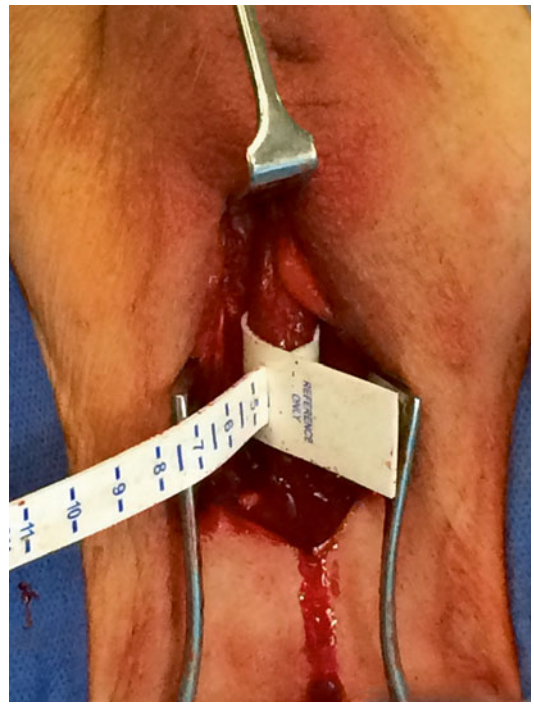

Fig. 14.9 Measurement of urethral circumference

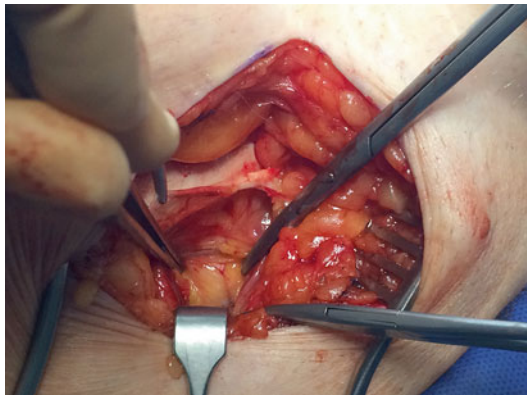

Fig. 14.10 Inguinal dissection into space of Retzius

fascia transversalis the correct entry into the retropubic space (Space of Retzius) is confirmed by palpation of the back of the symphysis pubis or the external iliac artery.

For the placement of the pump a subcutaneous tunnel is then made through the inguinal incision using long blunt scissors introduced beneath Scarpa's fascia which then develops a dartos pouch deep in the scrotum (Figs. 14.11 and 14.12). This will harbor the pump.

The components of the AUS device (cuff, pump and pressure regulating balloon) are then prepared and filled with 0.9% Normal Saline solution. Moreover components not coated with antibiotics can be placed into a basin with antibiotic solution and the wounds are irrigated with a similar solution throughout the procedure (Fig. 14.13). A 61–70 cmH_2O pressure regulating balloon is typically used and is filled with 22–25 ml 0.9% Normal Saline solution. The pump is deactivated and all the tubes of the device are connected in the inguinal region beneath Scarpa's fascia using a quick-connect system (Fig. 14.14). The tubing from the cuff can then be passed from the perineal dissection to the abdominal wound using a small trocar. Before completing the connection, the tubing is shortened to the appropriate length and all air bubbles are meticulously removed with saline flushing of all sites at the time of connection. After connection, the device is cycled to ensure that it is working properly and then left in the deactivated position. The perineal and inguinal wounds are then closed in

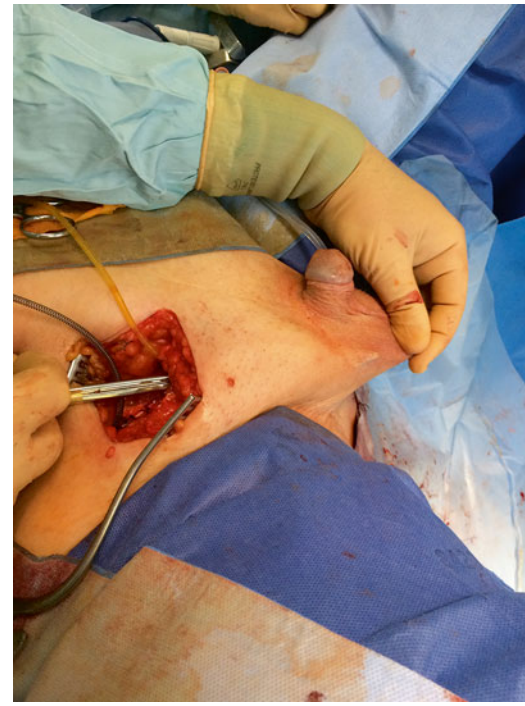

Fig. 14.11 Creation of dartos pouch for pump placement

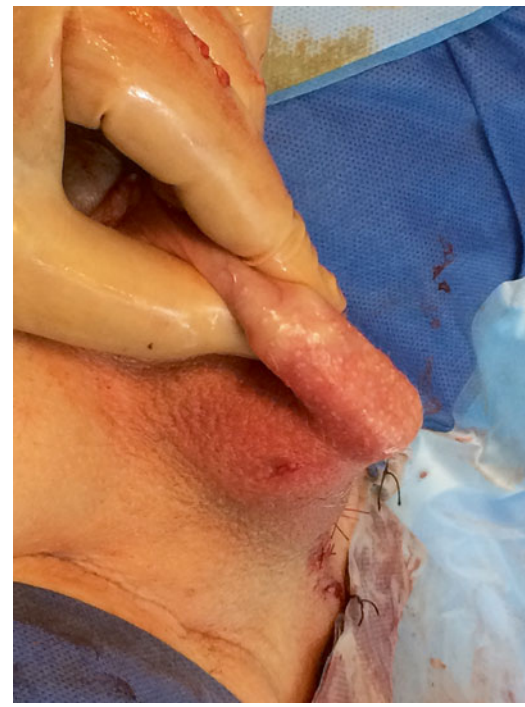

Fig. 14.12 Final position of pump in most dependent part of scrotum

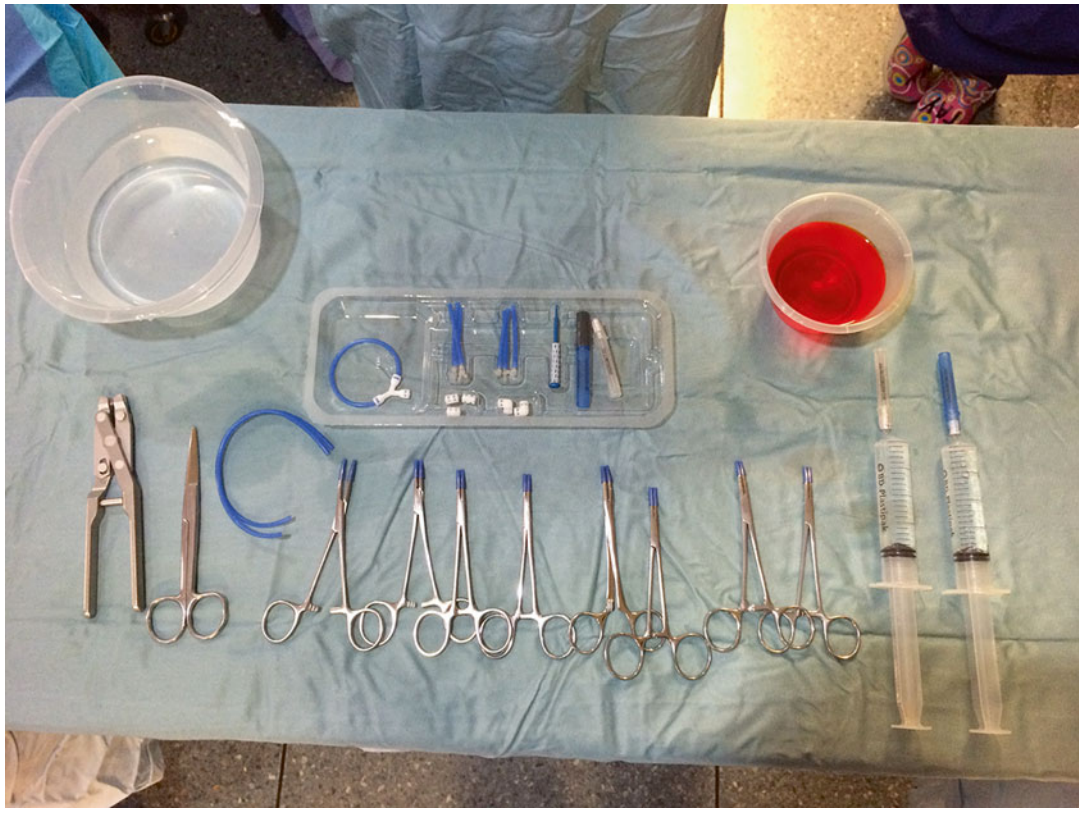

Fig. 14.13 Set up and components of the accessory kit used for AUS insertion

layers using 2/0 vicryl subcutaneously and 3/0 vicryl rapide for skin. Postoperatively the patient is usually hospitalized for 1 day and 2 more doses of intravenous antibiotics are administered. The Foley catheter is removed the following day and the bladder is checked for adequate emptying with a post-void bladder scan. The device is activated after 6 weeks in the outpatient clinic.

Outcomes of AUS

The European Association of Urology (EAU) guidelines report that the AUS device should be offered to men with moderate to severe male stress urinary incontinence (Grade B recommendation) [21]. The guideline also suggests that AUS surgery should be performed in high volume centres, however, men should be warned of the risk of complications, risk of mechanical failure or need for explantation. In general there is a lack of high quality studies comparing the AUS to other devices or surgical techniques. Only one study compared the AUS to bulking agents [22]. At present in the UK patients are being recruited to the MASTER – Male synthetic sling versus Artificial urinary Sphincter Trial: Evaluation by Randomised controlled trial which will assess clinical and quality of life outcomes over 24 months and provide level 1 evidence for these surgical procedures.

Currently the majority of data with regards to the AUS is from retrospective cohort studies (Table 14.2). In 2013 Van der Aa et al., published a systematic review of the long term outcomes following AUS implantation in male patients with non-neurogenic SUI [34]. The literature was reviewed up until October 2011 and all of the studies included had a mean follow up of at least 2 years after AMS 800 (narrow back cuff device) bulbar implantation via a perineal approach using a 61–70 cm water pressure regulating balloon.

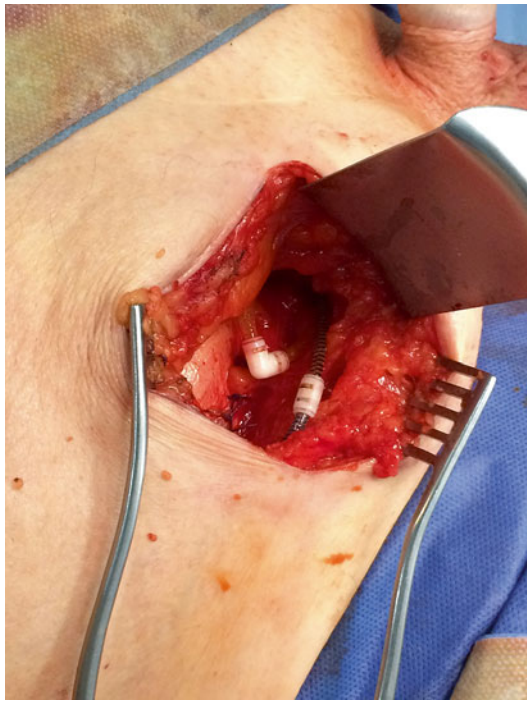

Fig. 14.14 Connection of tubing using quick connect system

Based on 420 identified records, 12 studies were included in the qualitative synthesis. The majority of the studies were retrospective single centre studies. Dry rates, which were assessed by no pad usage were reported in 7 studies. In these 329 patients the dry rate varied from 4.3 to 85.7 %. In the three prospective studies included in the analysis the dry rate was in the region of 50 % after medium term follow up. Dry or improved rates (1 pad or less, social continence) as assessed by 7 studies and 262 patients were 79 % (range 61–100 %). The authors of this review quite rightly state the need for an accurate definition of cure and suggest in those using pads for this purpose that studies report, no pad use, occasional pad use (including security pads) and regular pad use (stating pads per day). Only three studies assessed quality of life and improvements were seen using the AUA quality of life index, a 6 item Likert scale and the IIQ-7 [34]. One study reported on patient satisfaction after a 4 year follow up with results showing that 92 % of patients were either satisfied or very satisfied [35].

The rates of AUS infection and erosion was reported as 8.5 % (range 3.3–27.8 %) in 12 studies (n = 562). Urethral atrophy was reported in 7.9 % of cases (range 1.9–28.6 %) based on 6 articles and 456 patients. Urethral atrophy can occur between 3 and 23 months of follow up but the authors commented on the lack of reported timing of this complication in the papers analysed. Mechanical failure was seen in 6.2 % (range 2–13.8 %) in 562 patients analysed from 10 studies. Failures were reported from 11 to 68.1 months post insertion. Re-intervention rate in a pooled analysis of 549 patients from 10 studies showed this to be 26 % (range 14.8–44.8 %).

A recent meta-analysis has addressed the impact of radiotherapy on AUS implantation [36]. After screening, 23 articles were identified related to irradiated patients undergoing AUS implantation of which 16 were included in the meta-analysis. Fifteen of the studies were suitable for assessment of surgical revision outcome and 11 for persistent incontinence outcomes. In this analysis 'lack of social continence' at follow up was the marker of persistent incontinence post AUS implantation. Study quality was generally low and typically included retrospective cohort studies. Both this meta-analysis and the systematic review by Van der Aa report on the weaknesses of retrospective cohort studies including loss to follow up bias, recall bias and low response rates to patient surveys and lack of validated quality of life and satisfaction data [34, 36]. Of the 1886 patients in this analysis, 579 patients had radical prostatectomy and external beam radiotherapy prior to AUS implantation. In the radiotherapy group 37.3 ± 6.1 % (95 % CI 23.4–51.1) required surgical revision compared to 19.8 ± 3.6 % (95 % CI 11.9–27.6) in the non-irradiated group ($p < 0.007$). Also in the radiotherapy group 52.8 %, 36.5 % and 11.1 % of surgical revisions were performed for infection/erosion, urethral atrophy and other causes (such as haematoma, pump malfunction and leaks), respectively. Persistence of incontinence was also higher in the radiotherapy group (n = 290), being 29.5 ± 5 % (95 % CI 18.1–45.8) vs 12.1 ± 2.8 % (95 % CI 5.7–18.4) in 949 patients analysed ($p = 0.003$). The analysis suggested that

for every 4 AUS implantations in those who received radiotherapy, 1 surgical revision would need to be conducted. The authors concluded men who receive radiotherapy should undergo robust counselling indicating a higher revision rate for infection/erosion, urethral atrophy and higher rates of persistent UI.

Sandhu et al., reported on the learning curve for the procedure based on data collected from American Medical Systems (USA) [37]. The study showed a slow but steady decrease in the risk of reoperation with increasing surgeon experience (p = 0.020), being 24 % for an inexperienced surgeon, with 5 prior cases, which decreased to 18.1 % for an experienced surgeon with 100 prior operations and 13.2 % for a surgeon with 200 prior operations. Interestingly two thirds of patients were treated by surgeons with minimal experience and fewer than 10 % were operated on by surgeons with a case volume of >100 cases implanted. This study further highlights the need for AUS implantation to take place in high volume centres.

Surgical Considerations

The approach to placement has been challenged by some surgeons using a single transverse scrotal or penoscrotal approach compared to the traditional 2 incisions, one perineal and one in the groin. However a multicentre trial suggested the outcomes were better with the traditional perineal approach [38]. The completely dry rate was 27.4 % in the penoscrotal group and 44.1 % in the perineal group (p = 0.04) and subsequent tandem cuff placement for persistent incontinence was seen in 11.3 % of penoscrotal cases compared to only 5.4 % of perineal cases.

Complications Following AUS Implantation

Early Complications

Complications in the early post-operative period include AUS infection or erosion, haematoma, and urinary retention (Table 14.3). The presence of symptoms such as tenderness around the components, fever and erythema are signs of an infection and lead to fixation of the AUS components to the skin. Infection can be minimised by using a meticulous sterile technique combined with broad-spectrum intravenous antibiotics perioperatively. However, in the setting of a suspected infected device explantation is required in order to control the infection. Wound haematoma should be managed conservatively if possible as any further intervention risks damage and infection to the AUS components. Meticulous intraoperative haemostasis is essential in order to reduce the risk of haematoma formation combined with wound closure to reduce any dead space and the use of a compressive perineal dressing.

Erosion typically presents with a combination of haematuria, dysuria or urinary tract infection, and can be minimised be reducing the need for repeat urethral instrumentation as much as possible (Fig. 14.15). Early erosion is often related to an unrecognised urethral injury at the time of surgery and the risks are higher in patients who have had previous radiotherapy or perineal surgery. Again, device explantation is mandatory and re-insertion of the AUS can be considered after a further 3–6 months.

Urinary retention following removal of the urethral catheter in the immediate post-operative period may occur, although uncommon, and is typically related to local tissue oedema. This can be managed with careful re-insertion of a 12Fr urethral catheter after ensuring deactivation of the device, and a further trial-without-catheter performed after 1 week when the oedema has settled. It is our preference to insert a urethral catheter rather than a suprapubic catheter in this situation due to the potential risks of damage to the AUS components. It is important that the patient is given appropriate contact information for his specialist team in case of any difficulty in the immediate post-operative period, and he should carry a medical alert booklet or bracelet with him at all times so that general healthcare professionals are aware that he has an AUS *in situ* and that urethral instrumentation should only be performed by someone trained in the care of an AUS. Following AUS explantation for infection or erosion, repeat AUS implantation has been

Table 14.2 Outcomes of AUS implantation in largest contemporary series

Reference	*N*	Mean follow-up (months)	Continence rates	Infection %	Erosion %	Revision/removal %	Mechanical failure %	Patient satisfaction %	AUS durability %/year
Elliott and Barrett [23]	184	68.4	92	0.5	6.5	16.8	7.6		75/5
Lai et al. [24]	218	36.5	69 (0–1 PPD)	5.5	6.0	27.1	6		75/5
Litwiller et al. [25]	65	23.4	75 (0–1 PPD)	6	3.1	18		90	
Raj et al. [26]	554	68	90 (0–1 PPD)	1.74	5.2	19.1	8.3		79/5
Kim et al. [27]	124	81.6	82 (0–1 PPD)	7	10	9.5	29		
Venn et al. [28]	70	132	92	28.5 Infection/erosion	28.5 Infection/erosion	64	28.5		66/10
Haab et al. [29]	68	86.4	80 (0–1 PPD)		2.9	25		80	
Montague et al. [30]	113	73	40 (0 PPD)			12		73	
Gousse et al. [31]	71	91	59 (0–1 PD)	1.4	4	29	25	77	
Clemens et al. [32]	66	26.6	80 (0–2 PPD)	10.6	12	36.4	9		

Adapted from James and McCammon [33]

Table 14.3 Complications following AUS insertion

Early	Late
Infection	Mechanical failure
Erosion	Erosion
Haematoma	Urethral atrophy
Urinary retention	

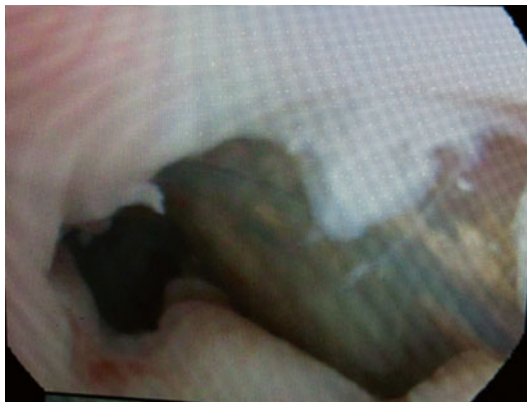

Fig. 14.15 Cystoscopic finding of cuff erosion into urethra

shown to have significantly higher rates of requiring further revision surgery, although adequate continence rates can be expected [39]. If the AUS has been explanted for mechanical failure or urethral atrophy, similar success rates can be expected as for primary AUS insertion [40].

Late Complications

Device malfunction occurs in up to 50% of patients at 10 years and presents with recurrent urinary incontinence. However, there are a number of other possible causes for persistent or recurrent urinary incontinence after previous AUS implantation (Table 14.4), and its evaluation should follow a step-wise approach (Fig. 14.16).

A detailed history regarding the timing and onset of recurrent incontinence (to distinguish mechanical from non-mechanical failure), presence of urgency symptoms, and a history haematuria or recent instrumentation that may have led to cuff erosion should be followed by abdominal X-ray (if contrast was used to fill the system) or ultrasound/MRI (if saline was used to fill the system) to assess for the presence of a fluid leak.

Table 14.4 Aetiology of persistent or recurrent incontinence after AUS implantation

Early or persistent urine leak	Late or recurrent urine leak
Accidental deactivation of control pump	Urethral atrophy
Early cuff erosion	Cuff erosion
Overactive bladder symptoms	Mechanical failure (e.g. fluid leak)

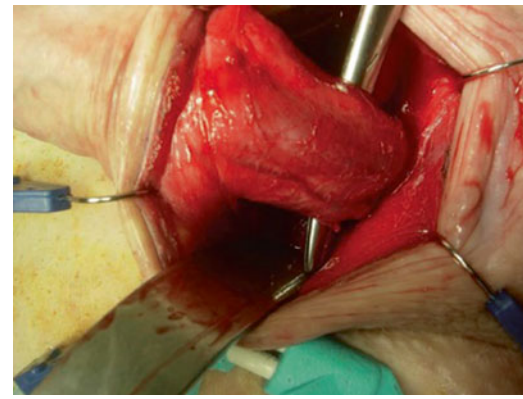

Fig. 14.16 Dissection through corpus cavernosum for placement of transcorporal cuff (Reproduced with permission from Lee et al. [41])

Cystoscopic visualisation will assess for cuff erosion and also visualise the degree of urethral coaptation on cycling the AUS. Urodynamic studies should be performed if concomitant bladder dysfunction is suspected, and appropriate treatment can be commenced once the degree of detrusor activity or bladder outflow obstruction is diagnosed. Loss of fluid from the system warrants replacement of the entire device, but if imaging confirms a full reservoir then cuff downsizing or inserting a higher pressure reservoir can be considered. The use of tandem-cuffs to improve continence rates or transcorporal placement to reduce erosion rates and provide better cuff fit have also been described with good results [42, 43] (Fig. 14.17). Insertion of a second cuff distal to the primary cuff has been reported for men with recurrent incontinence due to inadequate urethral occlusion, with DiMarco and Elliott reporting continence rates of 56% (0–1 pad per day) and high patient satisfaction rates [42]. A study of long-term follow-up in 22 men

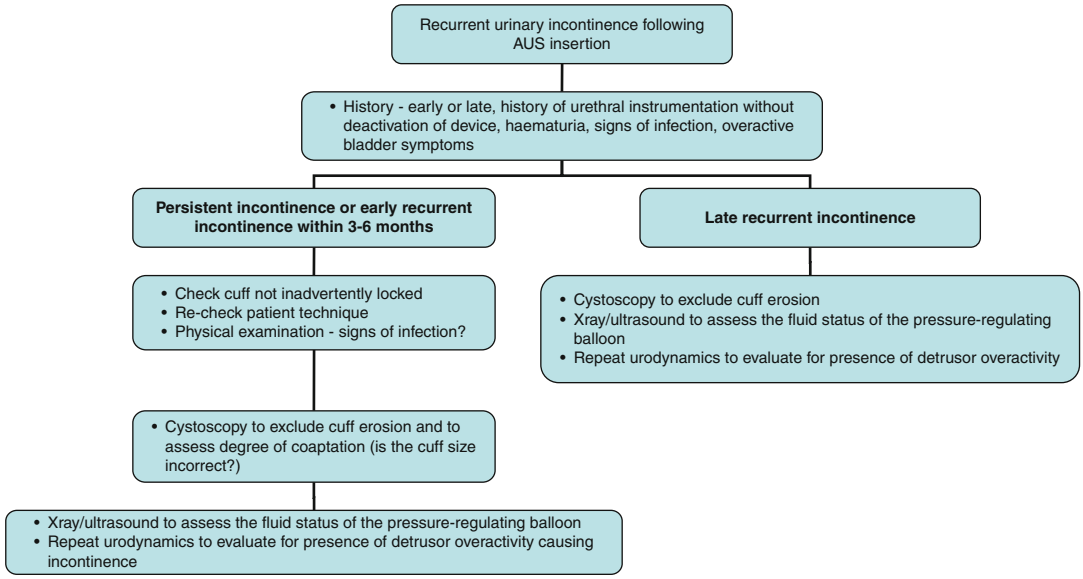

Fig. 14.17 Algorithm for diagnosis of AUS malfunction

with primary incontinence reported no difference in dry rates compared to men undergoing single cuff placement at an average of 58 months, but noted a higher re-intervention rate for complications in patients with a tandem cuff. Higher erosion rates have also been noted in other series [44, 45] and so the use of this technique for primary incontinence is not advised. Transcorporal placement has been described in a small number of case series in complex cases of recurrent incontinence after failed prior surgery in the presence of urethral atrophy or injury. In a recent series of 23 patients undergoing transcorporal cuff placement a success rate of 76% was reported (0–1 pad per day) for the 17 patients who had follow-up data over 1 year with a low rate of re-intervention. Furthermore, of the six patients who had good pre-operative erectile function, four had no deterioration in their erectile function [46]. Guralnick et al. reported on the largest series of men undergoing transcorporal cuff placement with a reported continence rate (0–1 pads per day) of 84% at a mean follow-up of 17 months in 31 men, with no erosions or infections reported. Deterioration in erectile function was reported in one patient although the majority of men had erectile dysfunction pre-operatively [43].

Conclusion

The artificial urinary sphincter remains the gold-standard surgical treatment for male stress urinary incontinence and has demonstrated high long-term success rates. The device has undergone a number of modifications since its original design with the aim of reducing complication rates and improving success rates further, and the AMS 800 is the most commonly used prosthesis worldwide. A thorough and systematic pre-operative evaluation is required in order to ensure appropriate patient selection for surgery and cases of recurrent incontinence require a detailed re-assessment and interrogation of the device, preferably in centres with expertise in the management of these complex cases.

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Male Urethral Slings

15

Christian Nayar and Hashim Hashim

Abstract

Iatrogenic male stress urinary incontinence (SUI) affects a small proportion of men who undergo urological procedures but has a profound impact on their quality of life. The prevalence of post-prostatectomy urinary incontinence (PPI) varies from 2.5 to 87 %. In the more recent series this is reported as 2–10 % (Haab et al. Urol Clin North Am 23:447–57; 1996, Majoros et al. Neurourol Urodyn 25:2–7; 2006). Incontinence can also occur in 1 % of patients undergoing surgical treatment for bladder outflow obstruction secondary to benign prostatic enlargement (Haab et al. Urol Clin North Am 23:447–57; 1996). The treatment of male SUI is continuing to evolve with multiple different surgical options. This chapter covers the increasingly popular option of using male urethral slings in men with SUI.

Keywords

Post-prostatectomy incontinence • Male sling • Bone anchored sling • Retrourethral trans-obturator sling • Adjustable retropubic sling

Introduction

Urinary Incontinence is estimated to affect between 12 and 17 % of males, with an increasing prevalence associated with aging [1–3]. More specifically, stress urinary incontinence (SUI) has now been defined by the International Continence Society (ICS) as the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing [4].

Prostate cancer is the most common solid organ malignancy in men accounting for 22–28 % of all male cancers and more than 500,000 men are diagnosed per year in the USA and

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Europe [5, 6] and mortality rates are estimated at about 10 %. However, despite a fall in mortality rates, the morbidity associated with SUI following prostate cancer treatment will affect the quality of life in the survivors.

The reported rates of SUI following radical prostatectomy varies between 2 and 10 % [2]. This range is a result of the different definitions of post-prostatectomy incontinence, differing surgical techniques as well as variable follow-up periods used in the reported studies. Other treatment modalities such as external beam radiotherapy are associated with SUI in 1–16 % of cases [7] and transurethral resection of the prostate (TURP) for benign disease is also a potential iatrogenic cause of SUI with reported rates of 1–3 % [8].

Since its popularisation in 1978, the artificial urinary sphincter (AUS) has been the gold-standard treatment for men with SUI. Since the late 1990s, the male urethral sling has been introduced as a surgical alternative to an AUS placement in men suffering from mild to moderate SUI. One significant difference between male slings and the AUS is the lack of mechanical components which reduces the potential for mechanical failure of the device as well as the risk of infection.

The concept of urethral slings dates back to when Kauffman described several surgical methods for compressing the urethra. These included compression of the bulbar urethra with the penile crura and subsequently compression of the bulbar urethra with polytetrafluoroethylene (PTFE) tape, which had a reported success rate of up to 70 % [9–11]. Male urethral sling placement is an option for men with post-prostatectomy SUI. It is usually offered to men who remain dissatisfied following conservative therapy for SUI including pelvic floor muscle training, biofeedback and electrical stimulation.

Alternative surgical treatments include injection of peri-urethral bulking agents or insertion of an AUS. All peri-urethral bulking agents share similar problems including the need for repeat injections, deterioration of effect over time and very low success rates. For example macroplastique shows a rapid deterioration after initial improvements with success rates of 40 %, 71 %, 33 % and 26 % at 1, 3, 6 and 12 months respectively [12].

Indications

Sling procedures to treat male urinary incontinence are indicated for bothersome mild-to-moderate stress urinary incontinence. They may be offered to men who remain dissatisfied or symptomatic following conservative management. The definition of mild incontinence remains to be defined in the literature but is usually less than 200 mL of urine loss in 24 h. Similarly moderate incontinence has been described at 200–500 mL per day and severe incontinence as more than 500 mL per day. Other studies have described mild incontinence as one to two pads per day, moderate at two to five or fewer pads, and severe at more than five pads per day [13].

Contraindications

Absolute Contraindications to Male Urethral Sling Procedures for Male Incontinence

Absolute contraindications include:

1. Stress urinary incontinence which is unlikely to be resolved with a sling procedure.
2. Bladder dysfunction that can jeopardize renal function, such as loss of compliance and vesicoureteric reflux at low bladder pressures.
3. Inadequate tissue integrity of the bladder neck or urethra.
4. Untreated urinary tract infection.

Relative Contraindications to Sling Procedure

Relative contraindications include:

1. Prior history of radiotherapy as this is associated with an 85 % failure rate [14]

2. Further need for transurethral procedures, for example patients with bladder cancer or with refractory urethral strictures, as transurethral access may be required and repeated instrumentation may increase the risk of erosion or infection.
3. Previous AUS placement (noting however, that slings do not preclude future placement of an AUS) [15]. However, investigators have shown that residual SUI following AUS insertion can be "salvaged" by insertion of a sling [16]

Types of Male Sling

Currently, several variations on male sling design exist, the most commonly published series available report on three different designs. Retrourethral transobturator slings (RTS), sub-urethral bone anchored slings (BAS) and adjustable retropubic slings (ARS). Postoperative success is defined as cured (no pad use or 1 pad for security reasons) and/or improved (1–2 wet pads or a reduction of pads ≥50 %).

Retrourethral Transobturator Sling

The RTS is passed outside-in through the obturator foramen (Fig. 15.1a). It is made of a polypropylene mesh which is sutured in place on the ventral surface of the bulbar urethra, tensioning results in cranial displacement of the urethra. In a pilot study by Rehder and Gozzi [17], urethral pressure profiling was used to demonstrate that the membranous urethral length and the mean urethral closure pressure increased. Magnetic resonance imaging showed that the ventral urethral bulb moved 6–9 mm cranially after RTS placement. Two studies have reported that there is a significant increase in Valsalva leak point pressure after sling placement but no increase in detrusor voiding pressures [17–19].

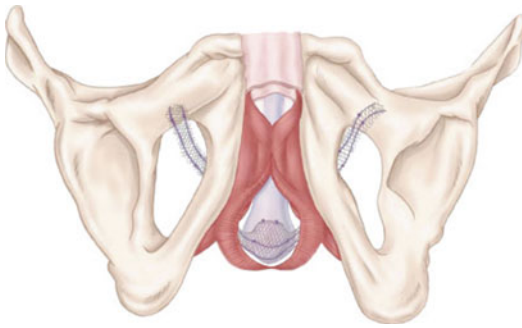

Fig. 15.1 Diagrammatical representation of a retrourethral transobturator sling (AdVance)

The group which has the best chance of benefiting from the RTS sling has yet to be properly defined. It has been suggested that patients with severe SUI, UI whilst supine in bed and prior pelvic irradiation are poor candidates for the RTS. The urethral repositioning test has been advocated as a method of predicting whether the patients UI will respond to placement of an RTS. The urethral repositioning test is performed with the patient in the lithotomy position and a flexible cystoscope is positioned just distal to the membranous urethra. For a successful test, perineal pressure directed cranially (but not directly into the urethral lumen) should produce 1–1.5 cm of circumferential coaptation of the membranous urethra. This is distinct from the ability to voluntarily contract the urethral sphincter.

The use of the RTS in patients with previous radical prostatectomy and adjuvant radiotherapy has been reported in a number of studies. Bauer et al. reported a 50 % success rate in 24 men with a median follow up of 18 months [20]. This lower success rate is consistent with other published series which have demonstrated lower success rates in patients who have had adjuvant radiotherapy indicating that it is a risk factor for sling failure [18, 21, 22]. It is difficult to transfer this efficacy for post-TURP SUI. Following TURP, the prostate and its supporting structures remain in place and therefore significant prolapse of the membranous urethra does not occur and as such the RTS mechanism of action may not be applicable. Rehder et al. suggest that in this situation the RTS sling should only be offered if there is a sphincteric defect between the 5 and 7 o'clock positions and the acknowledgement that in these situations the mechanism may be obstructive rather than re-positional [23].

Another important prognostic factor in the success of all male slings including the RTS is the degree of SUI. The series by Cornu et al. [22]

is the only one that reported a significantly increased risk of failure of the RTS in patients with a >200 g pad weight/day [22]. However, subgroup analyses in the other RTS series have not been sufficiently powered to answer this question (Table 15.1).

Efficacy

After RTS placement, success is achieved in 76–91 % of cases at 12–27 months of follow up [18, 21, 22] although smaller case series have demonstrated lower success rates [24, 25]. Actual cure rates are lower at 9–74 %. Efficacy is reduced in previously irradiated patients [18, 22] but careful patient selection may allow some men to achieve good results [20]. The RTS sling has also been suggested as a possible salvage procedure as an alternative to AUS revision in patients with recurrent urinary incontinence secondary to AUS related urethral atrophy. From a series of 19 men who had an RTS inserted in addition to their AUS, 15 of them became completely dry [26], and half of these men did not require reactivation of their AUS after undergoing a sling insertion. Solijanik et al. [16] described their attempt to salvage men who had early (between 1 and 13 weeks) failure of their first RTS. A second RTS was inserted but this time the sling was fixed with nonabsorbable sutures, to the outside of the bulbar urethra. At 17 months 72 % were dry or only using a security pad. This would suggest that early failure of an RTS is likely to be secondary to sling loosening or slippage.

Adverse Events

Acute urinary retention can occur in the immediate post-operative period either due to perineal pain, urethral manipulation, post-operative swelling or urethral compression (although cadaveric studies have demonstrated that <4 % of the RTS tension is directed on the urethral lumen [27]) and reported rates range from 3 to 21 %. This can last for up to 12 weeks before it resolves. Perineal pain is to be expected post-operatively, however, ongoing perineal pain occurs in 0–20 % of patients after RTS. Different definitions of post-operative pain probably contribute to the wide range. Most of these patients did not require any treatment and the symptoms abated within 3 months.

Fortunately post-operative wound infection is a rare complication and although only two cases have been described in case series, one of which required sling explantation, this is likely to be under reported.

A single case has been reported of a patient that presented 2 weeks after AdVance sling insertion with significant perineal and adductor compartment haematoma. However, this patient had an increased bleeding risk due to anticoagulant therapy for a metallic heart valve. Overall, severe complications that require removal or revision of the RTS are rare. Urethral erosion has only been reported in abstract form to date and eventually required a urethroplasty [28].

The AMS AdVance system (American Medical Systems, Minnetonka, MN) is a self-anchoring device, using a trans-obturator pathway for implantation and fixation. The technique is similar to that used in female SUI management with a transobturator tape. The theoretical principle behind the AdVance is relocation of the bulbar urethra rather than compression.

Surgical Technique: The AdVance Sling

1. Prior to surgery, urinary tract infection is excluded. Antibiotic prophylaxis to cover gram positives, gram negatives and anaerobes is given intravenously at induction in theatre (e.g.: triple therapy with Flucloxacillin 1 g, Gentamicin 3–5 mg/kg lean body weight, and Metronidazole, 500 mg). The patient is placed in a dorsal lithotomy position with the hips and knees flexed and slightly abducted. The perineal, genital and groin areas are shaved and then prepared with a 10 minute betadine scrub. Draping of the operative field includes covering the anus.
2. Cystourethroscopy can be performed to confirm the anatomy of the bladder and urethra. This also allows assessment of the mobility of the bulbar urethra, with the gloved index finger pushing the urethral bulb forward which simulates the anterior relocation of the urethral bulb which will be achieved by placement of the AdVance sling (Fig. 15.2).

Table 15.1 Comparison of outcomes following retrourethral transobturator sling placement in adult males with SUI

Study	Patient, n	Mean/med f/u (mo)	Pre-op continence (mean/med)	Success definition	Success (%)	Improved (%)	No improvement (%)	Complications (%)	Notes
Rehder et al. [18]	118	12	2.3 ppd	≤1 ppd	87 (74)	20 (17)	11 (9)	Retention 6 (5), perineal pain 23 (20)	Prospective
Cornel et al. [24]	35	12		0 ppd, <2 g urine loss/day	3 (9)	16 (46)	16 (46)	Removal 1 (3), retention 1 (3), mod-severe pain <3 months 12 (34)	Prospective, 2-center study
[a]Christine and Knoll [26]	19	13		0 ppd	15 (79)	4 (21)	0 (0)	None	Patients with recurrent incontinence after AUS placement
[a]Soljanik et al. [16]	29	17	4.3 ppd	0 ppd	10 (35)	16 (55)	3 (10)	Urethral injury 1 (3), retention <2 weeks 9 (24)	Patients previously with a failed sling placement
[a]Bauer et al. [20]	24	18	4.5 ppd	≤1 ppd	6 (25)	6 (25)	12 (50)	Removal 1 (4)	All patients undergoing RP and adjuvant radiotherapy
Cornu et al. [22]	136	21	2.1 ppd	0 ppd	84 (62)	22 (16)	30 (22)	Pain 14 (10), dysuria 19 (14)	Prospective study; failure associated with 24-h pad >200 g, trend toward radiation therapy
Bauer et al. [20]	126	27	4.9 ppd	≤1 ppd	65 (52)	30 (24)	31 (25)	Removal 2 (2), retention <10 weeks 19 (15), persistent pain 1 (1)	Prospective study; 17 patients (14 %) with pre-op radiation
Berger et al. [27]	26	22	5.6 ppd	0 ppd	16 (62)	7 (27)	3 (12)	Pain ≤4 weeks 5 (19)	

[a]Salvage patient populations

At the end of the cystourethroscopy the bladder is emptied and a 16Fr 2-way Foley urethral catheter is inserted.

3. From 1 cm below the dependant portion of the scrotum (where the urethra bends below the inferior pubic ramus) to approximately a point 2 cm above the anus, a 5 cm lower perineal midline incision is made (Fig. 15.3).
4. The subcutaneous tissue and Colles fascia are divided with electrocautery down to the level of the bulbocavernosus muscle (Fig. 15.4).
5. The muscle is elevated away from the urethra and divided using electrocautery or McIndoe scissors. The bulbocavernosus muscle is then retracted laterally, using a Lone star retractor, which exposes the corpora cavernosa and the proximal urethral bulb. The urethra is easily identifiable here with a urethral catheter *in-situ*. The bulbocavernosus muscles and the urethra are dissected away from the bulbospongiosus muscle (Fig. 15.5).
6. The fibres of the perineal body are extensions of the superficial anal sphincter, however they can be cut without compromising the anal sphincter integrity as this depends upon the intact internal sphincter. After cutting these superficial fibres the central tendon of the perineal body is cut. Sufficient mobility can be demonstrated by using a finger to displace the bulb cranially, which will replicate the displacement of the urethra by the mid-urethral sling. However, dissection should not extend past the perineal body as this may inadvertently allow the sling to slip past the urethral bulb. This area can be identified either using a marker pen or a 4/0 absorbable suture. The dissection is continued laterally between the medial bulb and lateral corpora cavernosa and up to the central tendons on both sides using a blunt dissection technique.
7. The insertion of the adductor longus tendon into the body of the pubis is identified; this should be easily palpable with the patient in the lithotomy position. The medial border of the obturator fossa lies 1 cm beneath and 1 cm lateral to the insertion of adductor longus. Small stab incisions are made at these points (Fig. 15.6, marked X). A long needle such as a spinal needle that can be bent is used to identify the point of entrance to the medial obturator fossa; it can be left in place as a guide prior to the insertion of the introducer needles. Local anaesthetic, such as bupivacaine 0.5 % can also be injected at this point (Fig. 15.6).
8. The insertion of each introducer needle should be rehearsed in free space above the patient with the aim of visualising the path of the trocar and to maintain a constant axis at about 45°. The needle is passed outside-in through the stab incision, resistance is felt as the needle tip reaches the external obturator muscle and membrane. A 'pop' can then be felt when the membrane is punctured by the introducer needle followed by some give as the needle tip

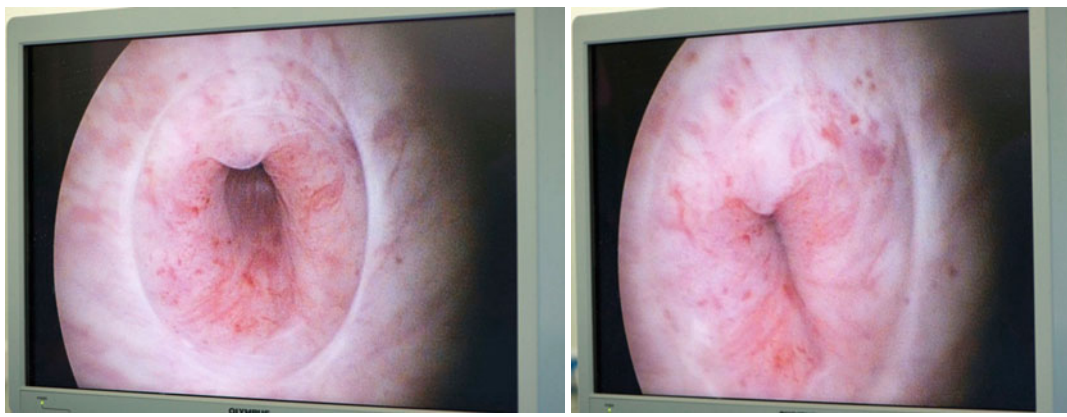

Fig. 15.2 Cystoscopic appearance of the urethral bulb. The *left* picture shows the bulbar urethra open without any external pressure and the *right* shows good co-aptation with external pressure with an indexed finger

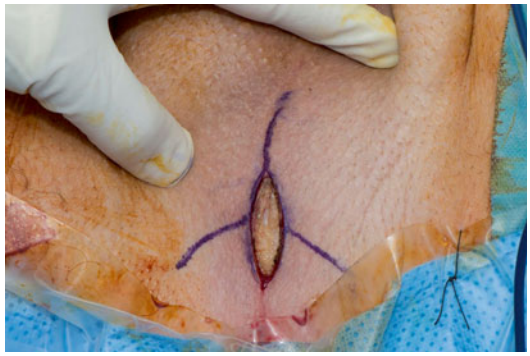

Fig. 15.3 Perineal incision is marked and the skin incised

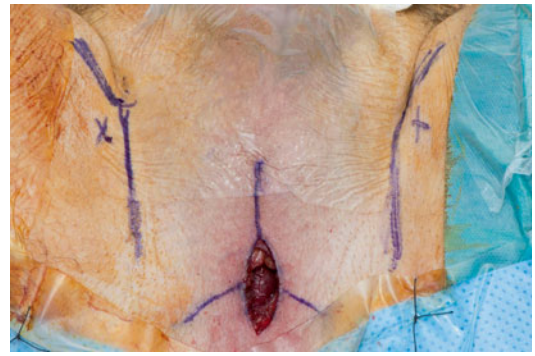

Fig. 15.6 Points of entry marked relative to the adductor longus tendon

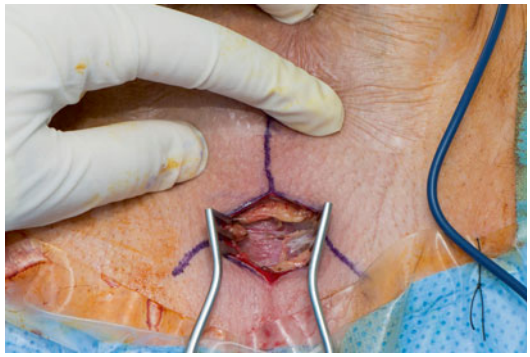

Fig. 15.4 Incision though the subcutaneous and fascial layers down to the bulbocavernosus muscle

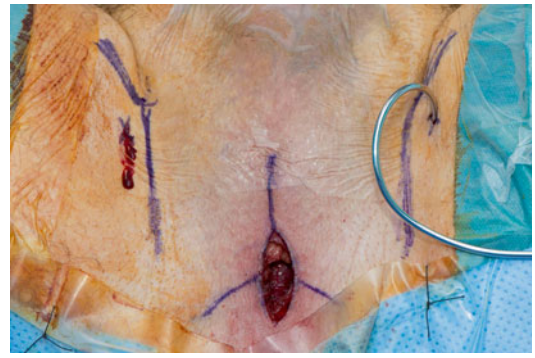

Fig. 15.7 Introduction of the trocar through the stab incision

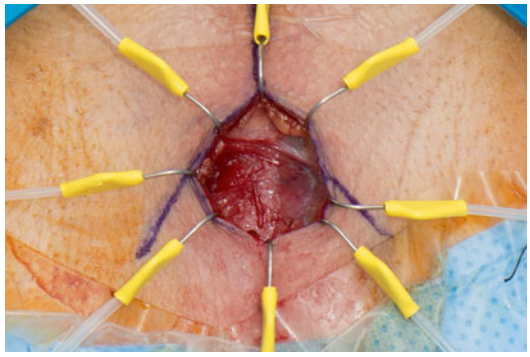

Fig. 15.5 Exposure of the corpora and proximal urethral bulb

passes through. Some gentle finger pressure with the thumb of the hand that is not holding the trocar on the introducer needle may be necessary to allow this to happen. The needle tip can be palpated under the inferior pubic ramus with the index finger of the opposite hand (Figs. 15.7 and 15.8).

9. Using a rotational movement of the introducer needle the needle tip is guided by the index finger into the apex of the triangular area formed by the corpus cavernosum and corpus spongiosum (Fig. 15.9).
10. One end of the sling is clipped into position on to the tip of the guidance needle. The sling

tensioning sutures and blue dots should face away from the urethra and towards the surgeon. The sling is pulled into position by reverse rotation of the introducer needle and pushing the trocar with the other hand to aid movement, only minimal force should be required. The same procedure is then repeated on the contralateral side having identified the insertion of the adductor longus tendon.

11. The centre portion of the sling is positioned over the proximal urethral bulb – the mesh here is sutured in place with 4 tacking sutures using 3-0 absorbable sutures (2 sutures are placed proximally and 2 are placed distally). The aim is to spread out the central portion of the sling to prevent it from rolling up or kinking (Fig. 15.10).
12. To tension the sling both sling ends are pulled simultaneously. This aims to cause proximal relocation of the posterior surface of the proximal urethral bulb by about 2.5–3.5 cm. The surgical wound and the AdVance sling are washed at this stage with a solution of Cefuroxime and Gentamicin to reduce the risk of infection. Further sling fixation can be achieved by creating a subcutaneous tunnel; this is reported to increase the sling fixation by 50% [29].
13. The dead space created by proximal displacement of the bulbar urethra should be obliterated as much as possible prior to wound closure. In order to achieve this the bulbospongiosus is closed in the midline and the wound closed in layers. In experienced hands the entire procedure can be performed in less than 45 min. The catheter can be removed the day following surgery, and the patient discharged with instructions to avoid strenuous exercise for 4–6 weeks including squatting, climbing and sexual activity, this allows for tissue ingrowth into the mesh to improve sling fixation (Fig. 15.11).

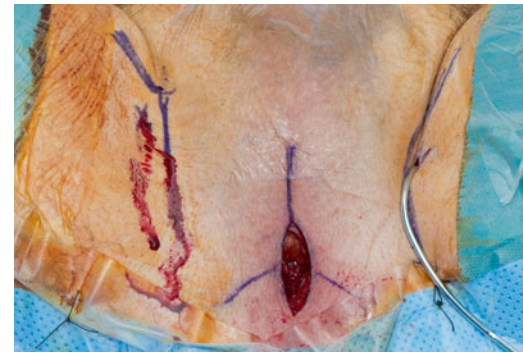

Fig. 15.8 Trocar being advanced in a rotational movement

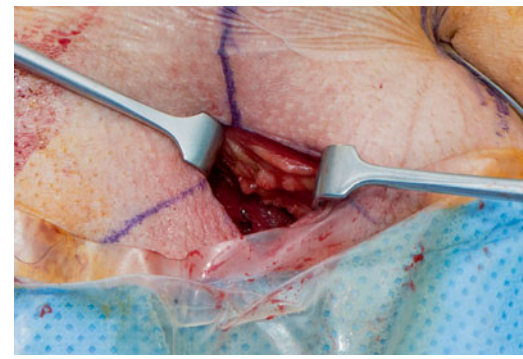

Fig. 15.9 Introducer being advanced and guided into the triangular area formed by the corpus spongiosum and corpus cavernosum

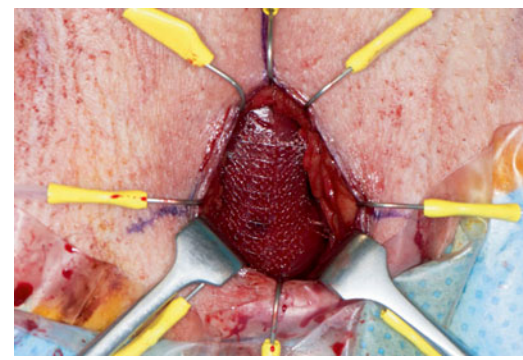

Fig. 15.10 Sling in position

Bone Anchored Sling

The BAS (Fig. 15.12) compresses the urethra with a silicone-coated polypropylene mesh that is fixed to the bony pelvis. This procedure has been described both with synthetic mesh [30] and with organic grafts [30, 31]. The bulbar urethra is compressed by the sling which is fixed to the inferior pubic rami with bone screws. Synthetic mesh is now the primary material used for the bone anchored sling (e.g. InVance sling). Organic sling

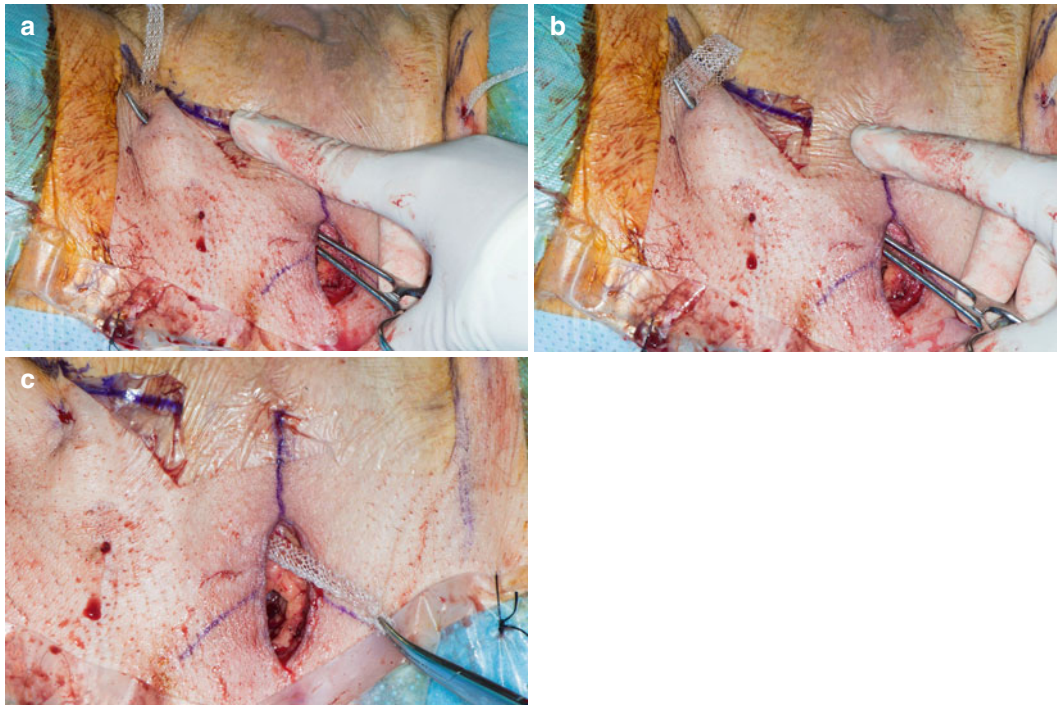

Fig. 15.11 (**a**–**c**) The sling ends are cut level with the skin, making sure they are properly buried under the skin

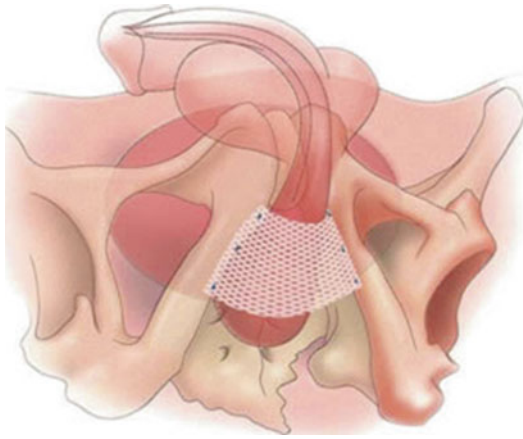

Fig. 15.12 Diagram to illustrate the position of the bone-anchored sling

materials have been shown to degrade in this situation [32–34]. The degree of sling tension is a vital part of the procedure and various methods have been used: retrograde perfusion pressure of 30–50 cm H_2O or >60 cm H_2O, cough test or maximal compression with or without a urethral catheter in place. Dynamic MRI has been used to demonstrate the compressive effect of the BAS on the urethra. Ullrich and Comiter demonstrated that mean detrusor pressure and maximum flow rate (Q_{max}) do not change significantly despite a doubling of the retrograde leak point pressure (RLPP) from 30 to 60 cm of H_2O following BAS insertion [35]. A significant increase in the Valsalva leak-point pressure (VLPP) after BAS implantation has been described [34]. BAS is thought to improve continence by causing urethral obstruction and allowing better transmission of intra-abdominal pressure to the bulbar urethra [36].

Success Rates

As the BAS has been around longer than the other types of slings there are more studies available for review with consequently longer mean/median follow up rates. Overall results of the BAS suggest cure rates ranging from 37 to 67 % with a further improvement noted in an additional 10–40 %. The wide range of results is thought to be secondary to surgical technique, the definition of continence utilised and case complexity (Table 15.2 [37–43]).

Adverse Events

Postoperative urinary retention is a recognised complication of BAS reported in 0–12 % of patients. This is thought to be related to urethral compression, in addition to post-operative swelling and pain. In most cases it is self-limiting and resolves in 1–15 days. Infection of the perineal incision and mesh has also been described. These infections usually require removal of the implanted sling in order to treat the infection although some superficial infections have been successfully treated with antibiotics. Most infections occur early following the procedure but later infections have also been reported at 3 months and even at 1 year. Osteomyelitis is a potential complication of this procedure and has occasionally been described [44, 45].

Abnormal post-operative pain or paraesthesia is thought to be from compression or intraoperative disruption of the superficial perineal nerves [46], or from healing around the newly inserted bone screws. The pain generally resolves after less than 3 months.

By compressing the bulbar urethra, the BAS increases bladder outflow resistance, this can cause *de novo* detrusor overactivity or urinary urgency. Rates have been reported at 0–14 %, and have been successfully treated with anticholinergic medication when required. The bone screws can become loose, or displaced as a late complication leading to recurrent urinary incontinence. Therefore these slings have been withdrawn from most markets around the world due to their complications.

Adjustable Retropubic Sling (ARS)

The ARS was based on the Schaffer et al. retropubic urethral bolsters [47]. The sling is surgically placed at the proximal bulbar urethra with traction sutures placed retropubically (Fig. 15.13). The sutures are then "tensioned" at the level of the rectus fascia utilising silicone columns and washers (Argus sling, Promedon SA, Cordoba, Argentina) to provide an appropriate level of urethral compression. It is positioned using a trocar which passes through the perineal membrane, retropubic space and abdominal fascia. The sling tension is set to a RLPP of 45 cm H_2O [48] or 37 cm H_2O which was associated with significantly less erosion [49] and also with reduced pain and urinary retention [50]. The primary advantage of this design is that the sling tension can be modified and maintained through a superficial suprapubic incision. The Remeex sling (Neomedic International, Terrasa, Spain) was originally designed for female incontinence. It is a monofilament polypropylene mesh bulbar urethral sling which is attached to sutures that are passed through the retropubic space. These sutures are connected to a subcutaneous veritensor that sits above the abdominal fascia, and allows the sling sutures to be tensioned on post-operative day 1 with a "manipulator" that is temporarily left protruding through the incision. This veritensor can also be utilised with further adjustments in tension if required.

Efficacy

Results of initial and longer-term follow up demonstrate success rates of 13–100 % with the larger series reporting rates of 54–79 % [49–55]. Patients required adjustments in 10–100 % of cases, many of which required repeated anaesthesia. Outcomes of the Reemex sling in two small case series were encouraging [51, 52]. A multicentre case series of 50 men has been reported [53] with almost all patients needing a second adjustment at between 1 and 4 months. There was a 65 % cure rate, and a 20 % improvement rate at a median of 32 months of follow-up (Table 15.3).

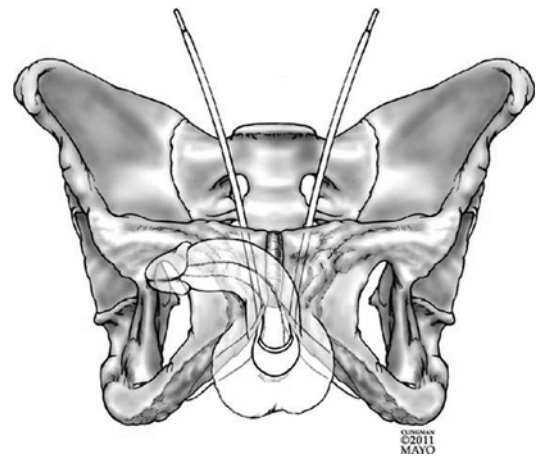

Fig. 15.13 A diagrammatic representation of an adjustable retropubic sling

Table 15.2 Comparison of results of bone anchored sling placement in adult males with SUI

Study	Patients (no.)	Mean/med f/u (mo)	Pre-op continence (mean/med)	Success definition	Success (%)	Improved (%)	No improvement (%)	Complications (%)	Notes
Cespedes and Jacoby [31]	58	6			26(45)	11(19)	21(36)	None	
Ullrich and Comiter [37]	36	25	≥3 ppd	0 ppd	24(67)	9(25)	3(8)	None	Mean pads decreased from 4.6 to 0.64
Comiter [38]	48	48	≥3 ppd	0 ppd	31 (65)	10 (21)	7 (15)	Infection 1 (2), erosion 1 (2), perineal pain ×3 months 7 (16), 2 (4) screw dislodgement	Mean pads decreased from 4.6 to 1.0
Castle et al. [39]	38	18		≤1 ppd	15 (40)			Infection 3 (8), erosion 1 (3), majority with significant perineal pain ×3–4 months	
Gallagher et al. [40]	31	15		≤1 ppd	18 (58)			Infection 2 (6), Sling removal 4 (13)	3 pts lost to f/u, 4 pts w/sling removal
Fischer et al. [41]	62	15	Pad wt 352 g ± 43	PGI-I 1 question	36 (58)	6 (10)	26 (42)	Infection 3 (5), erosion 1 (2), pain >5 months 5 (8), total 13 (21)	Prospective study; 71 % chance of success if preop pad weight <423 g
Guimarães et al. [42]	62	28		0 ppd	40 (65)	14 (23)	8 (13)	Infection 2 (3), pain 12 (19), bone anchor dislodgement 1 (2)	3 year f/u w/21/30 (70), 4 year 8/12 (67) successful
Giberti et al. [14]	40	35		pad weight 0-1 g	22 (55)	5 (13)	13 (33)	Infection 6 (15), de novo detrusor overactivity 2 (5), pain 29 (73)	
Athanasopoulos et al. [43]	43	24		≤1 ppd	22 (51)	8 (19)	13 (30)	Infection 5 (12), ne novo urgency 6 (14), pain 1 (2)	Pre-op incontinence: 1–2 pads in 6/43 (14), 3–5 pads in 23/43 (53), and ≥6 pads in 14/43 (33)
Carmel et al. [36]	45	36		0 ppd	16 (36)	18 (40)	11 (24)	Infection 1 (2), pain ≤3 months 10 (22)	12 pts (27 %) w/preop radiation

Table 15.3 Comparison of results of adjustable retropubic sling placement in adult males with SUI

Study	Patient (no.)	Mean/med f/u (mo)	Pre-op continence (mean/med)	Success defn	Success (%)	Improved (%)	No improvement (%)	Complications (%)	Notes
Romano et al. [50]	48	45		0 ppd	31 (66)	6 (13)	10 (21)	Infection 3 (6), erosion 6 (13), removal 9 (19), pain 2 (4)	Argus sling; adjustment required in 5 (10)
[a]Tuygun et al. [54]	8	10	6.8 ppd	0 ppd	1 (13)	1 (13)	6 (75)	Pain 3 (38)	Argus sling; pts w/prior AUS erosion; study compares AUS to sling as salvage option
Bochove-Overgaauw and Schrier [48]	95	27	See notes	≤1 ppd	51 (54)	17 (18)	27 (28)	Infection 6 (6), erosion 3 (3), removal 11 (12), total 55 (58)	Argus sling; Pre-op continence: 1–2 ppd in 13/100, 3–5 ppd in 46/100, and 6–10 ppd in 41/100
Dalpiaz et al. [55]	29	35	5 ppd		5 (17)			Infection 2 (7), erosion 3 (10), bladder perforation 3 (10), retention 10 (35), removal 10 (35), significant pain 8 (27)	Argus sling; Dissatisfied with clinical outcome 21 (72)

Hübner et al. [49]	101	25		≤1 g 20-min pad test	80 (79)			Bladder perforation 5 (5), infection 5 (5), erosion 13 (13), removal 16 (16), pain <3 weeks 15 (15)	Argus sling; adjustment required in 39 (39)
Sousa-Escandón et al. [53]	51	32		≤1 ppd	33 (65)	10 (20)	8 (16)	Infection 3 (6), removal 1 (2), bladder perforation 5 (10), majority with perineal pain	Remeex sling; multicenter study; adjustment required in 51 (100)
Verdejo et al. [52]	5	15	5–8 ppd	≤1 ppd	5 (100)				Remeex sling
Parra et al. [56]	15	19			5/12 (42)	4/12 (33)	3/12 (25)	Removal 3 (21), readjustment 12 (86), bladder perforation 4 (29), retention 5 (36)	Remeex sling

PPD pads per day, *PGI-I* patient global impression of improvement, *RP* radical prostatectomy, *RLPP* retrograde leak point pressure
[a]Represents specialized/salvage patient populations

Adverse Events

Overall erosion rate was initially reported at 13 % [50], infection requiring sling removal was reported in 3–11 % of patients. Intraoperative bladder perforation was reported in 5–6 % of cases [48–50]. If bladder perforation is recognised during intra-operative cystoscopy, then repositioning of the trocar is required. Transient perineal pain was reported in 9–15 % of men and persistent perineal pain in 4–5 %.

Reported complications with the Reemex sling included a 10 % rate of bladder perforation, 4 % rate of veritensor infection necessitating explantation and a 2 % urethral erosion rate [53].

ProAct Device

The ProAct device (Uromedica Inc) is a minimally invasive treatment for male SUI. It is composed of two silicone elastomer balloons inserted paraurethrally at the bladder neck in men with post prostatectomy incontinence. Each balloon is attached to a titanium port which is buried in the anterolateral part of the scrotum. These ports allow adjustments of the balloon pressures postoperatively to achieve the desired urethral resistance without further surgical intervention. A further advantage of the ProAct device is that it can easily be removed if the balloons prove to be painful, erosive or become infected [57].

Between 1999 and 2004, 117 patients were implanted with a ProAct device at a single centre. Device implantation took between 14 and 56 min. On the first post-operative day only 5 men were fully continent and needed no further percutaneous adjustment of the balloon volume. 112 men (96 %) needed a median of 3 (range, 1–15) adjustments to achieve a satisfactory result. Median balloon volume at implantation was 2 ml (0.5–7.5 mL) and the final mean volume after adjustments was 3.5 ml (1–10 mL). In 15 men there were perforations (bladder/urethral) at the time of surgery.

At 1 year, 92 % of men were wearing fewer pads compared to baseline and 88 % were described as continent or mildly incontinent. From this series 28 men have gone on to have an AMS 800 AUS inserted [57].

Crivellaro et al. compared the efficacy of the ProAct device against the BAS in men with post prostatectomy incontinence. Forty-six men received the ProAct and 38 had the BAS inserted by two different surgeons in two different centres. Both groups were followed up prospectively by pad usage per day and using the UCLA/RAND questionnaire. Complication rates and operating times were also compared. At 19 months post insertion 30/44 (68 %) of the ProAct patients were dry and at 33 months 23/36 (64 %) of BAS patients were dry. The UCLA and RAND questionnaires showed an 11.7 point improvement on average with ProAct and 10 points for BAS. Mean operative time was 18 min with the ProAct and 45 min for the BAS. Complications included removal of the ProAct or BAS in 6/44 (14 %) and 2/36 (6 %) respectively. The authors concluded that ProAct and BAS are both associated with a satisfactory outcome. The ProAct results seem better for more severe incontinence and BAS for mild incontinence [58].

ATOMS Device (Adjustable Transobturator Male System)

This device is a self-anchoring adjustable system to support the bulbar urethra using a transobturator approach. Unlike the AUS which compresses the urethra circumferentially the ATOMS device only compresses the dorsal aspect of the bulbar urethra. In one series temporary urinary retention occurred in two patients (2 %) and transient perineal/scrotal discomfort or pain was reported by 68 patients (68.7 %). There were 4 (4 %) cases of wound infection at the site of the titanium port leading to explantation. The mean (SD; range) number of adjustments to reach the desired result (dryness, improvement and/or patient satisfaction) was 3.8 (1.3; 1–6). After a mean (SD; range) follow-up time of 17.8 (1.6; 12–33) months, the overall success rate was 92 % and the mean pad use decreased from 7.1 to 1.3 pads/24 h ($P < 0.001$). Overall, 63 % were considered dry and 29 % were improved [59].

A further category of male urethral sling which has recently been introduced is the Virtue quadratic sling (Coloplast, Humlebaek, Denmark).

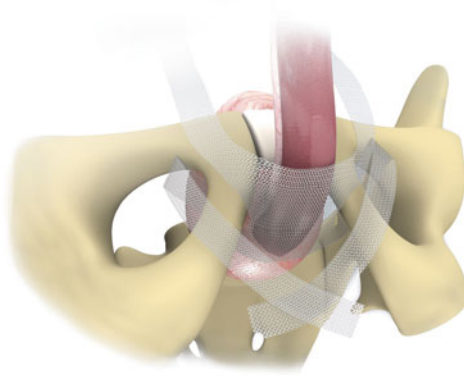

Fig. 15.14 Diagrammatical representation of the quadratic sling

The sling consists of a broad based mesh material placed over the bulbar urethra in a similar fashion to the BAS. The mesh is then secured by four mesh arms, two transobturator and two prepubic (see Fig. 15.14). The aim is to achieve proximal urethral relocation and bulbar urethral compression. However at present only minimal data is present.

Autologus Slings for Male SUI

Autologus slings using harvested rectus fascia have been described to treat male SUI. Athanasopoulos et al. described a series of 32 male patients with SUI treated over a 3 year period by insertion of a bulbourethral free rectus sling. Neurogenic dysfunction was the most common cause of incontinence in this group. They described modest success with 31.3% being cured (15.6% totally dry and 15.6% on one pad per day). However, morbidity was significant with 21.9% presenting with a mild complication- most commonly de-novo urgency [60].

Conclusions

Iatrogenic male SUI remains a significant problem affecting a large number of patients with resultant adverse effects on quality of life. Patients presenting with SUI should be adequately assessed prior to any decisions being made regarding treatment. Several treatment modalities are available for low to moderate volume incontinence including the AUS and several male slings. Male slings add to the urologists' armamentarium in the treatment of SUI. The MASTER trial (Male synthetic sling versus Artificial urinary Sphincter Trial: Evaluation by Randomised controlled trial) which is running in the United Kingdom and funded by the National Institute for Health Research, aims to ascertain which surgical intervention is best for any severity of incontinence.

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Injectable Agents in Urology

16

Tina Rashid and Ian Pearce

Abstract

Bulking agents are inert substances which when injected into luminal tissues increase coaptation of the submucosal walls thus increasing the resistance either through causing a physical obstruction or improving mucosal sealing. This results in improvements in both continence and vesicoureteric reflux. This chapter examines the historic and current use of injectable agents in urology, focussing on urinary incontinence and vesicoureteric reflux.

Keywords

Urethral bulking • Injectable agents • Stress urinary incontinence • Vesicoureteric reflux (VUR) • STING • HIT

Introduction

'Injectables' within urology encompass materials injected around the urethra for the management of stress urinary incontinence (SUI) in both men and women, and those injected around the ureteric orifices to prevent vesicoureteric reflux (VUR). This chapter considers available agents, their properties, injecting techniques, outcomes and potential complications.

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The Use of Injectable Agents in Stress Urinary Incontinence

Urinary Incontinence: Definition and Epidemiology

Addressing urinary incontinence (UI) with a health professional can be distressing for both men and women, and is often perceived to be stigmatised, consequently prevalence figures are usually underestimated. A study in the late 1970s suggested that the prevalence of UI reported to healthcare professionals was 0.2 % in women

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aged 15–64 years and 2.5 % in those aged 65 years and over, whilst a postal survey of the same population reported a prevalence of 8.5 % in women aged 15–64 and 11.6 % in the older group [1].

More recent studies have estimated that UI affects a considerable proportion of the population, both men and women, with one study suggesting 33.6 % of 15,904 community dwelling adults older than 40 years reporting significant symptoms [2]; a further European study of 29,500 women aged over 18 reported UI to be prevalent in 15 % of the population in Spain, 32 % in France, 34 % in Germany and 32 % in the UK [3]. On appraisal of the available evidence, the Fourth International Consultation in Paris concluded that some degree of incontinence is experienced in between 25 and 45 % of women and in 11–34 % of men [4]. The increasing incidence of UI in men is likely to relate in part to changes in patterns in diagnosis of prostate cancer and the rise in radical management of early and intermediate disease.

UI is associated with significant resource burden to both the individual and the health care system. Costs are attributed to general practitioner (GP)/hospital specialist visits, pad usage, medical or surgical treatment and loss of productivity. In the United Kingdom (UK), the cost of UI in women is equivalent to that of gynaecological cancers, osteoporosis and breast cancer [5] with the combined costs borne by both the individual and the National Health Service (NHS) estimated to be close to £743 million per year in 2006 [6], representing just less than 1 % of the total NHS annual budget. In the United States, over $12 billion dollars are spent annually on the management of SUI alone [7].

Stress Urinary Incontinence: Pathophysiology and Classification

SUI is the complaint of involuntary leakage of urine on effort or exertion, sneezing or coughing [8].

The precise pathophysiology of SUI is beyond the scope of this chapter, but in brief, the cause of SUI in men is secondary to external sphincter weakness combined with a poorly functional internal sphincter at the bladder neck level. This is most commonly (but not exclusively) seen following radical prostatectomy for prostate cancer or following resection of the prostate for benign disease. Any disease process affecting the sacral plexus with subsequent deleterious effects of bladder neck and sphincteric control, e.g. non-urological pelvic surgery (anterior resection) or neurological disease may also result in SUI.

In females, SUI is both more common and more complex, and may be caused by ‘urethral hypermobility’ or ‘intrinsic sphincter deficiency’, in addition to pelvic surgery and neurological disease as seen in men.

Urethral Bulking Agents

Mechanism of Action

Bulking agents are presumed to improve continence by increasing coaptation of the urethral walls when injected into the submucosal tissues of the urethra, resulting in an increase in urethral resistance either through causing a physical obstruction or improving the mucosa-to-mucosa sealing. Although small studies have suggested that injection with bulking agents increases the length of muscle fibres within the urethral sphincter with a subsequent increase in sphincter power [9], robust evidence for the mechanism of action is lacking (Figs. 16.1 and 16.2).

Table 16.1 demonstrates the characteristics which an ideal injectable agent should possess.

Patient Selection

Urethral bulking agents have been, and continue to be used in the treatment of SUI in men and women as an alternative to bladder neck suspension procedures, slings and artificial urinary sphincters. Conventionally, urethral bulking is reserved for patients in whom conservative treatments have failed and who either decline surgical treatment or who have a medical history that precludes them from it. In addition, urethral bulking may be an appropriate measure for young women who are yet to complete their family or utilised as “top up” therapy for patients in whom surgical treatment eg : mid urethral tape insertion has been only partly successful.

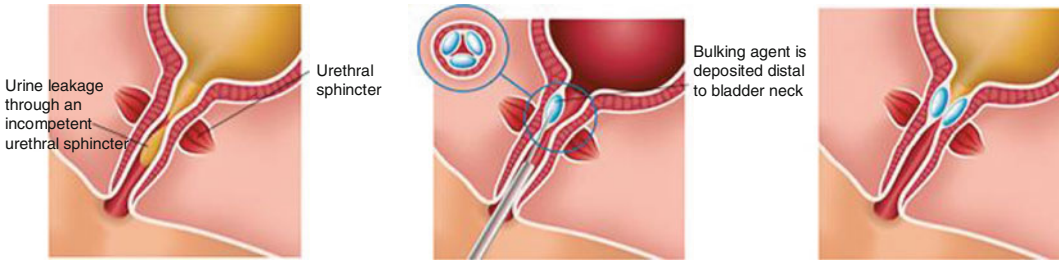

Fig. 16.1 Diagrammatic demonstration of the effect of urethral bulking agents placed in the female urethra (Reproduced with permission of Contura International ©, Denmark. All rights reserved)

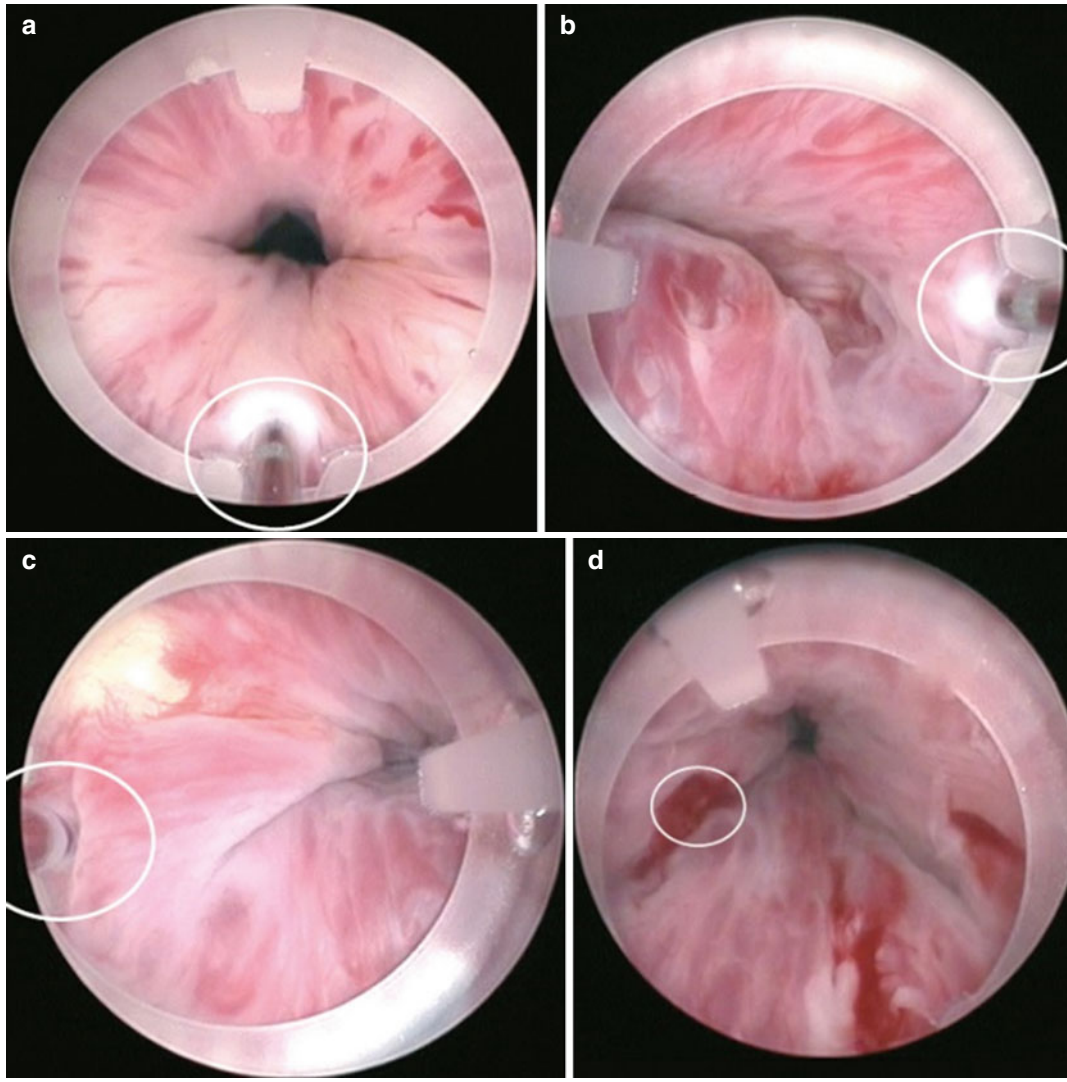

Fig. 16.2 Photograph demonstrating the effect of urethral bulking in the female urethra: (**a**) bladder neck is gaping, first injection is placed; (**b**–**d**) bulking effect after placement of bulking material at three points (Reproduced with permission of Contura International©, Denmark. All rights reserved)

Table 16.1 Desirable characteristics of the ideal injectable agent

Non-immunogenic
Hypoallergenic
Biocompatible
Permanent
Non-erosive
Non-migratory
Heal with minimal fibrosis
Easy to store and handle

When offering urethral bulking agents, patients must be aware that repeat treatments are likely to be necessary as the effects are short-lived and that medium to long term outcomes are inferior to those of more invasive techniques. Urethral bulking agents are not recommended in those patients seeking a cure for their symptoms, however, their risk profile is comparatively lower and this can be appealing to some.

Historical Use of Urethral Bulking Agents

Injection therapy was first described in 1938 by an obstetrics registrar, Bryan Murless [10] who utilised **sodium morrhuate**, a mixture of the sodium salts of saturated and unsaturated fatty acids of cod liver oil. Prior to this, sclerosing agents had been described in the treatment of hydrocoeles, ganglions, varicose veins and inguinal herniae, with the sclerosant causing local irritation and subsequent fibrosis. He described *'a fair degree of success'* in 20 women whose main complaint was SUI with varying degrees of anterior vaginal wall prolapse '*too slight to warrant operation'*. Sodium morrhuate fell out of favour following reports of anaphylaxis and death following its use in the treatment of varicose veins.

In the 1970s, Berg described the successful injection of polytef paste (Teflon®, Polytef, polytetrafluoroethylene, PTFE) into the submucosal tissue of the urethra in three patients to augment urethral thickness for the correction of urinary incontinence [11] following its long successful use in the treatment of reflux in children [12]. However, there were significant concerns of particle migration and embolisation as well as the induction of inflammatory reactions and granuloma formation. This was corroborated by X-ray microanalysis which confirmed migration of injected periurethral PTFE in female dogs and male monkeys to pelvic nodes, lungs, brain, kidneys and spleen. Polytef granulomas were found at all injection sites and some sites of distant migration [13]. PTFE never received Food and Drug Administration (FDA) approval in the United States (US) and has not been recommended by the National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) [14].

In order to avoid these complications, **autologous fat** was investigated in 2001. Fat harvested from a patient's abdominal wall using liposuction was injected periurethrally under transrectal ultrasound guidance to treat SUI. Despite early reports of success in individual [15] and small case series [16, 17], there were difficulties harvesting the fat and unacceptably high rates of reabsorption from the injection site which impaired results and hampered the technique. In addition, when compared to newer techniques using collagen, only 13% of the autologous fat group were cured (compared with 24% of the collagen group) with lower subjective improvement (70.9% versus 31.2% respectively, $p<0.001$) [18]. When compared to periurethral injections of saline [19], periurethral fat injection did not appear to be more effective than placebo, with 22.2% cured in the autologous fat group compared to 20.7% in the saline group at 3 months. A strong recommendation against the use of autologous fat was finally made by NICE [20] in 2006 and in a Cochrane review [21] in 2007 following a case of a death associated with pulmonary adipose tissue and lipid droplet embolism [22].

Non-animal stabilised hyaluronic acid/dextranomer (NASHA/Dx, Zuidex®) comprises dextranomer microspheres in a carrier gel of non-animal stabilised hyaluronic acid. There remains

only one randomised controlled trial (RCT) comparing dextranomer (placed in mid-urethra) to collagen injection (at the bladder neck). At 12 months, results were inferior in women given dextranomer [23]. This product was eventually withdrawn from the market for use in SUI because of high complication rates.

Porcine dermal implant (Permacol™) is a sterile saline suspension of acellular cross-linked porcine collagen matrix that maintains its original three-dimensional form once injected. There is one very small RCT comparing its use to silicone particles, which demonstrated no significant difference in failure rates between the two at 6 months' follow-up [24].

Ethylene vinyl alcohol copolymer (EVOH, Uryx®, Tegress®) is a solution of ethylene vinyl alcohol suspended in dimethyl sulfoxide, approved for use by the FDA in December 2004 for the treatment of SUI. The mixture shows minimal foreign body reaction and has been used successfully in the treatment of brain aneurysms by direct implantation into the aneurysm itself. To date, there is one RCT (n = 210), comparing ethylene copolymer to collagen, which demonstrated similar efficacy at 6 months' follow-up [25]. However, a greater than 50 % complication rate including urethral erosions and pain have left this agent low on the list of favourable agents [26].

Until its production ceased in 2011, the 'gold standard' bulking agent was considered to be **glutaraldehyde cross-linked bovine collagen (GAX, Contigen®)**. Implantation of GAX collagen promotes fibroblast invasion in 93.3 % of patients, collagen formation in 73.3 %, capillary ingrowth in 46.6 % and an inflammatory reaction in 20 % [27]. The recruitment of host fibroblasts is key, eventually replacing the injected collagen and it is this mechanism that is responsible for continued continence when the collagen inevitably disappears. In contrast to previous discussed agents, there is a proven lack of migration of GAX collagen after injection and its safety in children with VUR is also supported.

Fig. 16.3 Macroplastique™ (Reproduced with permission from ©Uroplasty, Inc. All rights reserved)

Newer Injectable Agents

More recently, newer agents with improved safety profiles have emerged.

Silicone, polydimethylsiloxane microparticles (Macroplastique™) comprises heat-vulcanized polydimethylsiloxane suspended in a polyvinylpyrrolidone (PVP) carrier gel. When injected, the synthetic polydimethylsiloxane implant remains in place at the implantation site whilst the carrier gel is exchanged for tissue fluids containing host fibroblasts that subsequently deposit a collagen matrix around individual implants, as well as around the periphery of the implanted material. After the exchange, the carrier gel is removed by the reticuloendothelial system and excreted, unmetabolized, from the body via the kidneys.

Silicone particles have been compared to collagen in two RCTs, only one of which has been published as a full article [19], with no significant difference in efficacy detected (Fig. 16.3).

Synthetic **calcium hydroxylapatite (CaHA, Coaptite®)** is suspended in a mainly glycerine and water gel with a chemically-modified naturally occurring polysaccharide sodium carboxymethylcellulose as support. CaHA is inert in soft tissue, and does not generate an inflammatory reaction. When injected, healthy tissue grows through the injected deposit to form a tissue-CaHa matrix which remains soft, pliable and stationary within the injection site. A small study comparing collagen with CaHa suggested the failure rate to be significantly higher at 6 months

for collagen compared to CaHa (6/18 vs. 3/22, respectively) [28].

Pyrolytic c**arbon-coated zirconium oxide beads** are suspended in a water-based carrier gel containing beta-glucan to form **Durasphere®**. Once injected, collagen is slowly deposited around the pyrolytic carbon-coated beads, resulting in bulking from both the beads and the collagen. Although a good quality RCT comparing carbon beads to collagen [29, 30] demonstrated no difference in efficacy, the former product is associated with technical shortcomings. The biogel that suspends the beads flows fairly easily through the injection needle without carrying the beads along at a steady rate, with the result that the beads clog the needle, and the remaining material in the syringe is rendered useless. Sterile abscess formation has been reported with carbon-coated beads, an issue with many injectables that remain in a solid phase [31].

Hydrogel cross-linked with polyacrylamide (PAHG, Bulkamid®) was introduced in Europe in 2006 [32]. It is a polymer gel consisting of 2.5 % cross-linked polyacrylamide and 97.5 % water for injection. It is non-toxic [33, 34], resistant to degradation [35, 36] and has a widespread use in ophthalmic surgery, drug treatment, food packaging, and water purification [37]. PAHG has also been used in plastic surgery for aesthetic purposes in the former Soviet Union and China for the past 20 years.

The polymer gel stays within the soft tissues for at least 8.5 years after injection and gives rise to little or no tissue reaction with an absence of capsular fibrosis or calcification [35]. A recent study in rabbits has shown that the bulking effect is preserved for at least 7 months [33] and a study in pigs has documented that PAGH is a stable viscoelastic bulking agent which is integrated into its host tissue by vessel ingrowth [36]. However, no RCT data are available and data comes from single-surgeon experience and case series. A single multicentre case series of 135 women reported a 66 % success rate with 35 % of participants requiring re-injection [38] (Fig. 16.4, Table 16.2).

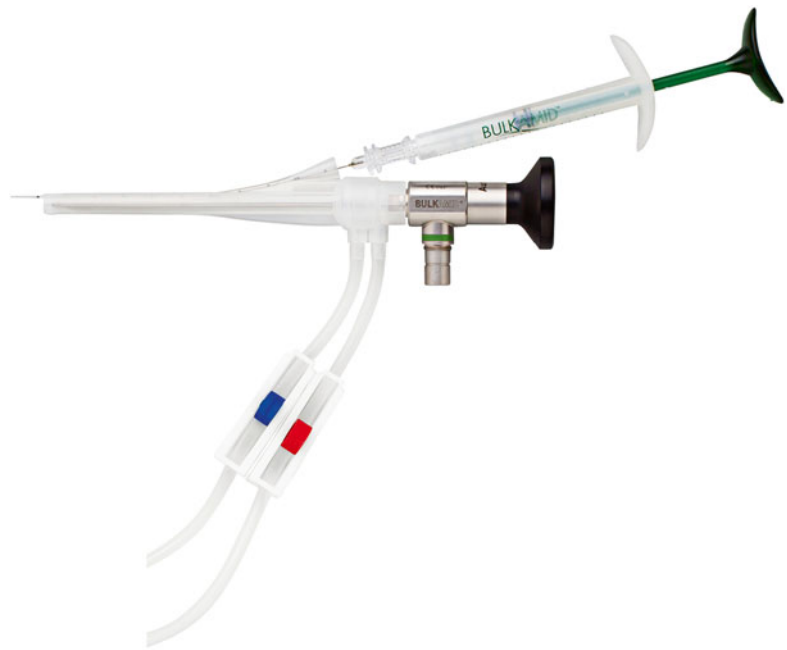

Fig. 16.4 Bulkamid Urethral Bulking System (Reproduced with permission from ©Contura International, Denmark. All rights reserved)

Table 16.2 Common bulking agents

Bulking agent (FDA approval)	Trade name	Gauge needle	Injection location	Total volume injected
Glutaraldehyde cross-linked bovine collagen (1993)	Contigen™ (Bard, Inc.)	22–23 g		2.5–5 mL
Pyrolytic carbon coated graphite beads (1999)	Durasphere EXP™ (Coloplast, Inc.)	Transurethral 18/20 g 15 in. Peri-urethral 18/20 g 1.5 in.	Between 4 and 8 o'clock At 3 and 9 o'clock	2–4 mL
Calcium hydroxylapatite (2005)	Coaptite™ (Boston Scientific)	21 g	4 o'clock 8 o'clock	2–4 mL
Polydimethylsiloxane particles (2006)	Macroplastique™ (Uroplasty)	18/20 g	6 o'clock 2 o'clock 10 o'clock	5.5 mL
Polyacrylamide hydrogel (not yet approved)	Bulkamid™ (Contura Intl)	23 g or Bulkamid Urethral Bulking System	3 o'clock 6 o'clock 9 o'clock	1.5 ml

Repeat Treatment

Each bulking agent requires different time intervals between successive treatments. Whereas GAX-collagen and Coaptite may be injected at 4-weekly intervals, Macroplastique injections can be performed at 12-week intervals. Durasphere injections require a minimum time interval of 7 days. In reality, the time interval between injections will vary on clinical response and patient desire.

Contraindications

Urethral bulking agents must not be implanted in patients with active urinary tract infection. Caution is also advised in patients with a fragile urethral mucosal lining such as that found post-radiotherapy or after bladder neck surgery.

Injection Technique

The recommended site of injection varies with the bulking agent. Injections may be transurethral or transperineal under urethroscopic control, or alternatively using a purpose-made device (implacer), which reliably positions the needle-tip under local anaesthetic at the required position in the urethral wall. Outcomes of transurethral versus the periurethral route are similar, although the latter is thought to require larger volumes of injected agent to achieve the same outcome and a subsequent higher risk of urinary retention compared to a transurethral injection. However, no difference has been found in efficacy between a mid-urethral and bladder neck injection of collagen.

Patient Preparation

1. Exclude a urinary tract infection.
2. Broad-spectrum antibiotics in line with current local/departmental microbiology guidelines are administered prior to injection.

Product Preparation

Carefully examine the sterile packaging and contents prior to use to confirm sterility and expiration date. Instructions for product preparation will vary with the product being used. Table 16.3 describes how to prepare Macroplastique® for injection; see Figs. 16.5 and 16.6 for illustrations.

Procedure

1. The patient is placed in a lithotomy or Lloyd Davies position and standard procedure is used to prepare the patient for cystoscopy.
2. Topical local anaesthetic may be applied in the urethra if the procedure is being performed under local anaesthetic.

3. Fill the bladder to approximately 50 % of its capacity with sterile water or saline.
4. Insert the cystoscope into the urethra and advance the needle through the working channel of the scope to visualize the needle tip.
5. Retract the needle tip and cystoscope back into the urethra 1.5–2.0 cm distal from the bladder neck.
6. Advance the needle with the bevel facing the lumen of the urethra.
7. In all positions, use the 'tissue tunnelling' technique (Fig. 16.3) and wait approximately 30 s before withdrawing the needle from the tissue to limit product loss from the implantation site
8. Recommended injection sites will vary with product, anatomy and any previous incontinence surgery.
9. Use caution and avoid passing the cystoscope over the implantation site, which could potentially disrupt product placement.
10. Use a small intermittent catheter (8–12 French) to drain the bladder when necessary

Table 16.3 Instructions for Macroplastique® product preparation

Macroplastique® is supplied in a pre-filled polypropylene syringe containing 2.5 ml of product. It is injected transurethrally through a cystoscope with an endoscopic needle
1. Place the syringe collar over the Macroplastique® syringe flanges, then firmly grasp the collar and lock the syringe/collar assembly securely onto the rotating hub of the administration device
2. Firmly twist and fasten the endoscopic needle hub onto the luer lock tip of the syringe to achieve a tight connection. Remove the protective sleeve from the needle (Fig. 16.5)
3. Prime the needle with Macroplastique® by engaging the administration device. To stop the flow, depress the release mechanism located on top of the administration device
4. The system is now ready to administer bulking agent
NB: Inject product slowly. Wait a few seconds between each pull of the administration device lever

Postoperative Care

Urethral bulking agents have a low risk profile. However, the main complication is postoperative urinary retention which tends to be transient. If the patient is unable to void immediately after treatment, urethral catheter placement must be avoided in case the bulking agent

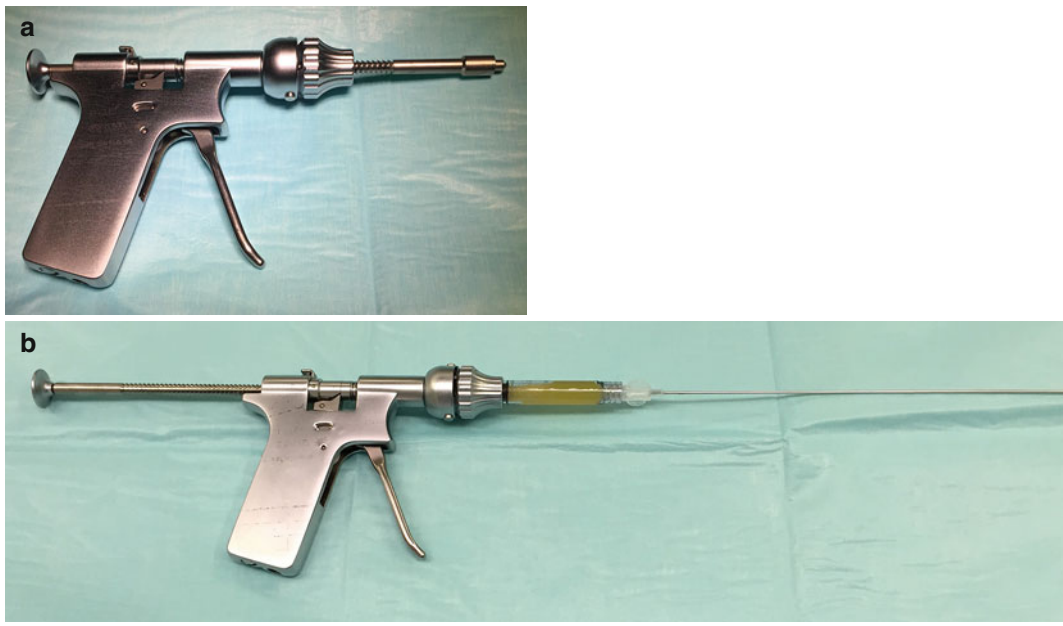

Fig. 16.5 (**a**) Macroplastigue 'gun'. (**b**) Fully assesmbled equipment with pre-filled syringe and needle attached

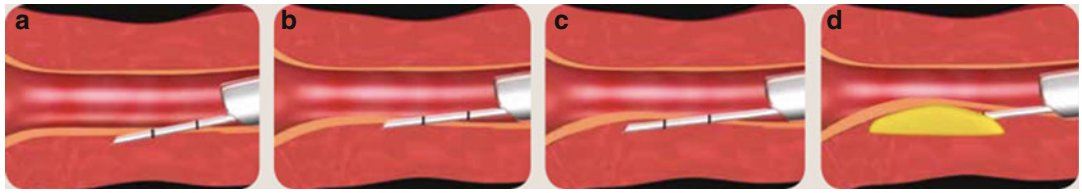

Fig. 16.6 Diagrammatic representation of the recommended 'tunneling technique'. (**a**) The cystoscope is tilted to a 30–45° angle with the bevel facing the urethral lumen. The needle is advanced approximately 0.5 cm into the tissue. (**b**) The scope angle is reduced to 0°. (**c**) The needle is advanced a further 0.5 cm, creating a 'tissue tunnel'. (**d**) A small volume of agent is injected to create a mucosal bleb, confirming accurate needle placement (Reproduced with permission from ©Uroplasty, Inc. All rights reserved)

becomes moulded around the catheter and thus loses its effectiveness. Instead, intermittent self-catheterisation or suprapubic catheterisation are the favoured solutions.

For most patients, multiple treatments with injectable agents will be necessary before achieving the desired therapeutic effect.

Outcomes

The available evidence assessing efficacy of injectable agents and comparing different agents is poor, many of the trials being moderate in quality, small in size and only reported in abstract form. All injectable agents investigated have shown *short-term* efficacy in reducing symptoms of SUI [20, 29, 39, 40]. When compared with open surgery, evidence from RCTs (silicone particles compared to autologous slings and collagen injections compared to assorted procedures) suggests that injectable agents are less efficacious, have lower complication rates compared to open surgery but equivalent levels of satisfaction [41].

Complex Use of Injectable Agents

The continence cutaneous urinary diversion (CCUD) utilises the appendix (or other suitable organ) as a catheterisable conduit between the skin and native or reconstructed bladder in congenital or neuropathic bladder dysfunction, complex incontinence, following cystourethrectomy and in pain syndromes. CCUD incontinence occurs in up to 50 % of patients and may be related to dysfunction of the reconstructed bladder or secondary to valve incompetence. Revision of the channel for the latter may require laparotomy. However, injection of bulking agents at the junction between the conduit and the reconstructed bladder may avoid or delay a complex reconstructive operation in up to 50 % of patients [42].

Complications of Urethral Bulking Agents

Polytetrafluroethylene, autologous fat, ethylene vinyl alcohol (Tegress®) and hyaluronic acid/dextranomer copolymer (Zuidex®) have been abandoned due to concerns regarding migration [43], hypersensitivity [43], urethral erosion [44], pseudocysts/abscess [45], and granuloma formation [46–49].

For those agents currently in use for urethral bulking, risks include transient retention, erosion of the agent into the bladder, haematuria, dysuria, urinary tract infection, urgency and frequency. In the case of erosion, during repeat injections the eroded side should not be reused for injection purposes until the epithelium recovers.

The Future of Injectable Therapy

Injectable chondrocytes, smooth muscle cells, muscle precursor cells (MPCs), adipose-derived stem cells, bone marrow stromal cells and stem cells [50] have all been the subject of recent research in the hope of finding the ideal injectable agent. The use of these cells is aimed at achieving coaptation of the bladder neck region by augmenting tissue mass or restoring sphincter function.

Autologous Chondrocytes

Chondrocytes are readily isolated, grown, and expanded in culture conditions and when implanted *in vivo*, possess an inherent ability to produce extracellular matrix and maintain their structural integrity, thus providing ideal tissue bulking for the treatment of urinary incontinence.

Bent et al. [51] harvested chondrocytes from auricular cartilage of women with documented ISD. Once expanded, the cells were suspended in alginate, a liquid solution of glucuronic and mannuronic acid, enabling delivery of the chondrocytes through an endoscopic needle. Of thirty-two patients who received a single outpatient injection of the chondrocytes just distal to the bladder neck, half (16/32) were dry at 12 months and approximately one third (10/32) had improved.

Injectable Muscle Cells

Strasser et al. [52] injected autologous myoblasts and fibroblasts transurethrally in 42 patients (29 women, 13 men) with urinary stress incontinence. In 35/42 patients, urinary incontinence was completely cured. According to the authors, the remaining seven patients had undergone multiple surgical procedures and radiotherapy, and their urinary incontinence improved but was not eliminated. No side effects or complications were reported postoperatively. The technique is still considered experimental and several FDA-approved cell therapy clinical trials targeting incontinence are on the horizon.

Stem Cells

Stem cells, defined by their ability to self-renew and differentiate into a variety of cell types, have been proposed as a promising cell source to replace, repair, or enhance the biological functions of the damaged sphincter [53]. Sources include fetal stem cells derived from amniotic fluid and placenta [54, 55]; adipose-derived stem cells [56] (processed lipoaspirate, PLA, cells) harvested from adipose tissue under local anesthesia and bone marrow derived mesenchymal-derived stem cells [57].

Whilst early reports of dose-ranging studies [58] suggest that stem cell injection is a safe procedure in the short-term, further studies are required to establish efficacy.

The Use of Injectable Agents in Vesicoureteric Reflux

VUR: Definition and Epidemiology

VUR is a pathological phenomenon in which urine flows retrogradely from the bladder into the ureter. It is a common urological anomaly within the paediatric population, but because invasive diagnostic procedures are performed only in select patients, the 0.4–1.8% estimated prevalence of VUR for all-comers is likely to be an underestimation [59].

Pathophysiology and Classification

VUR is classified as grades I to V, according to the severity of retrograde filling and dilatation of the ureter, renal pelvis and calyces on micturating cystourethrogram (MCUG) (Table 16.4).

The consequences of VUR include renal scarring which may result in renal insufficiency with up to 20% of children with VUR developing childhood hypertension and end-stage renal disease [60]. Therefore, the objective in managing these children is the preservation of renal function by minimising the risk of pyelonephritis.

Not all children with VUR require intervention. Who and how to investigate and treat remains one of the most debated subjects within paediatric urol-

Table 16.4 Grading system for VUR on MCUG, according to the International Reflux Study Committee

Grade I	Reflux into the ureter but does not reach the renal pelvis;
Grade II	Reflux reaches the renal pelvis but no associated dilatation of the collecting system and fornices are normal
Grade III	Mild or moderate dilatation of the ureter, with or without kinking; moderate dilatation of the collecting system; normal or minimally deformed fornices
Grade IV	Moderate dilatation of the ureter with or without kinking; moderate dilatation of the collecting system; blunt fornices, but impressions of the papillae still visible
Grade V	Gross dilatation and kinking of the ureter, marked dilatation of the collecting system; papillary impressions no longer visible; intraparenchymal reflux

ogy. It is, however, accepted that those children at increased risk should be the subject of investigation and possible intervention (Table 16.5).

The factors that affect spontaneous resolution of VUR include:

1. Age at presentation
2. Gender
3. Grade
4. Laterality
5. Mode of clinical presentation (e.g. prenatal screening for hydronephrosis versus febrile UTI in infancy)
6. Anatomy [62].

Good prognosis is associated with age <1 year at presentation, lower grade of reflux (grade I–III) and asymptomatic presentation on screening (in prenatal hydronephrosis or sibling reflux). High-grade VUR is thought to resolve in >25 % [63]. Poor prognostic indicators for resolution include: the presence of renal cortical abnormality, lower urinary tract dysfunction, and breakthrough febrile UTIs.

The assessment of VUR includes a fully history (including family history), examination (including measurement of blood pressure), urinalysis and culture, serum creatinine, urinary tract ultrasound, MCUG and nuclear medicine renography.

Ureteric Orifice Bulking Agents

There are two main treatment approaches to VUR: conservative (non-surgical) and surgical. Conservative therapy involves the prevention of febrile UTI and may employ the use of continuous antibiotic therapy, although this remains an area of controversy.

Table 16.5 Risk factors for VUR [61]

Risk factor	Risk (%)
Pre-natal hydronephrosis	16.2 (7–35)
Sibling with VUR	27.4 (3–51)
Parent with VUR	35.7 (21.2–61.4)
Recurrent UTIs	30–50
Lower urinary tract dysfunction	40–60
Gender	Male 29 %; female 14 %

Whilst surgical correction should be considered in patients with persistent high-grade reflux (grades IV/V), there is no consensus regarding the timing and type of surgical correction.

Surgical treatment may be endoscopic (see below) or ureteric reimplantation, using an open or minimally-invasive approach. Ureteric reimplantation is beyond the scope of this chapter.

Mechanism of Action

Bulking agents are injected submucosally via a cystoscope underneath the intramural part of the ureter, with the aim of elevating the ureteric orifice and distal ureter, thus increasing coaptation. The result is narrowing of the lumen, enabling antegrade urine flow but preventing reflux.

Historical Use of Bulking Agents

As with injectable agents used in the management of stress urinary incontinence, many agents have been used but only one has stood the test of time: dextranomer/hyaluronic acid (Deflux®, Q-Med, Scandinavia).

Deflux® was approved by the US FDA in 2001 for the treatment of VUR in children. As discussed earlier in this chapter, Deflux® comprises NASHA and dextranomer microspheres measuring 80 and 250 μm. Once injected, the NASHA stabilises to form a gel with increased viscosity and stability and the dextranomer microspheres minimise the risk of migration from the site of injection. The result is a stable agent that remains in position over time.

Injection Technique

Deflux® may be injected under general anaesthetic as a day case procedure. Urine must be sterile prior to intervention. Once in lithotomy position, sterile preparation and draping of the operative site is performed. Cystoscopy is performed in line with standard procedure.

The three techniques for injection of Deflux® are described below:

1. *Subureteral transurethral injection (STING):* the originally described technique in which

bulking agent is injected just outside the ureteral orifice at the 6 o'clock position, elevating a mound with a resultant compressed ureteral orifice located at the top of the hillock.

2. *Hydrodistension implantation technique (HIT):* the ureter is hydrodistended allowing the needle to be placed inside the ureter, a few millimeters within the orifice. This allows the bulking agent to track along the ureteral sheath resulting in more efficient coaptation.
3. *Double HIT:* a refinement of the previous techniques, involving a proximal and distal injection. The first injection is as with the previously described technique. The second 'hit' is slightly more cephalad than that of the STING and coapts the ureteral orifice and elevates a mound of bulking material along the course of the ureter.

The double HIT method is currently the most commonly performed technique for endoscopic correction of VUR amongst paediatric urologists in the United States [64].

Outcomes

A meta-analysis of 5527 patients (8101 renal units) suggested that reflux resolves with endoscopic treatment in 78.5 % (grade I–II), 72 % (grade III), 63 % (grade IV) and 51 % (grade V) [65]. An unsuccessful first injection may lead to success in 68 % after a second treatment and 34 % after a third treatment. Poorer outcome was seen in duplex (50 %) versus single (73 %) systems, and neuropathic (62 %) versus normal (74 %) bladders.

A randomised controlled trial comparing endoscopic injection to antibiotic prophylaxis and surveillance with antibiotic prophylaxis in children aged 1–2 years with grade III–IV reflux ascribed success rates of 71 % to endoscopic treatment versus 39 % for antibiotic prophylaxis and 47 % in the surveillance group. The recurrence rate at 2 years after endoscopic treatment was 20 %.

Further trials with longer follow-up and standardised methodology are awaited. In the future, autologous chondrocytes combined with alginate, may be the way forward. Early studies in 10 centers across the United States have shown a success rate similar to that with other injectable substances in terms of cure [66].

Conclusion

Many agents of different make and tissue interaction have been used for urethral and ureteric bulking. Injectable therapy is currently suitable only in specific patient groups due to its low effectiveness in comparison to its more invasive alternatives. This may change in the future if long-term methodological research favours the use of autologous agents.

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Penile Reconstructive Surgery Using Grafts

17

Joshua P. Langston, Giulio Garaffa, and David Ralph

Abstract

The evolution of grafting materials and associated surgical techniques has given the surgeon undertaking prosthetic surgery a number of options when approaching complex cases requiring penile reconstruction. Whether for trauma, malignancy, or Peyronie's Disease, available grafting options are able to provide excellent surgical results and restore patient quality of life.

Keywords

Penile reconstruction • Prosthetic surgery • Peyronie's disease

Introduction

Complex penile reconstruction using grafts may be required following trauma or excision of benign and malignant conditions of the penis, however the majority of cases involve correction of penile deformities in patients with Peyronie's disease (PD). The aim of surgery in cases of PD is to obtain a functionally straight and rigid erection sufficient to engage in penetrative sexual intercourse whilst minimizing penile shortening. This should only be considered once the inflammatory phase of PD has resolved, as generally noted by resolution of penile pain associated with the Peyronie's plaque and also stability of the penile curvature.

For patients with mild or moderate curvature, good erectile function, with or without the use of phosphodiesterase type 5 inhibitors (PDE5i), and reasonable penile length, the deformity should be corrected using a "plication type" procedure which may or may not involve excision of the tunica albuginea. These procedures achieve straightening by shortening the longer, unaffected side of the penis. These techniques are always associated with a degree of penile short-

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ening, which is directly related to the degree of the curvature correction. As a practical rule, patients are expected to lose 1 cm for each 20–30° of curvature corrected. However, indentations and penile shaft narrowing, or waist deformity, cannot be addressed with "plication type" procedures as it may result in the development of a hinge deformity which causes penile instability.

More challenging is the correction of the deformity in patients with significant (>60°) or complex curvatures combined with a waist or 'hourglass' deformities, and/or significant penile length loss. In this group of patients it is vital to assess the quality of the erectile function preoperatively in order to decide the most appropriate treatment option. Patients with good quality erections are better served with 'lengthening' procedures, which involve performing a relaxing incision in the tunica albuginea on the concave aspect of the penile shaft at the level of maximum curvature and repairing the tunical defect with a graft. Only patients with good erections should be offered this plaque incision and grafting, procedure as it is associated with a postoperative worsening of the quality of erections in around 20–25 % of cases [3]. Patients with a degree of erectile dysfunction (ED) are therefore not ideal candidates for this procedure and should be considered for penile prosthesis implantation. All patients with PD and refractory ED should be offered a penile prosthesis regardless of the degree of curvature. Often, prosthesis placement alone is sufficient to correct the penile curvature, but additional modeling procedures or plaque incision and grafting procedures may also be performed simultaneously. In cases of significant penile length loss, simultaneous lengthening procedures, such as the 'sliding technique' with its dual grafts, or circumferential grafting, may also be required.

Introduction to Grafting Materials

The ideal grafting material should be readily available and inexpensive, resistant to contraction and infection, reliably incorporate into the tissue, and preserve erectile capacity [1, 2]. Unfortunately this ideal material has yet to be identified, but tissue engineering technologies offer optimism for the future. Historically, Horton and Devine were the first authors to describe the use of grafting in the correction of penile curvature using primarily dermal grafts. Whilst a number of tissues have been used in the decades since, autografts such as tunica vaginalis, temporalis fascia, saphenous vein, dermis and buccal mucosa have little contemporary use in penile reconstruction as they are associated with donor site morbidity as well as added operative and recovery time [3]. Many synthetic materials have been considered as well but are found to have prohibitively high infection rates and are thus not used [4].

The modern generation of grafts are 'off-the-shelf' processed allografts from human cadaveric tissue or highly processed xenografts. These tissues, all representing an extracellular matrix from a variety of sources, have many potential applications in reconstructive surgery [4]. Their processing is such that they are entirely acellular and have all antigens removed to prevent any adverse immune response from the host [5]. This processing removes all the bacteria, viruses, and prions such that there have been no known infections transmitted to patients as a result of allograft or xenograft implantation [3].

Among the extracellular matrix grafts, human or bovine pericardium, porcine Small Intestine Submucosa (SIS), and human or porcine dermis are the most commonly used. These grafts integrate readily into the penile tissues acting like a scaffold allowing the influx of growth factors and extracellular components that produce an orderly healing process [6]. Because of this integration and ingrowth they produce a tissue with excellent tensile strength, which is critical to successful use in the reconstruction of the penis.

Practically there are very few differences amongst the various grafting materials. One relevant difference is that the pericardial graft does not contract, while SIS is known to contract in size by up to 25 % [7]. Published reports show that outcomes are very similar between the most popular materials used. In the largest studies reported to date, Knoll described the use of SIS in grafting for Peyronie's Disease and found that

91 % of patients had correction of the curvature whilst 21 % reported Erectile Dysfunction (ED), and none had diminished glans sensation [8]. A similarly sized study by Taylor and Levine reported on the use of pericardial grafts and found 92 % penile straightening and 35 % post-operative ED, with 31 % reporting a change in glans sensation [9]. Lue detailed his case series with venous grafting and showed 96 % straightening, 12 % post-operative ED, and 10 % diminished sensation. Numerous additional series exist; however, with regards to functional outcomes it is clear that the choice of grafting material is secondary to patient related factors.

One unique allograft option is Tachosil®, an off-the-shelf absorbable sealant patch for topical application, originally developed for cardiac surgery. It consists of equine collagen coated with fibrin glue, human fibrinogen and human thrombin, and has been adapted to a wide range of surgical procedures. In 2002 Lahme reported the outcome of patients with PD who had undergone plaque incision and grafting with Tachosil® [11]. The main advantage of this graft is that it has hemostatic and adherent properties such that it does not require suturing to the tunica albuginea and relies only on Buck's fascia closing over it for additional support. However, while this represents a novel approach to grafting, larger series of patients are required to test the reliability of this material [12].

Plaque Incision and Grafting Procedures

Plaque incision and grafting procedures are ideal for men with complex/severe curvature (>60°), waist deformity or a destabilizing hinge effect secondary to PD, and preserved erectile function [3]. Whilst patient history is often relied upon to obtain information regarding pre-operative erectile function, the use of Doppler ultrasound can be informative, with a Resistive Index >0.80 or a peak systolic flow >30 cm/s demonstrating sufficient erectile function for grafting procedures [13]. Patients with any degree of erectile dysfunction should be discouraged from undergoing this procedure, as the quality of their erection is likely to deteriorate postoperatively.

The procedure itself is carried out after the penis has been degloved using a sub-coronal incision. An artificial erection using saline identifies the point of maximum curvature. Once the site is identified, Buck's fascia is elevated together with the neurovascular bundle in order to expose the tunica albuginea. This can be performed from the midline and extended laterally after excising the deep dorsal vein or alternatively through two paraurethral incisions and elevating the Bucks fascia towards the midline. Once the tunica is exposed, a relaxing double-Y-incision is made transversely through the tunica at the point of maximum curvature. The graft is then sized with the defect on stretch and secured to the tunica albuginea using 4/0 absorbable polydiaxonone sutures. The Buck's fascia should be repositioned and closed, and finally the Dartos and skin reapproximated. Finally, a secure dressing is necessary to prevent hematoma formation under the graft, which could potentially lead to graft contracture and recurrence of the curvature. This can be accomplished by applying an elastic compression bandage around the penile shaft, with care taken to avoid significant compression, which could cause glans ischemia. This dressing can be left in place for up to 1 week to minimize post-operative hematoma formation (Fig. 17.1a–g – Incision and grafting steps).

After surgery, post-operative rehabilitation is recommended to minimize graft contraction, recurrence of the curvature and also penile shortening. Patients are encouraged to start manual massage and stretch therapy approximately 2 weeks postoperatively, once the incision has sufficiently healed. This is performed by grasping the glans penis and pulling it gently and repeatedly away from the body while also gently massaging the graft area. Ideally, this should be performed twice a day for 4 weeks. Phosphodiesterase inhibitors are also recommended to both enhance nocturnal erections and increase the overall blood flow to the surgical site, to improve healing, and to stretch the graft. PDE5i should be started 14 days after surgery and continued for at least 6 weeks [14]. Finally,

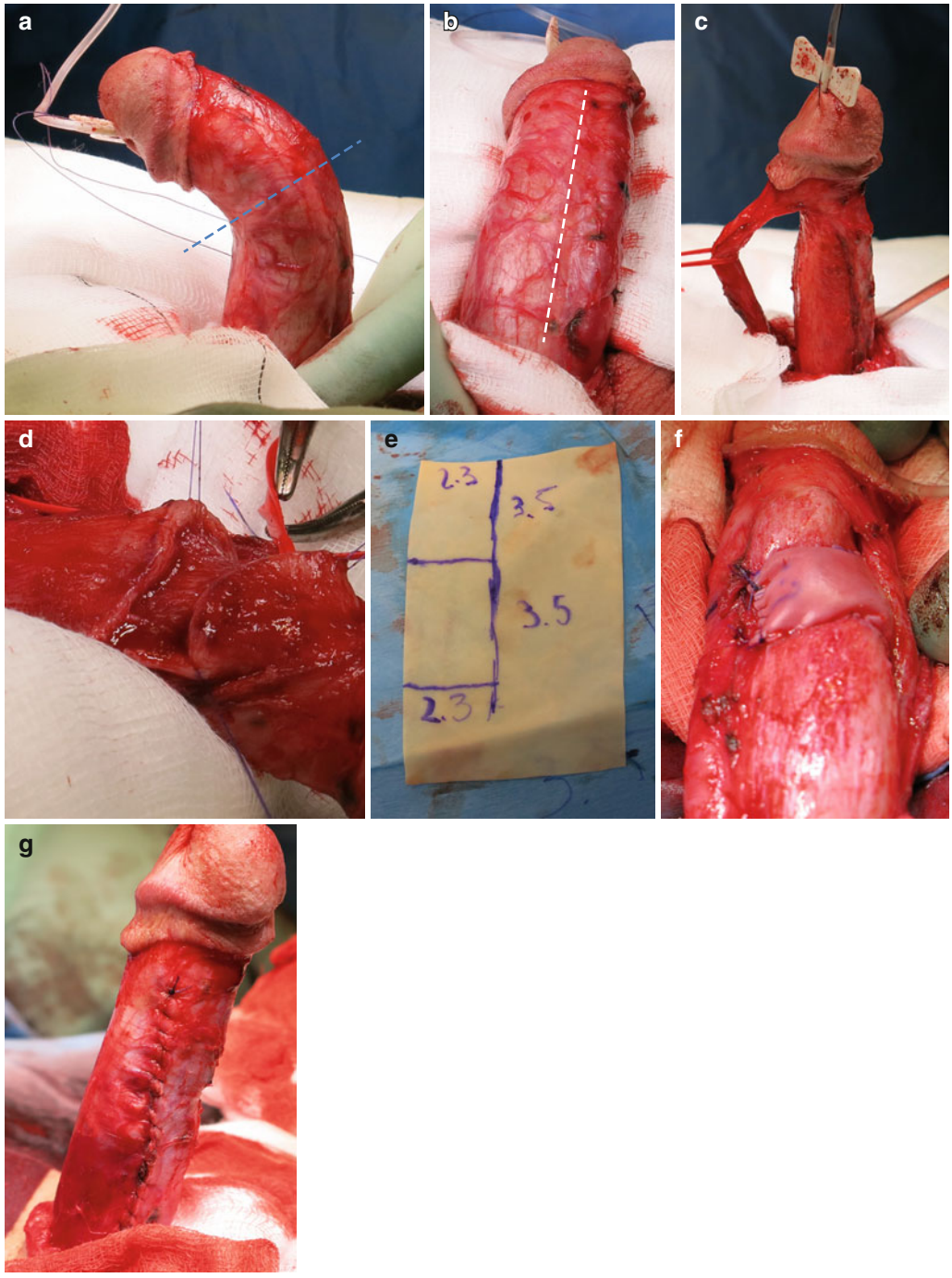

Fig. 17.1 Penile curvature secondary to Peyronie's disease. (**a**) Note the line marking the point of maximal curvature. (**b**) Degloved penis. Buck's fascia remains intact, note the suggested line for incision and reflection of Buck's fascia off of the tunica albuginea. (**c**) Buck's fascia elevated circumferentially. Note that all neurovascular structures are contained within Buck's fascia and should be dissected free leaving only the smooth homogenous surface of the Tunica Albuginea. (**d**) Tunical defect after relaxing incision. (**e**) Pericardial graft measured to fill defect. (**f**) Graft in place. The graft should be sewn into place using a running suture with care to create a water-tight closure in order to prevent post-operative hematoma and promote healing. (**g**) Final result. Note that Buck's fascia has been closed using running 4-0 absorbable suture bilaterally (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Table 17.1 Grafting outcomes

Author	N	Procedure type	% straight	% ED	% diminished sensation	Follow-up, mo	Year
Knoll [8]	162	Incision + SIS graft	91	21	0	38	2007
Sansalone et al. [25]	157	Pericardial graft	88	0	3	20	2011
Lue and El-Sakka [10]	112	Incision + venous graft	96	12	10	18	1998
Taylor et al. [9]	101	Pericardial graft	92	35	31	58	2008
Gelbard [26]	69	Incision + temporalis graft	74	14	n/a	n/a	1996
Hsu et al. [27]	48	Incision + venous graft	90	5	n/a	n/a	2007
Horstmann et al. [12]	43	Tachosil	84	21	58	59	2011
Levine et al. [28]	40	Pericardial graft	98	30	n/a	22	2003
Egydio et al. [29]	33	Incision + pericardium graft	87.9	n/a	n/a	19	2002
Breyer et al. [30]	19	SIS graft	63	53	n/a	15	2007
Hatzichristou et al. [31]	17	Tunica albuginea	100	0	n/a	39	2002
Cormio et al. [32]	15	Buccal graft	100	0	n/a	13	2009

the use of external penile traction therapy has been suggested to reduce postoperative penile shortening in patients who have undergone grafting procedures. If patients initiate this therapy, traction should be started 2–3 weeks postoperatively and performed on a daily basis using the traction device for a minimum of 2 h for 3 months [15]. As previously discussed, important post-operative outcomes include erectile function, penile straightening, postoperative penile length, and sensory deficits. Overall, compiling the largest series in the literature, 74–100 % of patients reported adequate penile straightening, and post-operative ED ranged between 5 and 53 %3. Length loss is reported in 35–100 %, and significant sensory changes are rare (Table 17.1).

Grafting with Prosthesis Placement

The technique of grafting simultaneously with penile prosthesis placement is uncommon, but can be the treatment of choice for patients with severe PD or corporal fibrosis and concomitant end-stage erectile dysfunction. Intraoperatively, residual curvature should be assessed after placement of the prosthesis. Often, device placement alone is sufficient to straighten the penis, likely due to fracture and release of the tethering corporal tissue during the dissection process [16]. However, studies using modern devices have established that between 19 and 42 % of patients will require additional maneuvers for straightening [17–19]. The standard for initial intraoperative treatment of residual dorsal and/or lateral curvature has become the modeling maneuver as initially described by Wilson and Delk [17]. As described elsewhere in this text, this process forcibly ruptures the plaque using the torque generated by the inflated cylinders. This can be repeated twice if residual curvature remains, and is effective in correcting curvature in up to 90 % of cases [15]. Importantly, this success rate is higher for three-piece inflatable devices when compared with two pieces inflatable and malleable prostheses [15]. In the 10 % of cases when the modeling procedure is not sufficient to correct the curvature, or in cases of ventral curvature where modeling should be avoided because of the risk of urethral injury, a number of strategies, including grafting, have been employed. Initially, one or multiple transverse relaxing incisions can be made at the apex of the concave side of the curvature. Grafting is not necessary if incisions

are small, as aneurysm of the cylinder through the defect is uncommon if the defect is less than 2 cm long [20]. In cases where this does not correct the curvature to a functional degree, the incision should be extended and grafting must be considered. In these cases grafting should be performed as previously described using extracellular matrix products, or autologous grafts, as these have shown to have no significant increase in infection rate as had previously been noted with synthetic materials [21] (Fig. 17.2a, b).

In patients with severe shortening as a result of PD, or fibrosis resulting from explantation of an infected penile implant or ischemic priapism, lengthening procedures using a circular graft or the 'sliding technique' with the use of two grafts, may be required to restore some of the penile length previously lost, in addition to the correction of ED and PD. These procedures should only be considered in patients with end-stage disease who have significant dissatisfaction with the shortening of the penis, and who understand the risks associated with the procedure. Circular grafts, which involve the subtotal disassembly of the penis followed by a circumferential incision of the tunica and septum at the point of maximal curvature have been described. The penis is placed on stretch and the longitudinal defect measured. An appropriate sized graft is then sewn in circumferentially. The authors have found that elongation was limited only by the stretch of the neurovascular bundle, which is less elastic than the spongiosum of the urethra. An inflatable penile prosthesis was then placed in the standard fashion through proximal corporotomies and left partially inflated for 2 weeks to establish the new restored length of the penis. No intra-operative or major post-operative complications were noted in their series of 23 patients and importantly the average length gain was 2.3 cm and overall patient satisfaction was 90% [22] (Fig. 17.3a).

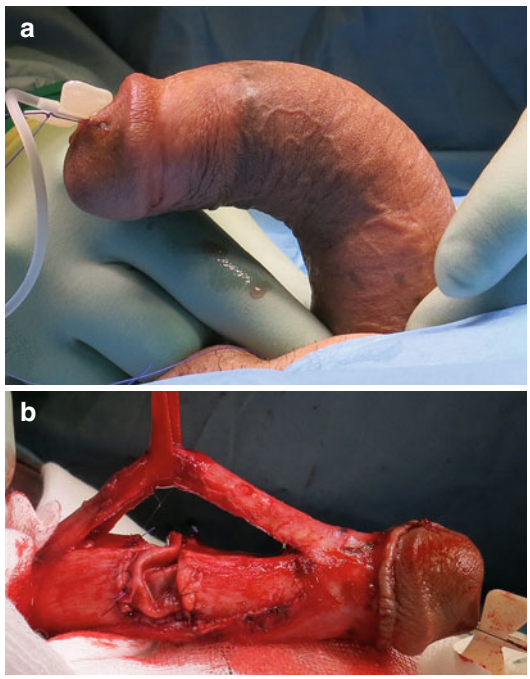

Fig. 17.2 (**a**) Ventral curvature in a patient with severe ED requiring penile implant. (**b**) Ventral pericardial patch in place. Note the urethra completely mobilized for placement of the patch prior to placement of penile prosthesis through standard penoscrotal approach (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

The sliding technique was developed to address concerns of increased axial traction on the neurovascular bundle at the time of circular grafting, which could potentially lead to neuropraxia. In the largest study to date, Rolle and Falcone reported on 28 patients who underwent the sliding technique. This procedure uses offset semi-circular incisions dorsally and ventrally through the tunica albuginea with longitudinal incisions along both sides of the tunica such that the distal portion of the penis can advance forward when placed on stretch and provide additional length. Two grafts are used, one dorsal and one ventral, to fill the gaps created by the advancement of the distal aspect of the penis (Fig. 17.3b). In their multicenter study a combination of SIS, dermis and Tachosil® were used for grafting. Again, the limiting factor was found to be the elasticity of the neurovascular bundle [23]. The average pre-operative stretched penile length was 8.2 cm and the average length gained through the technique was 3.2 cm. Complications included infection of the prosthesis in 2 patients (7%). Temporary glans hypoaesthesia was noted in 50% of cases but only 1 patient (4%) noted permanent sensory change. All patients showed

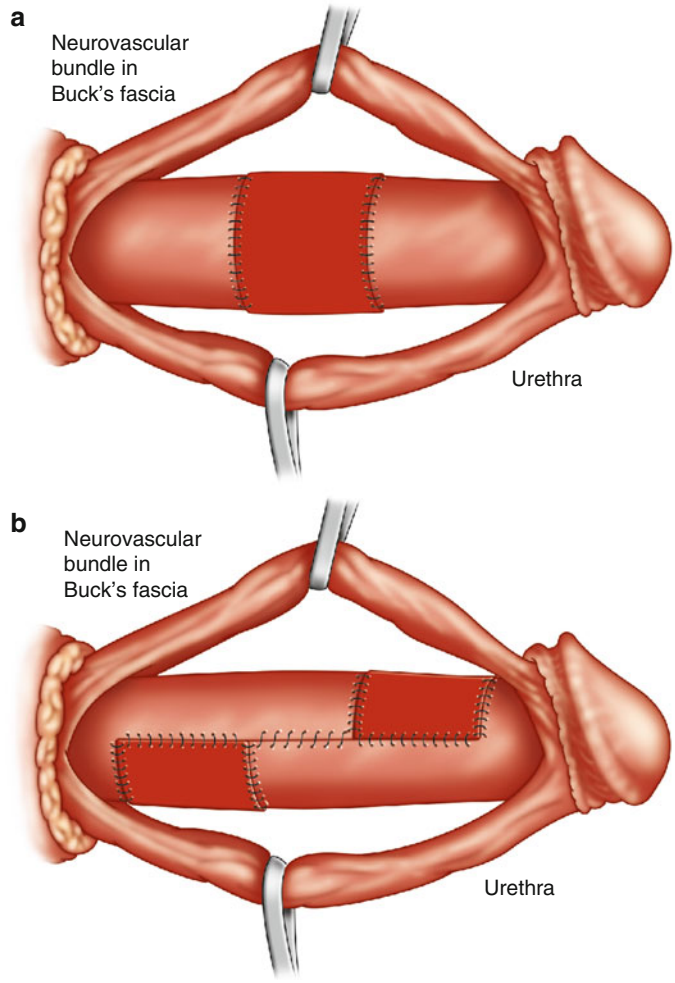

Fig. 17.3 (**a**) Circular graft. The penile prosthesis should be placed through separate corporotomy incisions in the standard location, either via the base of the penile exposure, or through a second penoscrotal incision. (**b**) Sliding technique. The penile prosthesis can be placed through the ventral graft site prior to complete closure of the site (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

improvement on post-operative validated questionnaires and 95 % were satisfied with the length gained [24]. These procedures require significant technical skill in the disassembly and reconstruction of the penis, and while they should continue to be performed only by experts in this area, they offer great hope for men who have lost significant penile length in the course of their disease.

Conclusion

Complex penile reconstruction represents one of the most challenging areas of surgical Andrology. With appropriate patient selection and meticulous technique, excellent surgical outcomes and patient satisfaction can be achieved.

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Penile Prosthesis Surgery

18

Joshua P. Langston, Asif Muneer, and David Ralph

Abstract

Penile prosthesis implantation represents the ultimate option for treatment of end-stage erectile dysfunction (ED). Originally developed in the 1970's, and refined in the following decades, it provides a durable and safe solution for men who have tried and exhausted all medical treatment options. Although the early versions of the penile prostheses were plagued with high mechanical failure and infection rates, the modern prostheses have a much higher mechanical reliability and are associated with low infection rates, translating into a high patient and partner satisfaction rate.

Keywords

Erectile dysfunction • Penile prosthesis

Patient Assessment and Counseling

Patients considered for penile prosthesis implantation should have a thorough physical and psychological assessment to ensure that it is the appropriate option for them and that they understand the aims of surgery. While implant surgery is quite effective at achieving functional goals, patients need to undergo adequate counseling and training prior to undergoing surgery. Penile prosthesis implantation usually represents the final step of a long diagnostic and therapeutic pathway. In addition to identifying and treating erectile dysfunction (ED) according to the etiology, patients should also be offered all of the available pharmacotherapies tailored according to the pre-existing medical conditions and patient preference.

Medical management usually follows a treatment algorithm, which is based on 1st line treatment using phosphodiestherase type 5 (PDE-5) inhibitors, while injectable or topical vasoactive drugs, such as alprostadil, and vacuum erection devices represent second line treatment when PDE-5 inhibitors have failed or are contraindicated.

When penile prosthesis implantation is indicated specific considerations in the medical and

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surgical history will often determine the best type of penile prosthesis for the patient. In particular, apart from the patient's preference, history of pelvic surgery, manual dexterity, systemic diseases such as diabetes mellitus and immunosuppression, and penile conditions such as Peyronie's disease, acute or chronic priapism must also be taken into careful consideration when choosing the most suitable penile prosthesis.

It is important to review the various device options with the patient and give him enough time to process all of the information and make his own decision. It is also critical to involve the partner, if possible. Patients should be shown samples of the various devices in order to allow them to appreciate the texture of the cylinders and familiarize themselves with the shape of the pump and the technique of cycling the device.

Adequate preoperative counseling and management of patient's expectations play a very important role in determining postoperative satisfaction rates. Modern patients have access to an overwhelming amount of information on the Internet, which can often be misleading and produce unrealistic expectations. Patients need to be fully aware that the goal of penile prosthesis surgery is to obtain a penis straight and firm enough for penetrative sexual intercourse with preservation of sensation and orgasmic and ejaculatory function. It should be clear that penile prosthesis implantation will not restore the penile length loss due to Peyronie's disease, cavernosal fibrosis or long-standing ED.

Penile Prosthesis Options

Coloplast Corporation and American Medical Systems produce the most popular and widely used penile prostheses. Coloplast currently markets the three-piece inflatable penile prosthesis Titan Touch™ and its narrow base version to allow for an easy implantation in fibrotic and narrow corpora (Fig. 18.1). The device offers hydrophilic coating on all of the components to allow the surgeons to coat the device in their preferred antibiotic regimen at the time of surgery. Their Cloverleaf™ reservoir has a lockout mechanism to prevent auto-inflation, and has been approved by the FDA for ectopic reservoir placement.

Fig. 18.1 Coloplast Titan Touch three-piece prosthesis with Cloverleaf reservoir (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Similarly, AMS produces their three-piece inflatable device, CX700™, as well as a CXR™ narrow cylinder option. They also offer the LGX™ cylinder option, which is the only cylinder that expands in both length and width upon inflation. AMS offers a standard reservoir which is 65 ml or 100 ml as well as the Conceal reservoir, which is a low-profile design approved for ectopic use (Fig. 18.2). AMS devices are precoated with Inhibizone™, which is a highly effective antibiotic combination of Rifampin and Minocycline. AMS also offers the only two-piece inflatable prosthesis on the market, the AMS Ambicor™, which functions without a separate reservoir and is often preferred for patients with a history of pelvic surgery or previous complex abdominal surgery where retropubic or intraabdominal reservoir placement is to be avoided. Both companies also offer a malleable prosthesis option which should be considered in patients with limited manual dexterity or who need prosthesis placement for penile exposure or reasons different from sexual intercourse. Alternatively some men prefer the simpler option rather than the three piece device. The Coloplast Genesis™ is hydrophilic coated for antibiotic adherence in the same manner as the three-piece devices, however the AMS Spectra™ does not have Inhibizone™ or any other antibiotic coating.

Design Considerations

Despite the numerous advances in three-piece prosthetics over time, the fundamental design has remained the same. Two inflatable penile cylinders are connected to a scrotal pump via silicone tubing, which in turn manages inflation and deflation using saline stored in a retroperitoneal reservoir. The cylinder components are specifically engineered to provide durable and reliable results whilst remaining malleable enough to provide a natural appearance and feel to the penis in the flaccid state. The AMS cylinder design, for example, involves a multi-layer approach incorporating Parylene™ polymer to coat the silicone layers and thereby reduce friction and silicone wear. This modification alone has been shown to greatly improve the longevity and function of the AMS device [1] (Fig. 18.3). The AMS 700 series offers both the girth expanding CX model as well as the length and girth expanding LGX model. To accomplish this, the Dacron-Lycra™ fabric cylinder of the CX model is woven unidirectionally while the LGX has a bidirectional weave to permit the additional length expansion. This allows the LGX device to expand 20 %, or 1–4 cm, upon inflation. Coloplast uses a proprietary "Bioflex" polyurethane for its cylinders which provides greater tensile strength, rigidity and tear resistance compared to silicone and thus provides a more rigid erect device which is felt by many to be more suitable for Peyronie's disease patients.

Fig. 18.2 AMS 700 series three-piece prosthesis with Conceal reservoir (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Other important technical differences exist between the two devices as well. The recent Coloplast Zero-degree™ input tubing modification has the tubing come out of the base flush with the cylinder. Given the stiffness of the hub, the tubing is not flexible enough to exit the corporotomy and make the 180° bend toward the scrotal pump until about 6–7 cm. Conversely, the AMS system tubing comes off at a 45° angle and is flexible enough to make the bend to the pump by about 4 cm (Fig. 18.4). This is crucial as you

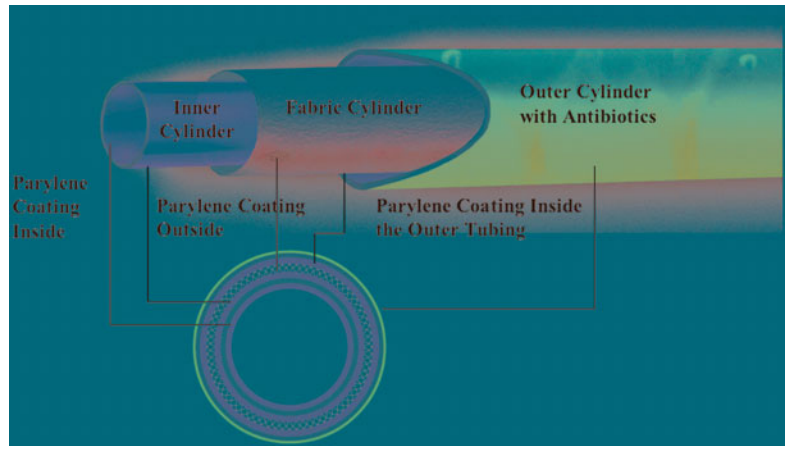

Fig. 18.3 AMS cylinder layered design (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

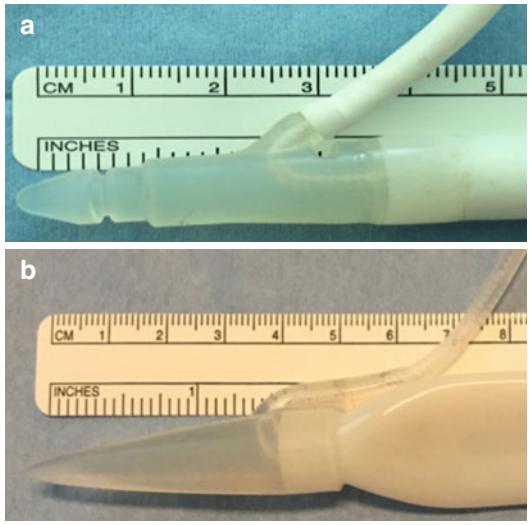

Fig. 18.4 (**a**) AMS cylinder hub. Note that the tubing exits at 3 cm and is flexible enough to make the turn down to the scrotal pump by 4 cm. (**b**) Coloplast Zero-degree cylinder hub. Note that the tubing exits at 4 cm and is flexible enough to make the turn down to the scrotal pump by 7 cm (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

size the implant and consider cylinder and rear-tip extender lengths. Importantly, rear-tip extender length must be added to the above measures to determine where the tubing will exit the corporotomy. The Coloplast devices are offered with cylinders ranging from 14 to 28 cm, in 2-cm increments, with 1.0, 2.0, and 3.0 cm rear-tip extenders. The AMS 700 series products come with cylinders ranging from 12 to 21 cm, in 3-cm increments, with a range of rear-tip extenders up to 6 cm. A 24 cm cylinder is available on special order. Pump features have also been continually refined for the two devices and it is important to note differences in size and release button position and prominence that patients should consider when selecting a device (Fig. 18.5a, b).

Patient Satisfaction and Modern Outcomes

Historical and modern overall satisfaction with penile prostheses is generally around 90% [2–4]. However, when subdividing patents in groups according to the etiology of their ED, there is a significant difference in terms of satisfaction rates amongst different groups. In particular, Menard et al. showed that, amongst implant patients, post-prostatectomy patients had lower pre-operative and post-operative IIEF scores. There was a significant difference between the groups, despite the expected improvement in erectile function in all groups, based largely on orgasmic function [5]. Mulhall's group has also shown that radical prostatectomy is predictive of lower overall patient satisfaction after prosthesis placement. In addition, his study showed Peyronie's Disease and BMI >30 to be factors predictive of lower satisfaction [6].

The currently available prosthesis models have undergone numerous design enhancements over the years in order to maximize success. Recent long-term data shows that the need for revision surgery for any reason is as low as 7% in modern devices [7]. Historically, functional longevity remains over 60% at 15 years [8]. Antibiotic coating for the devices has perhaps been the most significant improvement in design. American Medical Systems (AMS) introduced Inhibizone™ (Rifampin/Minocycline) coating for their prosthesis in 2001 and Coloplast introduced their hydrophilic coating, to allow for individual surgeon selection of antibiotic coating, around the same time. The results have been a greater than 50% decrease in infection rates for penile prostheses [9, 10]. In addition, certain subgroups have been shown to benefit significantly from antibiotic impregnation. A focused review by Mulcahy and Carson showed that diabetic patients were the group that benefitted most from the advent of coated prostheses with a drop in infection rate from 4.2 to 1.6% [11]. Patients undergoing revision implant surgery also benefitted from antibiotic impregnation, with significantly lower rates of device infection after revision surgery in this otherwise high-risk group [12].

Surgical Procedure (Peno-Scrotal Approach)

Surgical approaches for the implantation of inflatable penile prostheses include the infrapubic and peno-scrotal approach, whilst malleable prostheses can also be placed through a subcoronal or ventral penile shaft incision. Every access

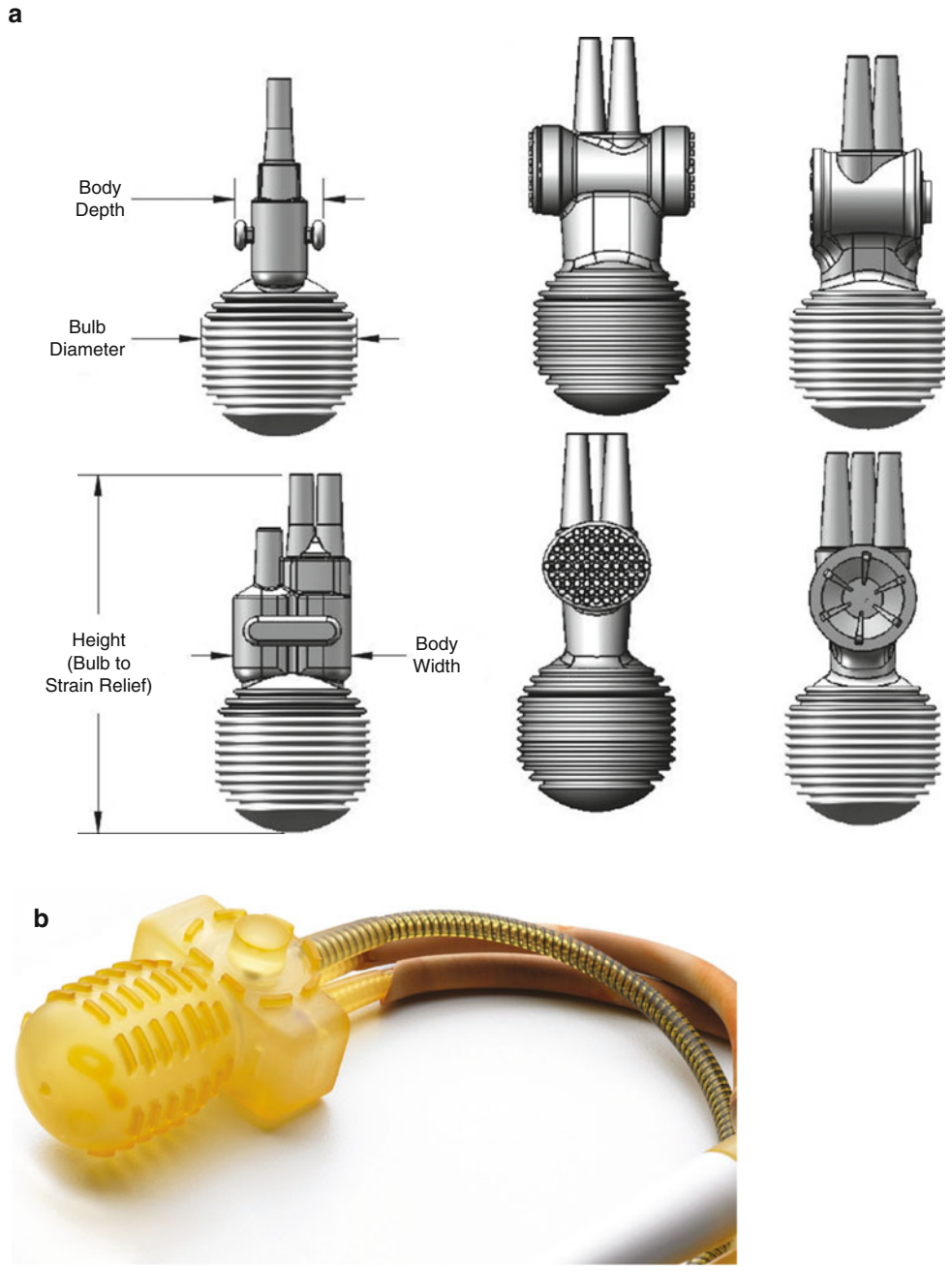

Fig. 18.5 (**a**) Coloplast Titan pump design. Note differences in size and release button prominence. (**b**) AMS 700 pump. Note the prominent release button and palpable ridges on the pump chamber (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

has its own advantages and drawbacks, although the majority of high-volume surgeons prefer the penoscrotal approach. This technique eliminates potential injury to the dorsal sensory nerves of the penis and allows for ease of placement of the pump in the scrotum and reservoir in the retropubic space. It also guarantees a good exposure of the crura, to allow for dilatation under direct vision – especially in the cases of corporal fibrosis as well as visualizing the distal bulbar urethra, if simultaneous placement of an Artificial Urinary Sphincter is contemplated.

The choice of pre-operative prophylactic intravenous antibiotics varies amongst surgeons. The only published guidelines regarding antibiotic prophylaxis are from the American Urological Association (AUA), which recommends Vancomycin or a first- or second-generation Cephalosporin in combination with an Aminoglycoside [13].

Patient Preparation

Prevention of prosthesis infection is a major concern during implantation of foreign material into the body. Studies have shown that early prosthetic infections are the result of bacterial entry and adherence at the time of surgery and are most commonly composed of skin flora [14]. Povidone-iodine based scrub has been a mainstay surgical site preparation, though more recently Chlorhexidine-alcohol based scrub has become more popular and has shown lower post-preparation positive skin cultures [15]. Also now widely published is the "No-Touch technique" which utilizes additional surgical draping to eliminate device contact with the skin and has decreased infection rates to 0.46 % in expert hands [16, 17]. A 10-min povidone-iodine scrub followed by chlorhexadine-alcohol prep and finally a 70 % alcohol paint is recommended to minimize infection rates (Fig. 18.6).

Instrumentation

While a minor surgical set is generally sufficient for the scope of the procedure, there are several specific instruments and tools that are essential in order to ensure successful placement of the prosthesis. Brooks and/or Hegar corporal dilators are necessary to dilate the corpora for cylinder insertion. The Furlow inserter is also an essential tool for measuring the size of the cylinders required as well as inserting the tips of the inflatable cylinders (Fig. 18.7).

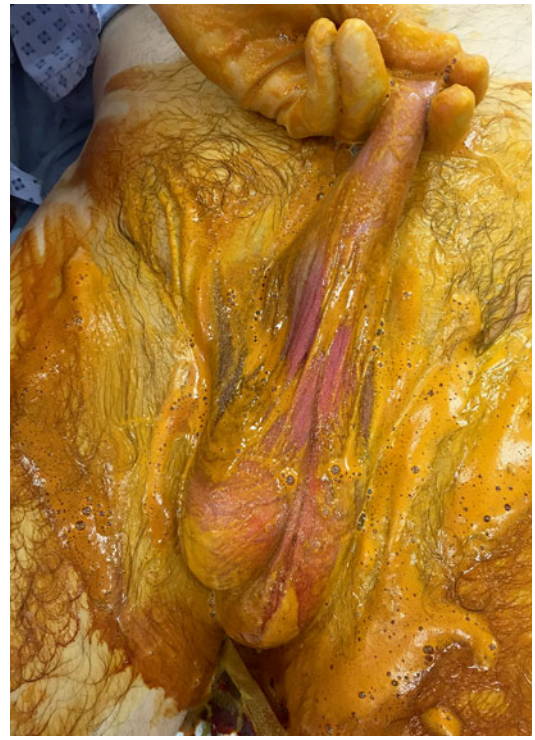

Fig. 18.6 10-min scrub. A 10-min povidone-iodine scrub prior to surgical preparation with chlorhexadine-alcohol solution (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Intraoperative Device Preparation

Both AMS and Coloplast three pieces inflatable devices will require preparation prior to implantation. This is generally performed on a second prep table to separate this process from possible contamination. Importantly, for Coloplast devices a solution of antibiotics will need to be prepared and the device should be placed immediately in this solution prior to handling (Fig. 18.8). A Rifampin/Gentamicin combination

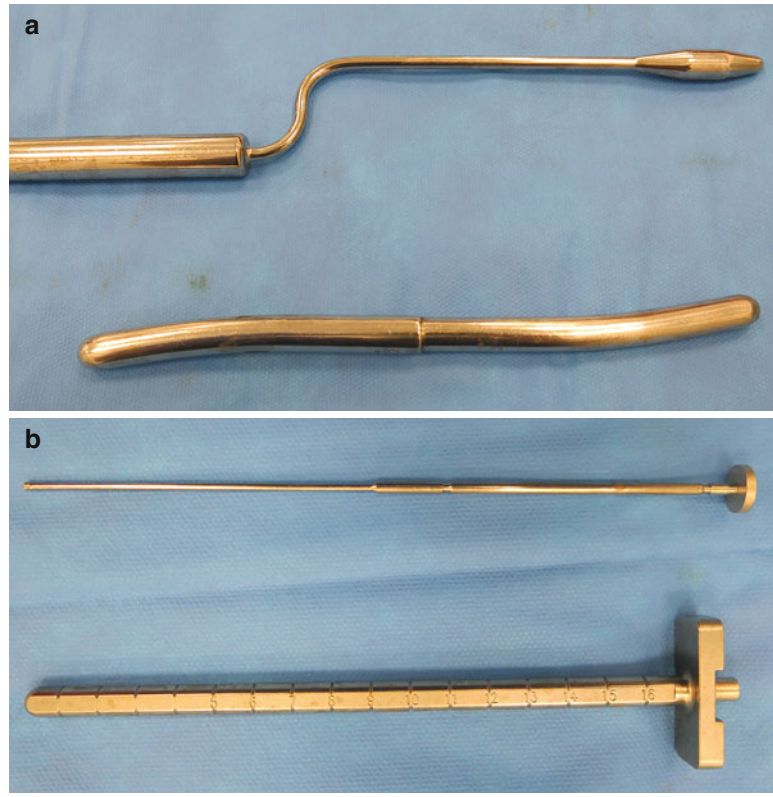

Fig. 18.7 (**a**) Brooks (*top*) and Hegar (*bottom*) corporal dilators. On a standard prosthesis instrument set Brooks dilators should be available sequentially from 8 to 14 mm. Hegar dilators are often available sequentially from smaller sizes, approximately 5 to 14 mm, though they are also available to much larger sizes. (**b**) Furlow Inserter. The Furlow inserter is critical for sizing and placement of the prosthesis (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

or Trimethoprim/Sulfamethoxazole combination have been shown to be highly effective [16]. As the AMS devices are already impregnated with Inhibizone additional soaking is avoided so that the antibiotic impregnation is not washed off. All of the air within the device should be carefully expelled from the system for both the cylinder/pump circuit as well as the reservoir, utilizing saline as the flushing fluid, and shodded-clamps placed on all tubing to prevent air egress.

Surgical Procedure

A standard-sized 14Fr Foley catheter is placed using an antibiotic soaked swab to hold the penis, thereby preventing contact with the meatus or excess lubricant, which could be contaminated by the colonized fossa navicularis. The swab should be discarded once the catheter is placed and the surgical gloves can be exchanged at this point. The catheter can be spiggoted at this point or placed to drainage to ensure that the urinary tract is a closed system in order to prevent contamination. The aim of the catheter is to allow for easier identification of the urethra and to empty the bladder prior to insertion of the reservoir in the retropubic space.

When a penoscrotal approach is used, a transverse scrotal incision is made 1 cm below the penoscrotal junction (Fig. 18.9). Alternatively, if a large scrotal web is present a vertical elliptical incision can be made to excise this excess tissue and offer a wider exposure. This has the additional advantage of increasing the subjective shaft length post-operatively. Once the incision is made, a Scott or Lone-star retractor is helpful in maintaining the exposure. A traction suture through the glans penis can be used to maintain a good stretch on the penis, or alternatively the sharp hook retractor for the Scott ring can be placed into the urethral meatus (Fig. 18.10).

The Dartos layer should be carefully dissected with the goal of identifying the urethra and then

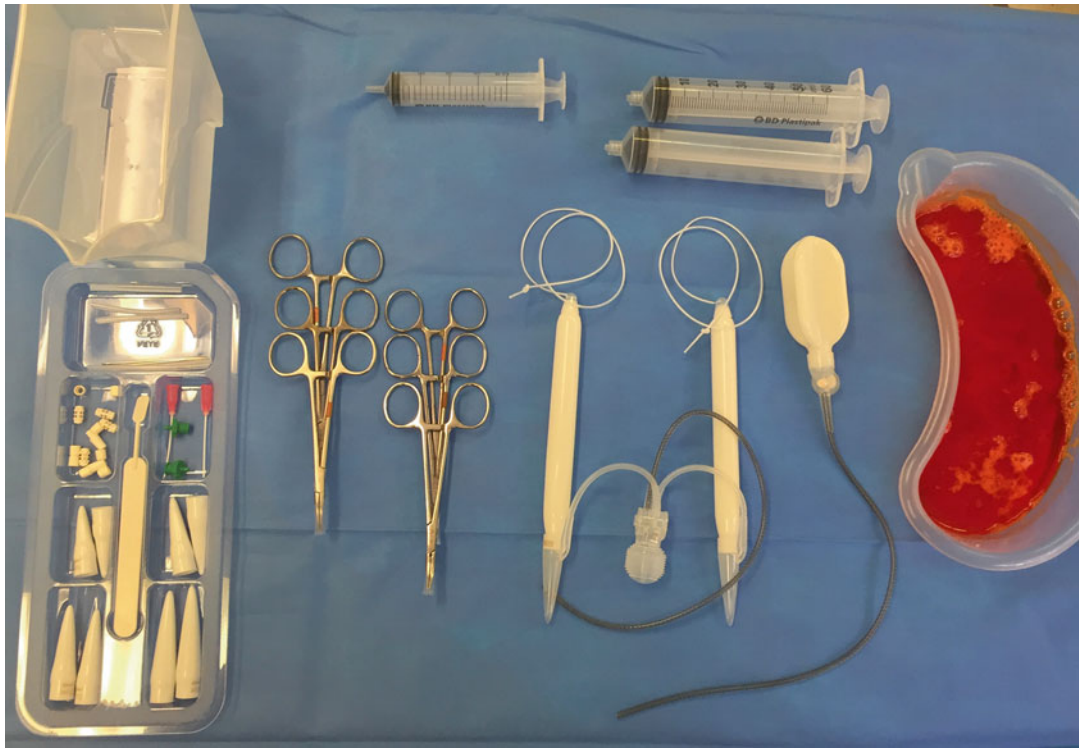

Fig. 18.8 Device preparation table. This demonstrates the set-up for the Coloplast Titan device. Note the antibiotic solution on the right for coating the implant (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

moving laterally to expose both corporal bodies. This can be achieved using a combination of electrocautery and Metzenbaum-type scissors. Once all of the structures are identified, corporotomy traction sutures should be placed parallel to the intended site of the corporotomy on either side. These will be used for the eventual closure of the corporotomy, so generally an absorbable suture with adequate tensile strength such as 0 polydiaxonone or PDS should be preferred (Fig. 18.11).

The corporotomy is made using cut-current cautery or a scalpel until spongy corporal tissue is clearly identified. Metzenbaum scissors can then be used to spread this tissue and develop the plane for corporal dilatation both proximally and distally. Importantly, the site of the corporotomy itself is not usually dilated by passage of dilators proximally and distally so in cases of a fibrotic corpora it is important to excise a small amount of tissue at this site to allow for a watertight closure of the corpora once the prosthesis cylinder has been placed.

Dilatation of the corpora should be undertaken carefully using either Brooks or Hegar-type dilators. Brook dilators have the advantage of being off-set, but they also provide less resistance during dilatation and therefore are more likely to cause perforation of the corpora compared to Hegar dilators. Whilst dilating distally, the surgeon should use one hand to identify the urethra, which is moved towards the contralateral corpora, while the dilatation should be carried out as laterally as possible in order to avoid inadvertent urethral injury or a cross over through the midline septum into the contralateral corpora (Fig. 18.12).

During proximal dilatation, it is important to remember the slightly lateral path of the corpora and carefully dilate until reaching the solid base of the corpora on the ischiopubic ramus. Generally, dilating to 12 mm is sufficient for standard cylinder placement. Once dilatation is complete, the

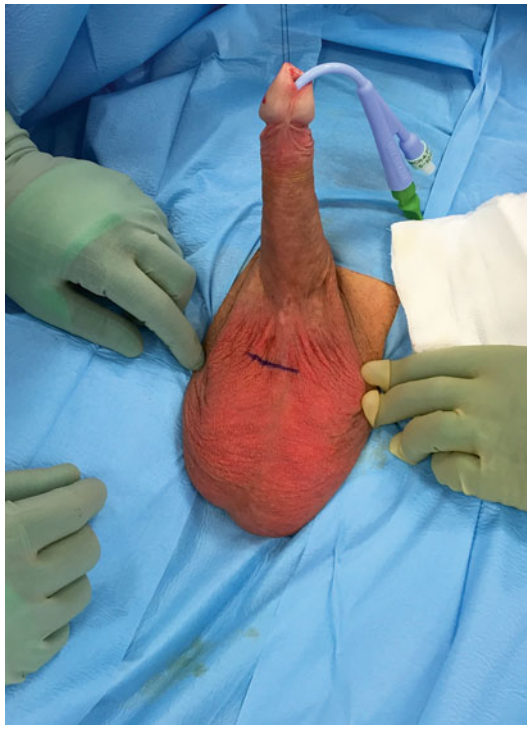

Fig. 18.9 Marked Incision and draping. A transverse scrotal incision is made one finger-breadth below the penoscrotal junction after placement of a Foley catheter and glans retraction stitch (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

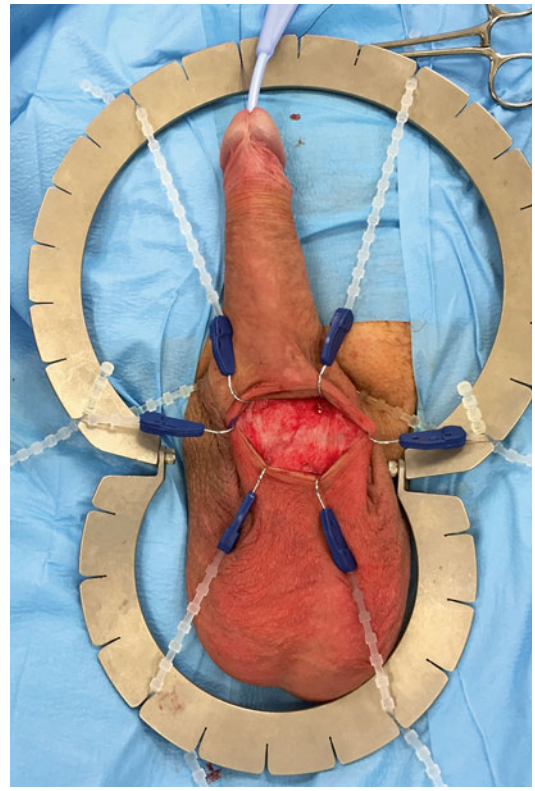

Fig. 18.10 Dartos dissection. After incision, a Scott or Lone-star retractor is very helpful in maintaining exposure. The Dartos should be carefully dissected with the goal of identifying the urethra and then moving laterally to expose the corporal bodies. This can be done using a combination of cautery and Metzenbaum-type scissors (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

dilators should be introduced simultaneously on both sides to test for a metal-on-metal sound indicative of a cross-over. The maneuver should be carried out both proximally and distally. Proximal passage of the dilators bilaterally is used to demonstrate that there is no proximal perforation (Fig. 18.13). Irrigation of the corpora with antibiotic solution should be carried out to minimize the chance of infection and to rule out inadvertent perforation of the urethra during distal dilatation. If there is a urethral injury then irrigant flows out through the meatus.

The corpora should be measured accurately both proximally and distally using a Furlow inserter. A clip may be used to mark the measurements at the edge of the corporotomy to ensure accuracy. Generally, the implant should be sized exactly to the measurement, without forcefully over extending the penis with the Furlow. It is usually best to maximize the cylinder size and not use an excessive length of rear-tip extenders. The devices are designed so that the exit tubing can run safely in the corpora alongside the cylinder, and care should be taken not to have excessive tubing in the scrotum that can be challenging to conceal.

A space should be made for the pump prior to the final cylinder placement in order to ensure that the tubing lengths are appropriate. Ideally the pump should sit in a sub-Dartos pouch in a dependent position in the scrotum between the two testicles in a location that is easily palpable for the patient (Fig. 18.14).

The cylinders are then placed into the corpora using the Furlow inserter and straight needle provided to guide the device distally. Once the

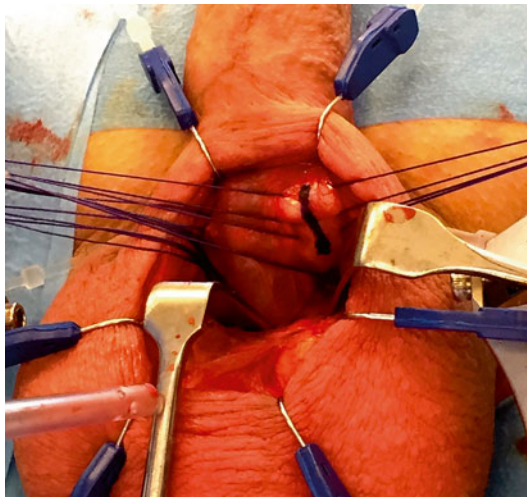

Fig. 18.11 Marked corporotomy position. Note that corporotomy traction sutures should be placed parallel to the intended site of the corporotomy on either side. These will be used for eventual closure of the corporotomy so generally a 0 Vicryl or PDS suture is preferred (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

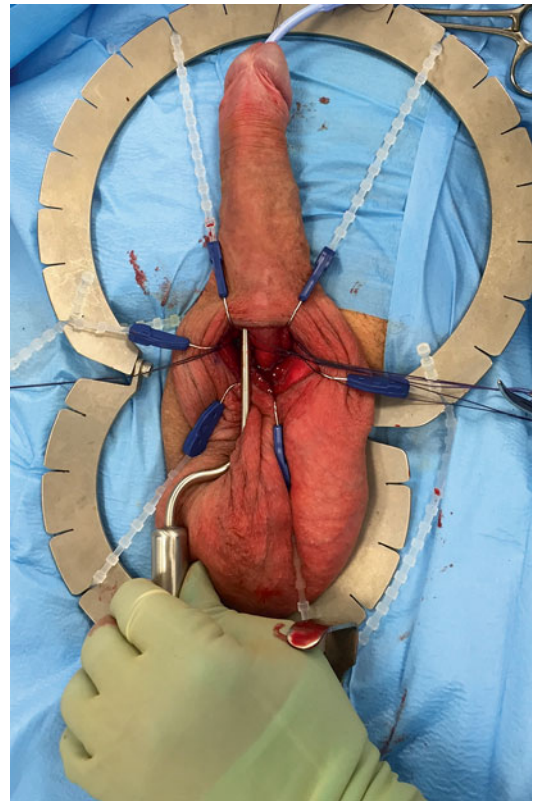

Fig. 18.12 Dilator in corpora. While dilating distally the surgeon should use one hand to identify the urethra and control passage of the dilator as laterally as possible in the corpora. When dilating proximally it is important to remember the lateral path of the corpora and carefully dilate until reaching the solid base of the corpora on the ischiopubic ramus. Generally, dilating to 12 mm is sufficient for standard cylinder placement (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

needle has been deployed through the glans it is often easiest to place the proximal portion of the cylinder first and then use the suture to pull the distal portion into position. Each device comes with a tool to help seat the device proximally, by pushing at the tubing hub. The Furlow inserter can be used for this as well. Once the cylinders are correctly placed in the corpora, the corporotomies are closed by accurately tying the stay sutures in a watertight fashion (Fig. 18.15).

Unless contraindicated by previous pelvic surgery, the reservoir is then placed in the retropubic space in a blind fashion though the external inguinal ring. The bladder has to be emptied first and the external inguinal ring should be identified on the selected side. Once the external ring has been identified, the fascia transversalis is punctured to enter the pre-vesical space of Retzius. A nasal speculum is then inserted through the puncture and should fall easily into the space without resistance to signify proper positioning (Fig. 18.16). The reservoir is then placed by spreading the nasal speculum and pushing the reservoir into the space using the Furlow inserter, or for the tougher Coloplast device a ring clamp can be used to grasp and insert the reservoir (Fig. 18.17). Once correctly placed, the reservoir should be filled completely and palpation of the lower abdomen performed to ensure that the reservoir is not palpable, which is usually indicative of incorrect positioning.

The system is then connected, using care to ensure that no air enters the circuit. The device should be inflated to ensure satisfactory positioning and to identify the presence of penile curvature or a droopy glans, which would have to be addressed intraoperatively. Many surgeons will leave the device at least partially inflated overnight to prevent corporal contraction and tamponade any bleeding.

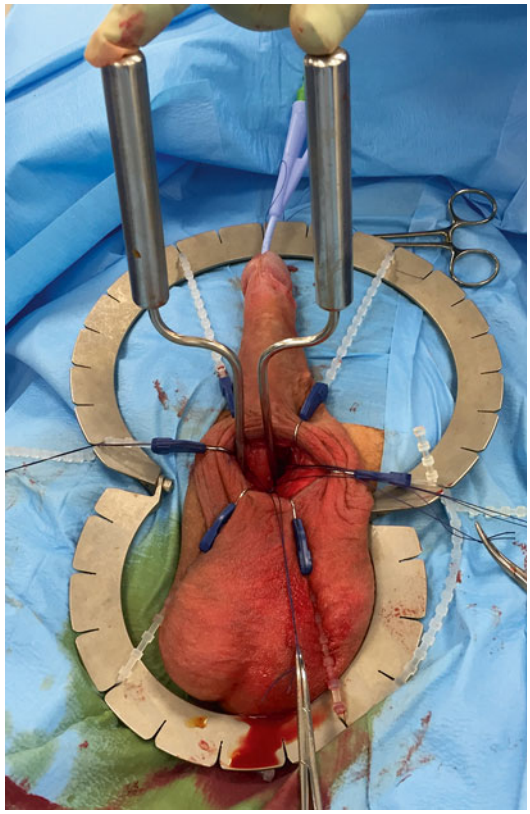

Fig. 18.13 "Goalposts" view of symmetrical Brooks dilators. After dilation ensure that there is bilateral symmetry of the dilators which proves there has not been proximal perforation and that you have not under-dilated (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

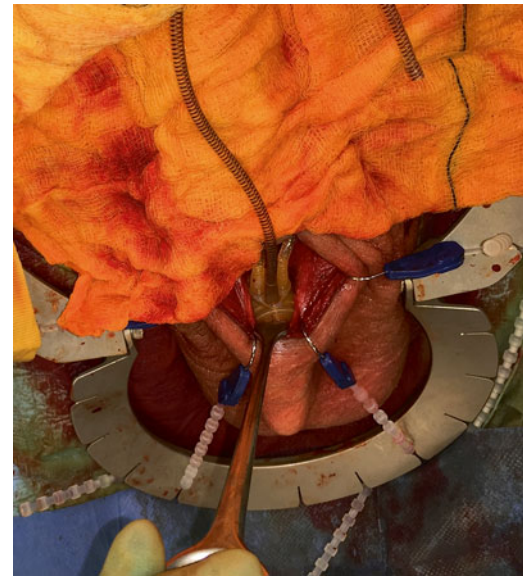

Fig. 18.14 Pump in position. Ideally the pump sits in a sub-Dartos pouch so that it is easily palpable for the patient. Incision and spreading of the Dartos with scissors can facilitate creating this space, which is ideally in the midline to avoid adherence of the pump to either testis (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

At this point hemostasis should be ensured and a decision made as to placement of a closed-suction drain. Available data shows no increased infection risk to doing this [18]. Closure of the surgical incision should be started by ensuring that the pump is anchored in its space with a purse-string suture to prevent the risk of migration into a position less accessible to the patient. The scrotum should be closed in multiple layers with absorbable suture with a focus on minimizing potential dead spaces for hematoma formation or fluid collection (Fig. 18.18). A compressive dressing such as the 'mummy wrap'™ should then be applied to the scrotum and penile shaft to minimize the risk of hematoma formation and to prevent the formation of edema. The dressing is usually left in place overnight and removed the following morning prior to discharge (Fig. 18.19). At the completion of the case it is important to document the details of the device placement, including both product device numbers as well as technique and indication details. Both device manufacturers include a form with the device that should always be returned to the company in order for this information to be on file as a future resource in case of revision, as well as contributing to available data for retrospective review (Fig. 18.20).

Post-operative Care

Patients are usually admitted overnight for monitoring and pain control. The following morning the dressing and urethral catheter are removed and the implant is deflated. In patients who have undergone previous implantation of an artificial urinary sphincter, this device should be reactivated at this point. If patients are able to void, and if the drain output has remained low after removal

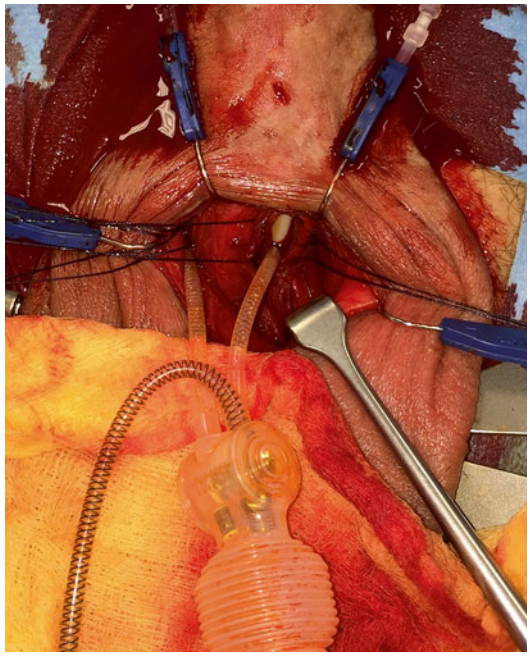

Fig. 18.15 Cylinders in position. The cylinders are placed into the corpora using the Furlow inserter and straight needle. Once the traction suture has been deployed through the glans it is often easiest to place the proximal portion of the cylinder first and then use the suture to pull the distal portion into position (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

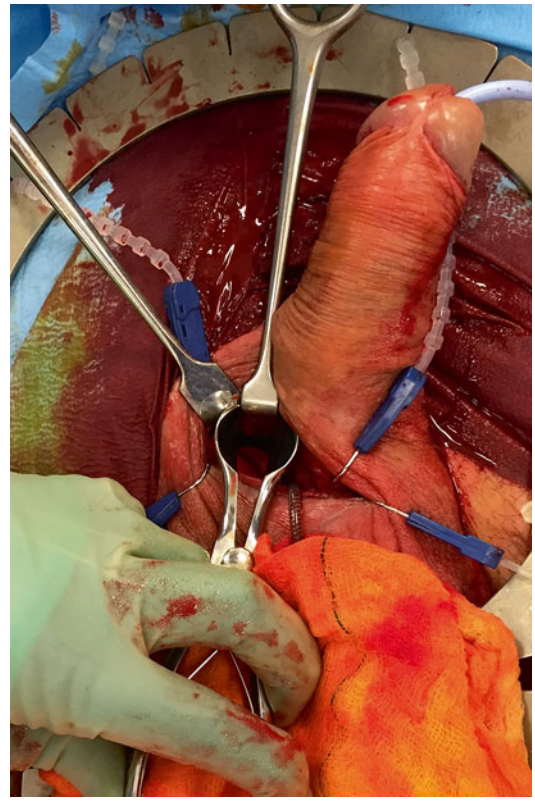

Fig. 18.16 Nasal speculum in position. If there are no contraindications, the reservoir should be placed through the external ring into the retropubic space. Once the ring is identified, a nasal speculum can be used to penetrate through the posterior rectus fascia into the Space of Retzius (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

of the dressing and deflation of the device, the drain is removed prior to discharge home. All patients receive two post-operative intravenous doses of antibiotics, and are discharged on oral antibiotics for 7 days. Guidance regarding post-operative antibiotic coverage is lacking, however, a survey of prosthetic surgeons revealed that 90% utilized post-discharge antibiotics for an average of 7 days [19]. Patients generally return to clinic at 2–3 weeks for follow-up assessment and cycling of the device and are instructed not to begin sexual intercourse with the device until 6 weeks post-procedure.

Special Situations

Ectopic Reservoir Placement

With the increasing need for prosthesis placement after radical pelvic surgery, prosthetic surgeons are forced to consider reservoir placement outside of the standard prevesical space. In fact, a survey of prosthetic surgeons found that over 90% believe that the safest option is to use an "ectopic" placement site in these patients [20]. Several techniques have been described to accomplish ectopic placement through the standard peno-scrotal incision, thus avoiding the morbidity of a second abdominal incision. As previously described in the section on reservoir placement, the external inguinal ring is identified, but instead of puncturing though the fascia transversalis into the prevesical space, a space is developed cephalad in a blunt fashion in a virtual space between the rectus muscles anteriorly and the fascia transversalis posteriorly [21]. This "high sub-muscular" type placement [22] avoids the peritoneal cavity while preventing the device from being palpable to the patient. It is important to remember that this is a

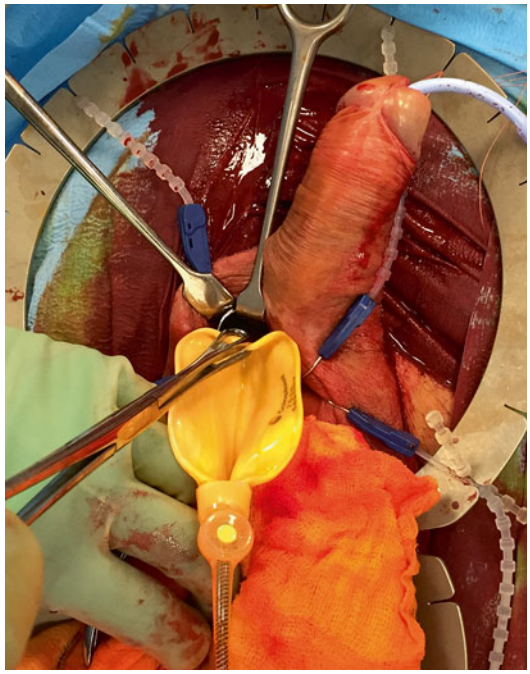

Fig. 18.17 Reservoir being placed. Once the route is established the reservoir can be placed by spreading the nasal speculum and pushing the reservoir into the space using the Furlow inserter, surgeon's finger, or ring clamp that will not damage the reservoir. Once the reservoir is filled the surgeon should palpate the lower abdomen to ensure that the reservoir is not palpable (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

potential space and will thus need to be developed appropriately using the clamp or nasal speculum to allow space for the inflated reservoir. Care should also be taken not to traumatize the reservoir when advancing it into the space. This can be accomplished either by using a blunt dilator or clamp or by grasping the hub of the reservoir with an atraumatic clamp [21] (Fig. 18.21).

Peyronie's Disease

Peyronie's disease patients can be a challenging group for prosthesis placement because of the associated fibrosis at the level of the plaque and because of the penile shortening and deformity frequently present in these patients. When erectile dysfunction precludes them from being eligible for plication or grafting procedures their curvature can be satisfactorily addressed at the

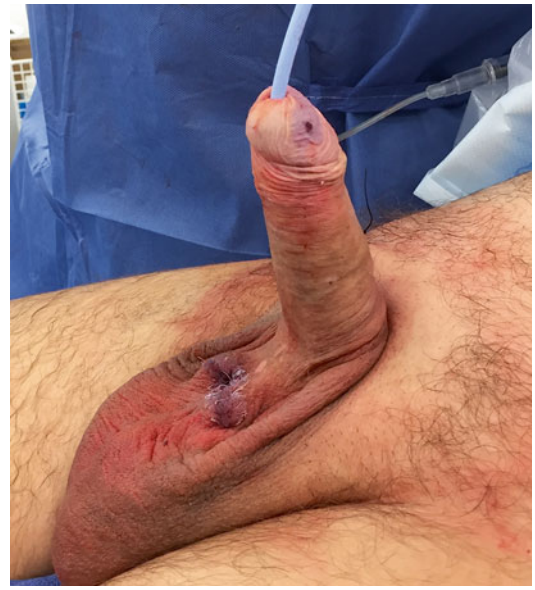

Fig. 18.18 Final result. The goal is a straight and symmetrical erection (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

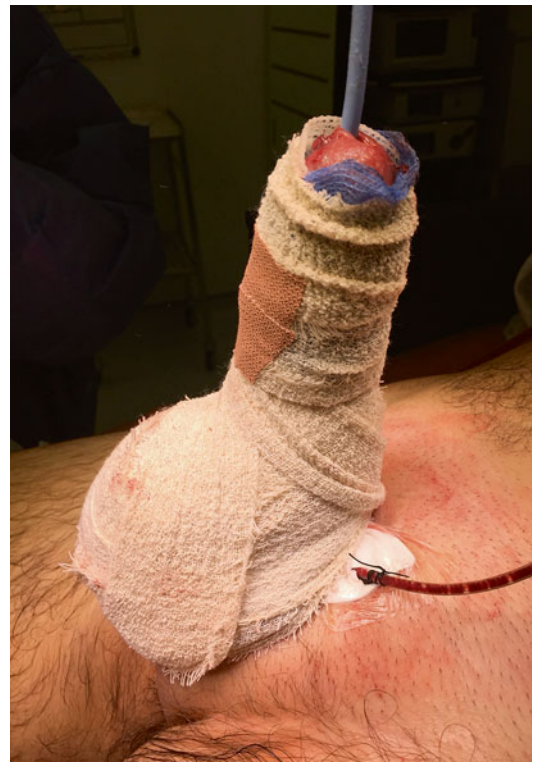

Fig. 18.19 Mummy wrap. To prevent hematoma formation we emphasize the use of a 'mummy-wrap' bandage around the penis and scrotum, using a combination of gauze and non-elastic 2-inch bandage (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Coloplast

Implantable Device
Voluntary Tracking Form

PATIENT INFORMATION (MAY USE PATIENT STICKER/LABEL)

Patient Name (Last, First, M.I.) | Date of Birth (MM/DD/YYYY)

Street Address | Apt. Number | Phone Number ( ) -

City, State, ZIP Code | Country | Email address

IMPLANTING PHYSICIAN/SURGEON

Physician/Surgeon Name (Last, First, M.I.) | Specialty

Street Address | Suite Number | Office Phone Number ( ) -

City, State, ZIP Code | Country | E-mail address

Account/CRM Number

IMPLANTING FACILITY

Facility Name | Office Phone Number ( ) - | **Date of Surgery (MM/DD/YYYY)**

Street Address

City, State, ZIP Code | Country | Account/CRM Number

DEVICE IMPLANT/EXPLANT DATA

Inflatable Penile Prosthesis (IPP)	Implant	Explant
Titan®	☐	☐
Titan OTR	☐	☐
Titan Narrow Base	☐	☐
Titan Zero Degree	☐	☐
Other (Name—be specific): _____	☐	☐

Circle below regarding rear tip extender(s) (RTE) and reservoir and their location implanted

RTE 3.0 cm Right Left
2.0 cm Right Left
1.5 cm Right Left
1.0 cm Right Left

Total cm of RTEs R ___ L ___

Reservoir Placement
Retropubic
Other (specify) _____

Reservoir Location
Left Right
Other _____

Corporal Measurements	Right	Left
Distal		
Proximal		
Total		

Malleable Penile Prosthesis	Implant	Explant
Genesis®	☐	☐

Other Prosthesis	Implant	Explant
Virtue® Male Sling	☐	☐
Torosa® Testicular Prosthesis	☐	☐
Other (Name—be specific): _____	☐	☐

ADDITIONAL INFORMATION

Was VED used pre-operatively? (Circle one) Yes No

How many weeks? _____

Was a drain used post-implant? (Circle one) Yes No

Start time of surgery (initial incision made) _____ End time of surgery (incision closed) _____

FOR DEVICE REPLACEMENT SURGERY ONLY (Please circle)

Please indicate the nature of the explantation/revision surgery:

☐ Malfunction Describe: _____

☐ Infection Describe: _____

☐ Size ☐ Erosion/Extrusion ☐ Patient preference

☐ Other (please specify): _____

Was the device returned to the Coloplast Product Evaluation Department? (circle one) Yes No

If no, reason: _____

Place all appropriate product record labels here

Device Label – Pump and cylinder

Device Label – Reservoir

Device Label – Assembly kit

Device Label – Miscellaneous

AQUEOUS SOLUTION USED TO DIP PRODUCTS (Check all that apply)

Rifampin	☐
Tetracycline	☐
Trimethoprim Sulfa	☐
Gentamicin	☐
Bacitracin	☐
GU Irrigant	☐
Vancomycin	☐
Saline	☐
Other:	☐

Please mail or fax this form when completed (white copy) to:

Coloplast Product Evaluation
1601 West River Road North
Minneapolis, MN 55411 USA
FAX: 612-287-4203

ETIOLOGY (Check one) and INDICATION FOR USE

Type of Erectile Dysfunction (Check one for primary indication):

Arteriogenic ☐ Venogenic ☐ Mixed ☐ Neurogenic ☐

Prostatectomy – Robotic	☐
Prostatectomy – Open	☐
Radiation	☐
Peyronie's Disease	☐
Diabetes	☐
Vascular Disease	☐
Neurogenic Disorder	☐
Trauma	☐
Psychological	☐
Other:	☐

NOTE: This data will be used for warranty purposes. Additionally, it may be used for research purposes, but only in a de-identified aggregate form.

Date Signature Title

White – Coloplast Copy Yellow – Patient Copy Pink – Surgeon's File Copy Green – Hospital/Chart Copy

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M2310N 08.12

Fig. 18.20 Coloplast Patient Information Form (*PIF*) (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

time of prosthesis placement. Often, placement of the prosthesis alone is sufficient to correct penile curvature in the erect state; this occurs because the dilatation of the corpora frequently breaks the fibrotic tissue responsible for the curvature. The percentage of adequate straightening with the placement of prosthesis alone varies significantly among studies, possibly because of differences in preoperative curvature or extent of dilatation of the corpora during prosthesis implantation. Certainly, a more aggressive dilatation, especially with the use of Rossello dilators or cavernotomes, is more likely to break the plaque and corporal fibrosis producing straightening of the penis. Large series have shown that 60–71 % of patients require no additional maneuvers at the time of prosthesis placement, as they have an adequately straight penis already

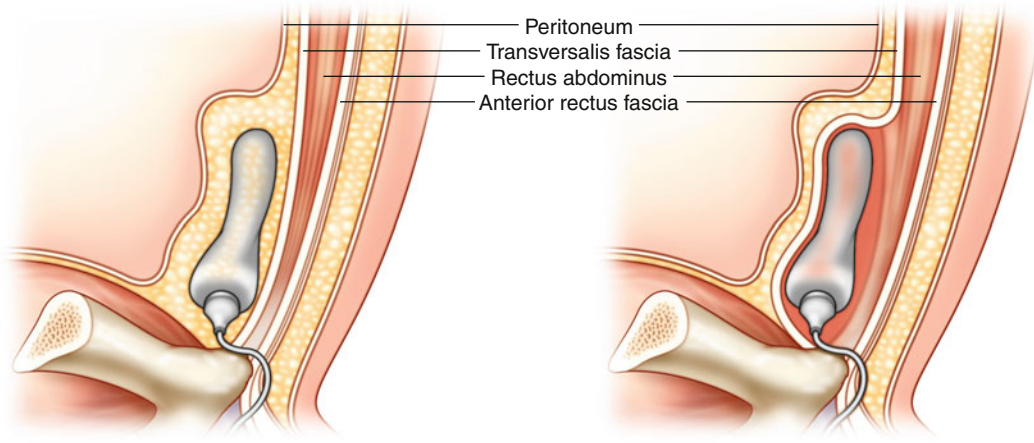

Fig. 18.21 Ectopic Reservoir placement. Note the key difference in the position of the reservoir relative to the transversalis fascia (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

[23, 24]. Generally, if residual curvature persists intraoperatively after device placement, penile modeling techniques can be employed. These techniques can be offered in patients with dorsal, lateral or dorsolateral curvatures only, as forcibly bending the penis dorsally to correct a ventral curvature is associated with a significant risk of urethral rupture. The modeling manoeuver is performed with a fully inflated prosthesis once the corporotomies have been closed and the exit tubing clamped to prevent pump damage secondary to backpressure. Protecting the corporotomies with one hand, the surgeon forcibly bends the penis in the direction opposite the curvature for up to 90 s (Fig. 18.22). The implant is then deflated and re-inflated to around 80 % of maximum capacity to allow for re-seating of the implant and to reassess the curvature. If the residual curvature exceeds 20°, the cylinders are inflated to maximum capacity and the modeling procedure is performed a second time if necessary. Inflatable prostheses have shown a clear advantage over malleable devices to correct the residual curvature during the modeling manoeuvre, possibly because inflatable devices provide a stronger support than their semirigid counterparts. Length/girth enhancing models (AMS LGX) do not perform as well as girth-only models (AMS CX and Coloplast Titan) during the modeling manoeuver [25]. Additional procedures after modeling are necessary in 4–8 % of cases [24–27]. These additional maneuvers include corporal plication, plaque incision, or plaque excision and grafting as necessary [28]. Wilson has shown that the straightening achieved at the time of device placement is durable, and is not associated with an increased rate of revision for mechanical failure [25]. Curvatures of less than 20° do not need to be corrected, as they generally do not interfere with penetrative sexual intercourse and because the regular use of the implant is likely to completely straighten the penis.

Fibrotic Corpora and Priapism

Dense fibrosis of the corporal bodies can pose a significant challenge during prosthesis placement. Fibrosis can be secondary to Peyronie's disease, priapism, intracavernosal injections for the treatment of ED, penile trauma and previous explantation of penile prostheses due to infection. In these cases dilatation under vision is necessary to minimize the chance of perforation, cross over and urethral injury. A penoscrotal approach guarantees adequate exposure to the crura while a second subcoronal corporotomy provides adequate exposure for controlled dilatation of the corpora (Fig. 18.23).

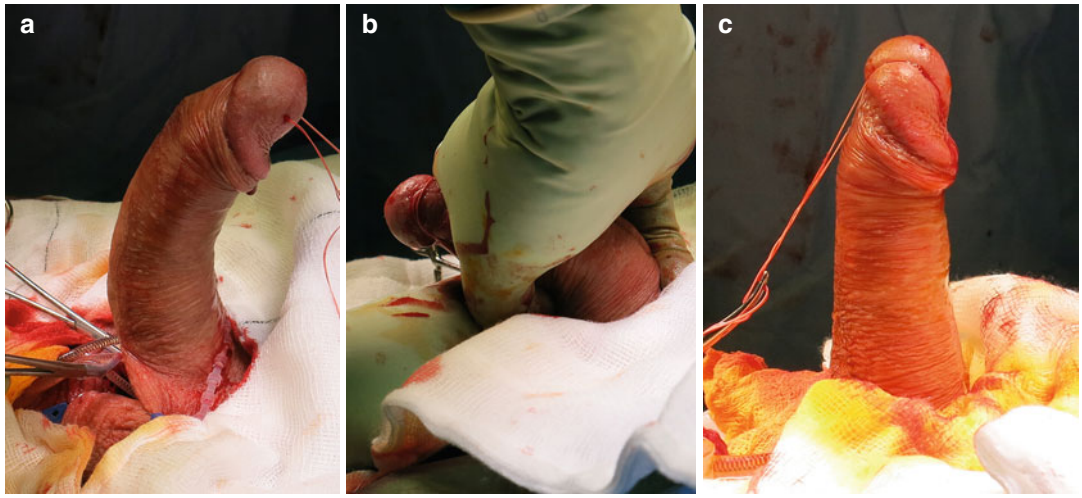

Fig. 18.22 (**a**) Residual Peyronie's Disease curvature after implant placement. Notice clamps in place on the cylinder input tubing in preparation for the modeling procedure. (**b**) Modeling procedure. Note the surgeon's hands in position to forcibly bend the penis in the direction opposite the curvature. The corporotomies will be supported by the assistant to prevent weakening of the closure. (**c**) Modeling procedure final result (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Surgeons may benefit from the use of special tools including Rossello dilators, or Uramix dilators which allow excavation of a channel in the fibrotic corpora. It is often best to perform the dilatation bit by bit potentially ulilizing multiple or extended corporotomies, to minimize the risk of perforation and cross over. Excavation of cavernosal tissue may also represent a useful step in selected cases. Consideration should also be given to using narrow cylinders (AMS CXR or Coloplast Titan Narrow Base) in which case corporal dilatation does not need to go beyond 10 mm. Studies have shown that in cases where narrow cylinders are required, regular cycling of the device over 8–12 months can produce a tissue expansion effect and allow for standard cylinder placement at the time of revision surgery [29].

Rossello dilators represent an extremely useful tool in cases of cavernosal fibrosis. These have a smooth side that should be kept facing the urethra, and the remaining surface is covered with small rasps that will break up the fibrotic tissue when passed in a linear fashion with slight rotation (Fig. 18.24).

Prolonged ischemic priapism causes diffuse necrosis of the cavernosal smooth muscle and

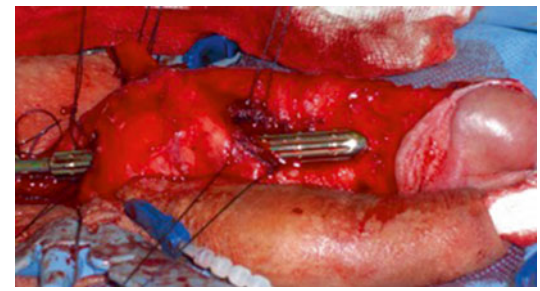

Fig. 18.23 Multiple Corporotomies. This extreme case demonstrates complete degloving of the penis. It is shown at an intermediate stage with a second corporotomy on the mid-shaft, prior to making an additional distal corporotomy to complete the dilation (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

ultimately leads to the formation of fibrosis, which typically is more severe in the distal aspect of the penis than in the crura. Due to the high complication rates and low patient satisfaction levels associated with penile prosthesis implantation in severe fibrosis, it is reasonable to consider immediate placement of a prosthesis in cases of prolonged ischemia, before the necrotic tissue has been replaced by fibrosis and penile shortening has occurred [30–32]. Although the exact time to implant in the acute setting is still debated, there is evidence that significant corporal fibrosis

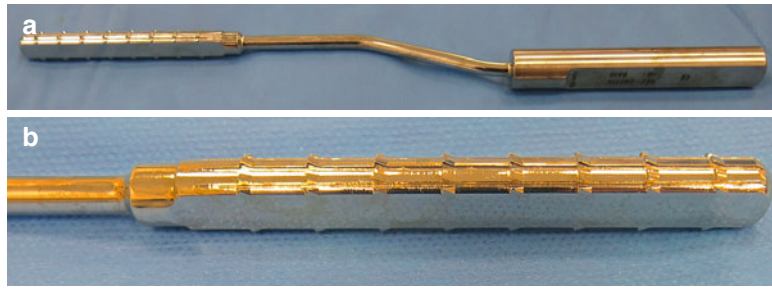

Fig. 18.24 (**a**) Rossello dilator. Like Brooks and Hegar dilators these should be available in sequential sizes for progressive dilatation. (**b**) Rossello dilator. Notice the rasps which fracture the tissue when withdrawn or rotated within the corpora. The smooth side should be kept toward the urethra at all times (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

has not yet occurred for up to 30 days from the onset of the episode. Because the increased risk of penile prosthesis infection after implantation in the acute setting is likely due to the presence of edema and bruising secondary to the failed attempt of aspiration, delaying the implantation for a few days, to allow for the edema and bruising to settle, and administering broad-spectrum antibiotics may be beneficial. As the necrotic cavernosal tissue will be replaced by fibrosis and contract around the cylinders, regular cycling of the inflatable device is necessary to prevent deformity. Therefore, malleable devices represent the first choice in these patients, with the potential to revise to an inflatable prosthesis if so desired in the future [32, 33]. Biopsy of the corporal tissue with frozen section analysis for smooth muscle necrosis at the time of surgery can ensure that the appropriate treatment is selected for patients with refractory ischemic priapism.

Revision Surgery

Surgical revision of implants may be required for mechanical malfunction or infection (see also Chap. 19). While reliability continues to improve with modern devices, revision surgery is still required in about 10 % of cases. Revision cases are associated with a higher infection rate, which can be up to ten-fold higher than virgin cases, as well as lower patient satisfaction [34–38]. Great progress has been made to minimize infection rates with the use of antibiotic coated devices [35] with large series showing a rate of 2.5 % at 6.6 years in revision cases [11]. Good data suggests that colonized biofilm present around the old device can be disrupted at the time of revision, even when there is no clinical evidence of infection [39] and lead to subsequent infection. It is therefore good practice to perform a thorough antibiotic washout, or 'mini-salvage', during the procedure [40].

Removal and/or replacement of the cylinders in revision cases can be challenging and morbid. Based on the concept of disrupted biofilm many have argued that the reservoir should be removed as well, however, retrospective data has shown that there is not an increased risk of subsequent infection according to the large published series [41, 42]. Many factors are important to consider, including patient preference as well as whether the revising surgeon placed the original implant and has a sense of where the reservoir is located. In the event that the reservoir is left behind it should be fully drained and consideration given to anchoring the cut tubing in place with a permanent suture to prevent migration of the device if there is potential communication with the peritoneal cavity.

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Complications of Penile Prosthesis Surgery

19

Joshua P. Langston, Asif Muneer, Giulio Garaffa, and David Ralph

Abstract

Complications are not an uncommon occurrence during and after penile prosthesis surgery. Fortunately, if complications are managed promptly according to established principles, the morbidity of the complications can be minimized.

Keywords

Penile prosthesis • Penile prosthesis complications

In prosthetic surgery, intra- and post-operative complications are not uncommon and can be extremely devastating for patients. Fortunately, if identified intra-operatively, many complications are suitable for immediate correction, which is usually straightforward and can yield excellent outcomes. Complications identified post-operatively are much more challenging to rectify and are frequently associated with a low patient satisfaction. For simplicity in this chapter, complications are subdivided into intra- and post-operative. However, it should be noted that many complications that manifest post-operatively do actually occur intra-operatively and are not promptly recognized.

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Intra-operative Complications

Cylinder Crossover

'Cylinder crossover' implies that one or both cylinders have perforated the corporal septum and passed through to the contralateral corpus cavernosum. According to the site of crossover, this complication can be subdivided into proximal and distal categories (Fig. 19.1). Crossover can usually be prevented during dilatation by intentionally keeping the dilators lateral as they

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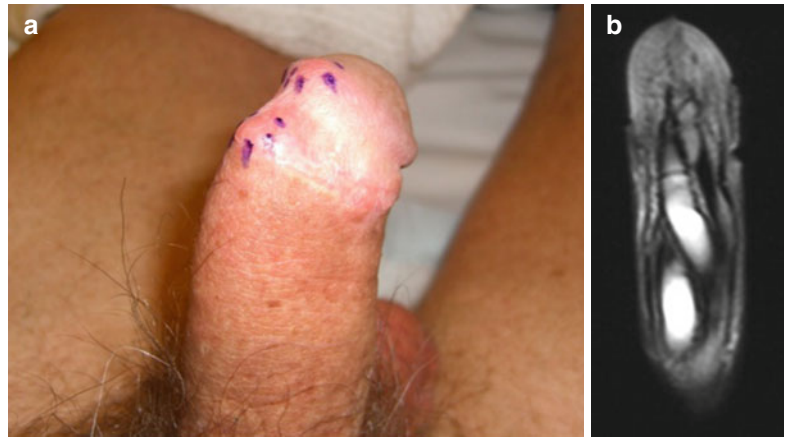

Fig. 19.1 (**a**) Distal crossover. Note the marked cylinder tips showing crossover from right to left. (**b**) MRI image showing distal crossover (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

are advanced into the corpora, in order to avoid inadvertently piercing the relatively weak corporal septum. As discussed previously, cases of corporal fibrosis may benefit from a second (distal) corporotomy made via a sub-coronal incision to allow for controlled dilation and minimize the risk of crossover, tunical perforation and/or urethral injury.

Crossover should be identified at the time of dilatation by simultaneously inserting a dilator into each corpus cavernosum (as described in Chap. 18, "Penile Prosthesis Surgery"). The presence of crossover can be ruled out if the simultaneous passage is easy, the corpora and the handle of the dilators are symmetrical, and there is no metal-on-metal sound caused by the two dilators making contact. If crossover is identified at this stage, correction is relatively simple and requires the creation of a new channel in the correct position. Leaving a Hegar-type dilator in the contralateral corpus cavernosum can be extremely helpful to prevent perforation of the septum again, or return into the wrong channel (Fig. 19.2).

Care should be taken to identify the problem early, specifically before the cylinders have been placed. Delayed identification will require temporary removal of the cylinders to allow for the creation of a new channel. This will significantly increase the time that the implant is exposed on the surgical field and may therefore increase the infection rate. Furthermore, if the crossover occurs only along a short tract at the midshaft, intra-operative identification after the insertion of the cylinders may not be apparent due to swelling and engorgement of the corpus cavernosum and surrounding tissues that may be present. Usually for these patients the cross over becomes evident a few months postoperatively, when the swelling has settled and the penile shaft appears deformed.

Urethral Injury

Urethral perforation represents one of the most feared intra-operative complications and should be subdivided into proximal and distal urethral injury, as management of the two entities is distinctly different. Distal urethral perforation typically occurs at the level of the fossa navicularis, as this location represents the weakest site along the tunica. Corporal dilatation in virgin patients is usually straightforward and simply keeping the dilators lateral against the tunica albuginea of the corpora cavernosa and protecting the urethra with the non-dominant hand can prevent urethral injury (see Chap. 18, "Penile Prosthesis Surgery"). Urethral perforation is more common in cases of corporal fibrosis or in the case of previous extensive penile surgery. This is because dilatation of the scarred corpora can prove extremely challenging for the surgeon and it is relatively easy, with the momentum required, to advance the dilators through the fibrotic tissue and inadvertently perforate the urethra. Exposing the corpora via a second subcoronal incision and

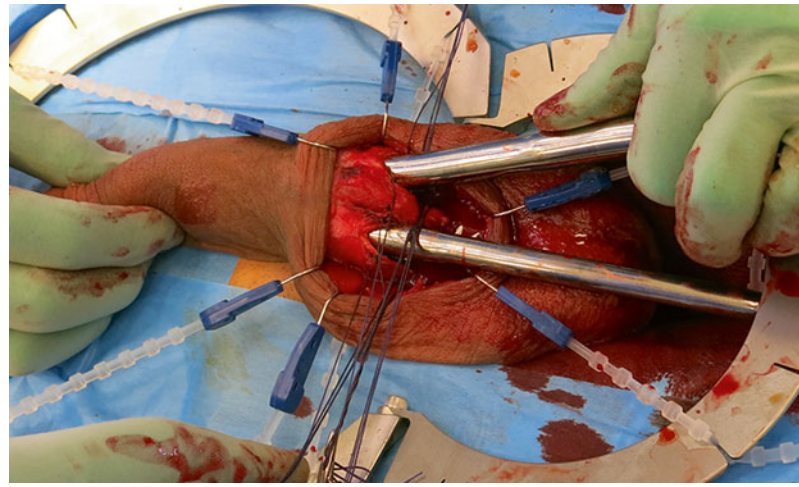

Fig. 19.2 Correction of intraoperative crossover. Note the Hegar dilator in place in the right corporal space while a new channel is created on the left with guidance by the non-dominant hand to remain lateral (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

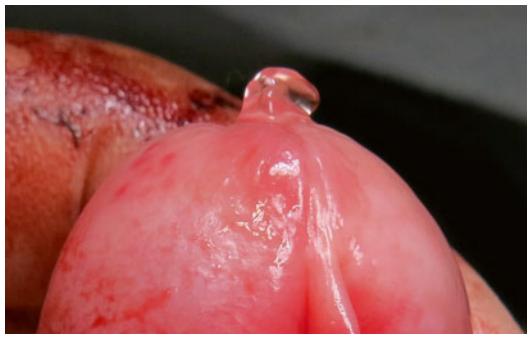

Fig. 19.3 Urethral leak during corporal irrigation (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

dilating with Rossello dilators may be extremely useful in these cases.

Urethral perforation should be suspected when blood is visible at the meatus. Routine irrigation of the corpora with antibiotic solution is recommended and can confirm the presence of a urethral perforation (Fig. 19.3). As the distal urethra is always contaminated, it is generally not advisable to continue with the cylinder placement in the affected corpora. If the perforation occurs during the dilatation of the first corpus cavernosum, the procedure should be abandoned and a urethral catheter left in place for at least 10 days to allow for a complete healing of the urethra to occur. In circumstances where the perforation is unilateral and the other corpus cavernosum has already been dilated, and there is no communication between the two corpora, a single cylinder of a malleable device can be left in the contralateral corpus to maintain the space and prevent the otherwise inevitable fibrosis and penile shortening. A long rear tip extender may also be left in the crus of the affected side, well away from the point of perforation, to render the delayed re-do penile prosthesis implantation easier. This is particularly useful in patients with corporal fibrosis, where communication between the two corpora cavernosa is unlikely.

Proximal urethral injuries can occur during initial dissection to expose the corpora and urethra or during the creation of the corporotomies. Because these can be well visualized and easily repaired via the penoscrotal incision, and since the bulbar urethra is usually not contaminated, it is reasonable to proceed with penile prosthesis implantation if the urethral injury can be repaired in a watertight fashion. If the injury was made with electrocautery it is critical to sharply remove any tissue at risk of thermal injury and delayed necrosis. Once the edges have been cleaned and well visualized the defect can be closed in at least two layers using a 5-0 or 4-0 braided absorbable suture for an inner mucosal layer and then 4-0 or 3-0 braided absorbable suture to close the corpus spongiosum. Additional adjacent tissue can be used as a flap to cover the site to reduce the chance of a urine leak from the anastomosis that could contaminate the prosthesis. If the defect can be closed satisfactorily in a tension-free

fashion and there is sufficient tissue to separate the injury site from contact with the prosthesis then the procedure can be continued. Copious antibiotic irrigation is always recommended, but is particularly useful in a situation such as this. The Foley catheter should be left in place post-operatively for at least 2 weeks and until a peri-catheter urethrogram demonstrates no extravasation at the injury site [1]. Urinary diversion with a suprapubic catheter is also an option.

Corporal Perforation

Perforation through the tunica albuginea of the corpus cavernosum can also occur during dilation. This most often occurs in cases of severe corporal fibrosis, when excessive force is required, and the true limits of the corporal bodies are difficult to discern, and/or when the surgeon fails to remain lateral along the course of the corpora proximally as it moves dorsolaterally toward the pubic rami. As previously described for the distal corpora, dilatation under vision is the key to reducing the risk of perforation. This can be easily achieved proximally through a penoscrotal approach, as the Dartos can be swept away exposing the proximal aspect of the crura. As with other complications, this can be subdivided based on location and managed accordingly.

Proximal (crural) perforation should be suspected when simultaneous placement of dilators in each crus yields an asymmetric result (Fig. 19.4). Although in the past proximal perforation was historically managed with creation of a 'windsock' out of Goretex to prevent proximal migration of the cylinder through the albugineal tear, this was associated with a significant increased risk of infection and is now obsolete [2]. At present, a rear-tip 'suture sling' represents the solution of choice to prevent proximal migration of the implant through the defect [3]. If a proximal perforation is confirmed the implant should be sized based on the measurements of the contra-lateral, non-perforated, corpora. Prior to placement of the cylinder on the affected side, a heavy non-absorbable or long-lasting absorbable suture should be passed outside-in through the tunica at the level of the corporotomy. It should then be passed through the rear-tip extender near its widest portion at the base (or cylinder base if no rear-tip extender is used) and then passed inside-out on the other side of the corpora. This will leave the suture arms outside of the corpora and ready to be tied (Fig. 19.5). The cylinder should be placed distally in the standard fashion, and then placed proximally with the suture sling in place. It is important to have an assistant keep the cylinder well positioned distally when the sling is tied down as this will ultimately determine the level at which the cylinder heals in place. The assistant should maintain distal traction on the glans suture and should ensure that the cylinder does not 'accordion' or heal in a contracted fashion by keeping proximal counter traction at the input tubing hub using the tool provided for this, or using the Furlow inserter. Now the sling suture can be tied down and this will prevent any

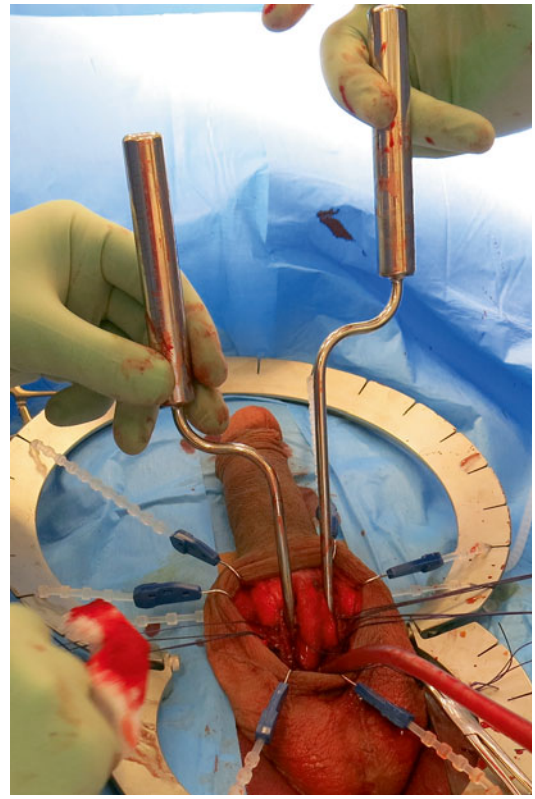

Fig. 19.4 Asymmetrical Brooks dilators indicative of proximal perforation on the patient's right (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

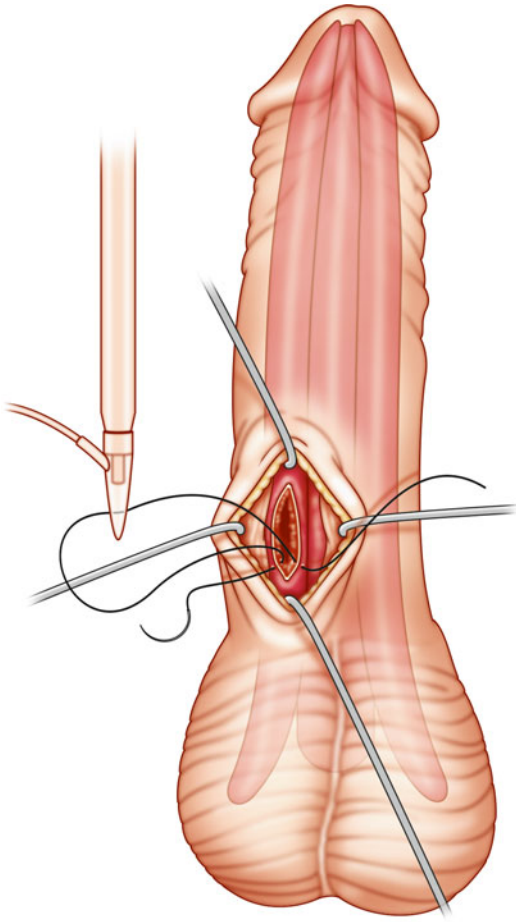

Fig. 19.5 Suture sling. A heavy non-absorbable or long-lasting absorbable suture should be passed outside-in through the tunica at the level of the corporotomy, then through the rear-tip extender near its widest portion (or through the cylinder base if no rear-tip is needed) and then passed inside-out through the other side of the corpora. This will leave the suture arms outside of the corpora and ready to be tied. The cylinder should be held in position proximally and distally before the suture is tied (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

proximal migration of the cylinder even if there is a substantial defect in the proximal tunica. Over time a capsule will form around the cylinder and scar tissue will solidify the tunical defect. These patients should not return to sexual activity for at least 8–12 weeks to allow for the initial healing process to occur [1].

Distal or lateral corporal perforation can be more routinely repaired intraoperatively given better accessibility to the site. Even minor defects should be addressed given that these will be noticeable to the patient and can create problems in the future. Generally repair of these complications will require an adequate exposure of the corpora cavernosa, which can be achieved either with a circumcoronal incision with partial or complete degloving of the penile skin or through the penoscrotal incision in a retrograde fashion. Often tunical closure can be completed primarily in two layers, using a smaller braided absorbable suture for the inner layer and a heavier version of the same suture for an imbricating outer layer of horizontal mattress sutures. The same technique is used to reinforce the site of a corporal aneurysm in revision surgery, and should be used in this instance to prevent a potential weakness where aneurysm could occur in the future. In these cases devices with controlled expansion should be utilized, such as the Coloplast Titan series or the AMS 700 series, in order to minimize future aneurysm risk [4].

Post-operative Complications

Infection

The most feared complication in prosthetic surgery is post-operative infection of the device. Based on the chronology of its clinical presentation, and underlying etiology, prosthesis infections can be subdivided into acute and chronic infection. The risk for infection is highest in the immediate post-operative period and usually acute infection manifests within 8 weeks of surgery. Chronic infections are much more subtle and may manifest even years after the implantation. The first signs of acute infection are sepsis and severe pain in the penis, which can appear oedematous, erythematous and warm (Fig. 19.6). Purulent discharge, skin necrosis and protrusion of components of the implant through the skin are not uncommon. Acute device infections are usually the result of bacterial entry into the body at the time of surgery; this is why a great effort is paid to sterilize and prep the surgical field and to minimize the contact between the components of

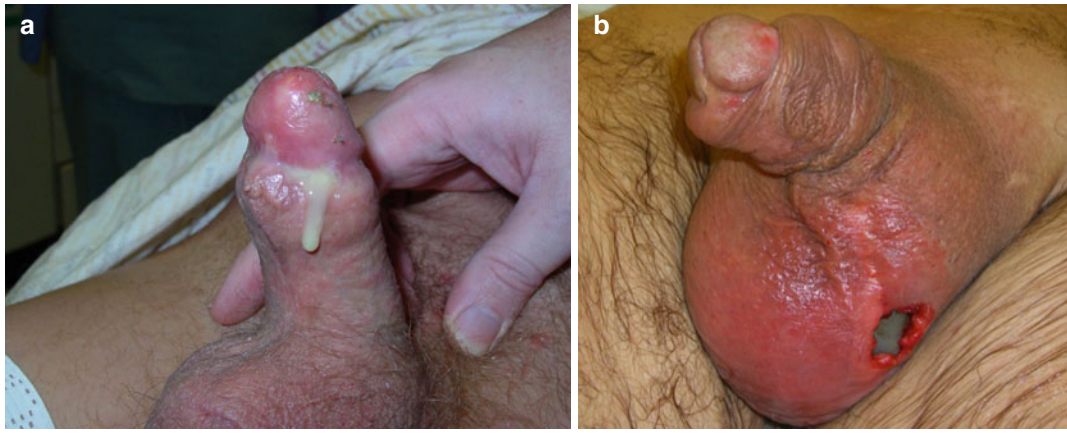

Fig. 19.6 (**a**) Purulent infection of penile prosthesis. (**b**) Scrotal erosion of prosthesis pump (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

the implant and the skin. Chronic device infections, in contrast, are thought to come from haematogenous sources and manifest with subtle pain over the components of the device, which may appear adherent to the skin [5].

The most common bacteria implicated in device infection is Staphylococcus epidermidis, while Methicillin-resistantant *Staphylococcus aureus* (MRSA), Pseudomonas aeruginosa, Escherichia coli, Proteus, Enterococcus, and Serratia species are less frequently involved [6]. Infections caused by fungi are rare, but are of particular concern in diabetic or immunocompromised patients and are not generally accounted for by implant antimicrobial coatings.

Patients and surgeons should be aware of the main risk factors for post-operative infection. Diabetes mellitus and immunosuppression are associated with significantly increased risk of penile prosthesis infection [7]. Other significant risk factors for infection include lack of genital sensation, as in spinal-cord injury patients, and prolonged operative time, such as in cases of severe fibrosis or revision surgery [8].

Ultimately, once a penile prosthesis becomes infected, the only successful management will involve removal of the entire device, as antibiotics are ineffective to clear the infection. This is because of the impenetrable mucopolysaccharide biofilm that forms around the device components and prevents antimicrobial activity [9, 10] as well as the poorly vascularized scar tissue around the surgical site, which prevents antibiotic delivery.

Removing an infected penile prosthesis represents an extremely traumatic event for a patient as it leads to penile deformity and penile shortening secondary to the fibrosis that will ultimately replace the corporal tissue. Performing delayed reimplantation of a prosthesis in these patient will be extremely challenging due to the diffuse fibrosis and will be associated with increased complication rates and lower patient satisfaction due to penile shortening.

In order to prevent fibrosis and penile shortening, a salvage device replacement procedure following removal of the infected implant should be considered in carefully selected patients [9, 10]. Salvage is always contraindicated in cases of sepsis, tissue necrosis, erosion of the implant through the skin, or urethral perforation [6]. In appropriately selected cases the success rate of the salvage procedure is around 85 % [6, 11, 12]. Despite this high success rate and acceptance in the literature for many years, Zargaroff and colleagues have shown recently that salvage procedures are only performed in 17 % of patients admitted with infected prostheses in the U.S [13]. Adequate counseling of the patient is extremely important in this situation and all potential risks and benefits of simple prosthesis explantation

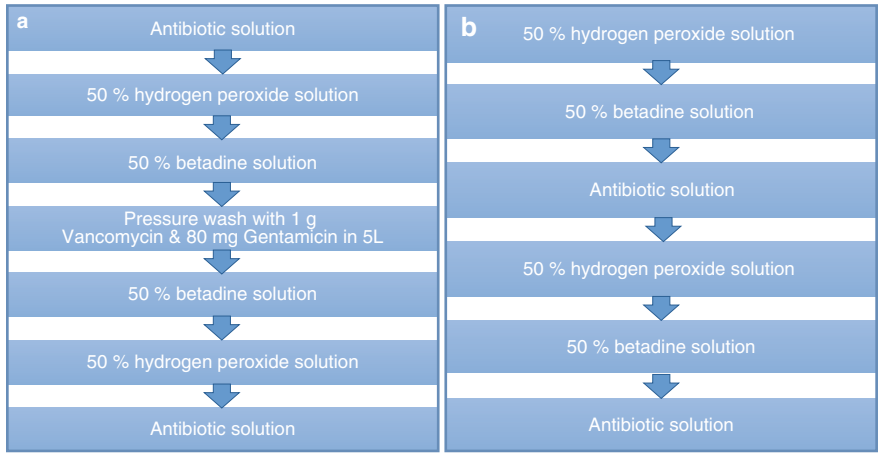

Fig. 19.7 (**a**) Mulcahy salvage washout protocol. (**b**) Modified salvage washout protocol (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

and of the salvage procedure should be clearly explained.

The salvage procedure should be carried out after the administration of broad-spectrum intravenous antibiotics. All the components of the device should be removed, ideally though the same approach by which it was placed. The dissection should be carried out using electrocautery to avoid inadvertently cutting implant components, which could then be lost in the surgical field. As each component is removed it is good practice to culture the space to gain information on the causative organism and guidance on post-operative antibiotics.

Once the device has been removed, the cavities are irrigated with a sequence of antimicrobial and antiseptic solutions. As originally described by Mulcahy (Fig. 19.7), all device spaces should be irrigated in a step-wise fashion using antibiotic solution, hydrogen peroxide solution and providone-iodine solution. A catheter can be inserted in to the deepest parts of the cylinder and reservoir spaces to ensure adequate delivery of the solutions (Fig. 19.8). It is important to remember that this washout needs to be mechanical in addition to antimicrobial in order to break up the biofilm, which will otherwise shelter the bacteria. This can be achieved with pressure irrigation of the surgical field with 5 l of antibiotic solution containing Vancomycin and Gentamicin. Finally, the initial 3 solutions are repeated in reverse order, finishing with the antibiotic solution. Many experts who perform salvage procedures have modified this protocol, and anecdotal reports suggest that some surgeons are restricted by hospital policy from using certain antibiotics or components of the irrigation.

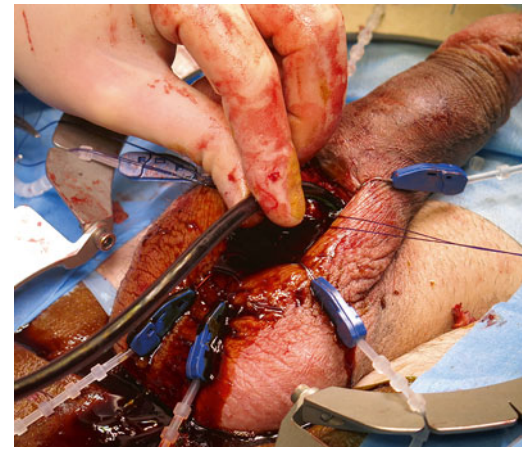

Fig. 19.8 Salvage procedure. Demonstration of catheter irrigation of corpora with povidone-iodine solution during salvage washout (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Once the salvage washout is complete, the drapes, gowns, and gloves of the surgeons and staff are changed and a different instrument set is used for the implantation of the new device. The implantation steps are the same as previously described for initial device placement. If there are no contraindications, it is reasonable to use the contralateral side for reservoir placement to avoid any potential infection from the old reservoir site. The patient should be continued on antibiotics for at least 2 weeks post-operatively. If no information is gained from intra-operative cultures then broad-spectrum oral antibiotics based on the local antibiotic protocol are recommended.

In cases where salvage is contraindicated, a period of 6–8 weeks should be allowed for the treatment of infection and healing of damaged structures prior to attempts at reinsertion. The patient should understand that this delayed replacement will result in penile fibrosis, which will inevitably lead to shortening and will significantly increase the difficulty of future surgery. In these cases, regular penile stretching with a vacuum device can be extremely useful to minimize penile shortening until a new attempt at implantation is carried out.

Fig. 19.9 Floppy glans/SST deformity (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

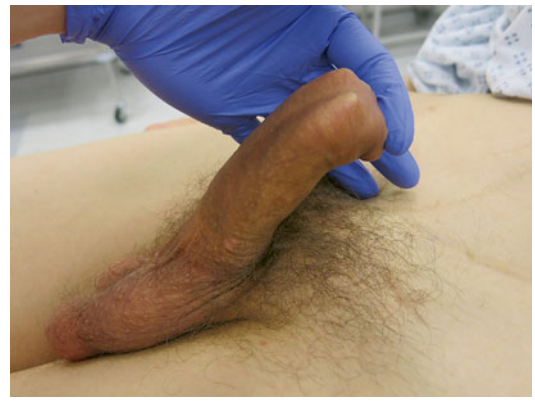

Fig. 19.10 Impending cylinder erosion (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

Distal Cylinder Malposition and Hypermobile Glans

The presence of glans irregularity in the erect state significantly affects patients' satisfaction with their prosthesis. If the glans is not well supported on the distal ends of the cylinders it will tilt ventrally in the erect state causing an 'SST (Supersonic Transporter) Deformity' (Fig. 19.9). This could be either due to short cylinders that do not extend to the distal end of the corpora, or more simply because of a 'hypermobile glans' that lacks good fixation to the erect corpora.

If the cylinders are too short, either because of mismeasurement or capsule formation that has restricted inflation, the device must be revised with implantation of longer cylinders. It is important to remember that replacement of longer cylinders into the same encapsulated cylinder space will not correct the problem. Generally speaking, proper revision of this situation would involve a distal corporotomy with incision of the old capsule and creation of an appropriate route for the cylinder up to the end of the corpora. The old distal capsule space should be closed off with interrupted sutures to prevent the cylinder from slipping back into this space when it is deflated (Fig. 19.10).

In the case of hypermobile glans, surgical repair should be offered when the use of PDE5 inhibitors and/or intraurethral application of topical prostaglandin-E have failed to provide adequate rigidity to the corpus spongiosum. Surgery involves fixation of the glans to the distal corpora

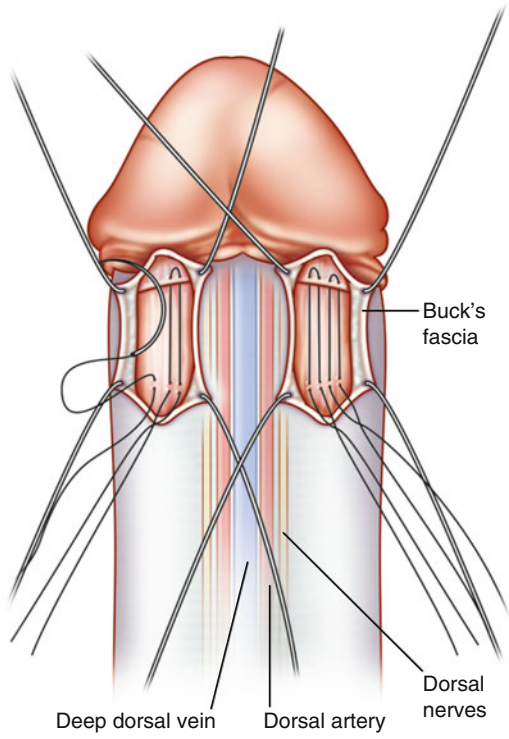

Fig. 19.11 Glanspexy (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

to achieve stability [14]. To accomplish this, a sub coronal incision is made just proximal to the coronal sulcus opposite to the direction of tilting of the glans. Sharp dissection is then used to carefully dissect the glans and the neurovascular bundle from the underlying tunica albuginea of the corpora cavernosa using two windows in Bucks fascia. The freed glans is now repositioned more proximally on the tips of the corpora and fixed with a long-lasting absorbable suture in a horizontal mattress configuration using two sutures on each side (Fig. 19.11). Buck's and Dartos' fascia can then closed over these suture lines [1].

Extrusion and Aneurysm

On occasion a cylinder can erode through the tunica albuginea in the absence of infection or device malfunction. If the skin or urethra is not perforated then infection is unlikely and the possibility exists to reposition the cylinder in the corpora without replacement of the device. Many repair techniques, using a variety of biologic [15], synthetic [3], and autologous grafts [16] as well as primary repair using local tissue [18] have been described for the management of impending erosion.

If the extrusion site is fairly distal, correction is best achieved through a subcoronal incision with partial degloving of the shaft. As discussed previously, it is safest to do most of the dissection with electrocautery. The cutting current should be set to less than 30 W in order to prevent damage to the cylinder. Once the boundaries of the defect in the corpora are defined the cylinder should be reflected out of the corpora and folded proximally. The distal capsule of the cylinder space should now be visible. A careful incision should be placed in the medial aspect of the capsule in order to find the remaining corporal tissue medial to the old capsule. A new route should then be developed for the cylinder into its correct position in the distal corpora. The medial and lateral edges of the old capsule should be closed together and sutured to the lateral aspect of the tunica albuginea to prevent the cylinder from slipping back into the old space, and to provide extra support to the weakened tunica albuginea. Once the cylinder has been redeployed into the distal corpora using the Furlow inserter, the two edges of the tunical incision should be approximated in a watertight fashion using interrupted absorbable sutures with strong tensile strength. If the defect cannot be closed primarily, a xenograft or allograft should be considered for tunical repair (Fig. 19.12).

Management of medial extrusion and impending erosion into the fossa navicularis can be managed in a similar fashion with retunneling of the cylinder laterally. Expert recommendation is to always use a biologic graft in these cases to reinforce the medial wall by placing graft between the two old capsular layers and thus further protecting from urethral erosion [1]. Aneurysm of the tunica can be managed in a similar fashion by repairing the defect in the corpora in two layers and considering a graft only when the defect is too large for primary repair.

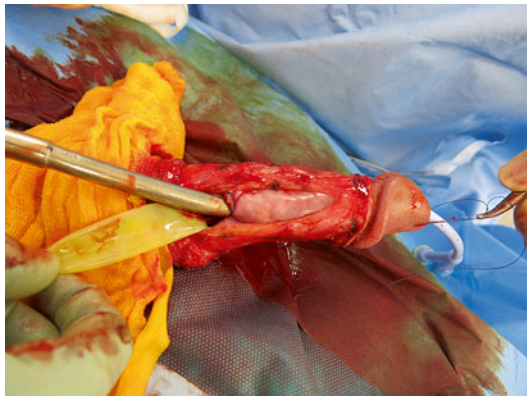

Fig. 19.12 Re-tunneling cylinder. The Hegar dilator is inside the new cylinder space which is created medial to the previous space seen with its capsule intact (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

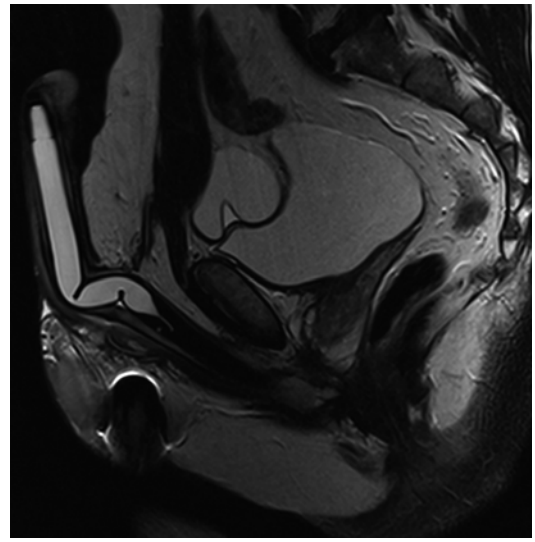

Fig. 19.13 MRI image demonstrating S-shaped deformity (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

S-Shaped Deformity

Buckling or kinking of the cylinders during inflation of the device can be extremely uncomfortable and prevent patients from utilizing the prosthesis for intercourse. This so called "S-shaped deformity" is generally due to oversizing of the cylinders or the use of length-expanding AMS LGX cylinders [17, 18]. Occasionally, capsular contraction around non-length-expanding cylinders can also produce buckling of the cylinders [19]. Although newer models in the AMS LGX series have limitations to length expansion in order to minimize the risks of buckling, the possibility still remains. Although the diagnosis of "S-shaped deformity" is generally made on physical examination, penile MRI may be useful to confirm the suspicion and to exclude the possibility of corporal scarring or capsule formation preventing proper cylinder positioning and thus causing the irregular inflation (Fig. 19.13). Proper management of this complication requires surgical revision, as no conservative measures can adequately address the underlying problem. If the cylinders are felt to be too long they must be replaced and downsized. If capsular contraction or corporal scarring is implicated then revision can be undertaken with repositioning of the cylinders in the corpora without downsizing the cylinders.

Reservoir Complications

Reservoir complications are rare, but can be serious. Blind placement, especially in cases of prior prostatectomy or other pelvic surgery, has been reported to lead to significant vascular and visceral injury [20]. In addition to the possibility of vascular injury there is the possibility of iliac vein compression, which can lead to deep venous thrombosis and its related complications [21] (Fig. 19.14). These vascular complications can be avoided by staying medial during the puncture of the external inguinal ring. In case of previous pelvic surgery, the reservoir should be placed under direct vision through a second abdominal incision. Alternatively, in order to avoid the morbidity of a second incision, the reservoir can be placed ectopically through the external inguinal ring in a virtual space above the fascia transversalis. (See reservoir placement technique in Chap. 18). In patients who have not undergone previous

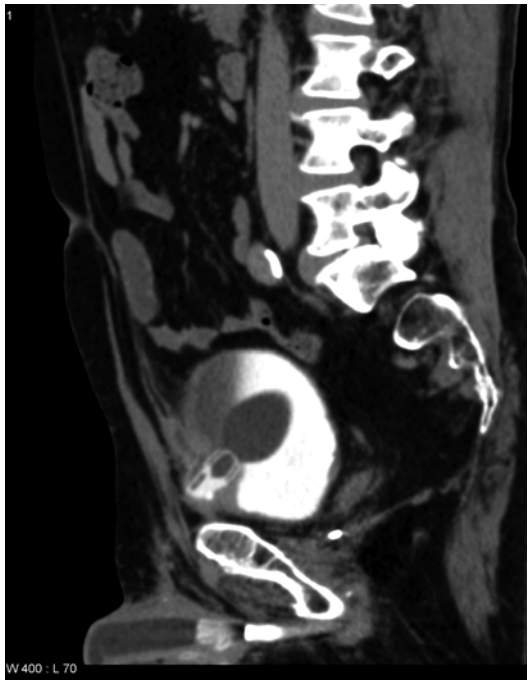

Fig. 19.14 MRI image demonstrating reservoir erosion into the bladder (Published with kind permission of © Joshua P. Langston, 2016. All Rights Reserved)

pelvic surgery, the reservoir can be easily placed blindly in the extraperitoneal space underneath the fascia transversalis though a puncture of the external inguinal ring. In case of blind insertion of the reservoir in the extraperitoneal space, the surgeon should always empty the bladder prior to puncturing the fascia transversalis to minimize the risk of inadvertent bladder injury.

Bladder and bowel perforation may be difficult to identify intraoperatively. The presence of hematuria may be an indicator of bladder injury while postoperative ileus suggests bowel perforation. Occasionally, bladder injury may manifest only with mild lower urinary tract symptoms and recurrent urinary tract infections after surgery. Cystoscopy represents the best investigation to rule out bladder injury while a computed tomography (CT) scan of the abdomen and pelvis is always necessary to confirm a suspected bowel injury. In cases of bladder or bowel injury, all the components of the implant need to be treated as infected and should be removed. Laparotomy and surgical repair of bowel injuries is always necessary while bladder injuries often only require prolonged catheterization, as they tend to heal spontaneously if there is no communication with the peritoneal cavity.

Conclusion

Complications in penile prosthetic surgery are unfortunately unexpected but, if managed according to the principles presented here can have minimal impact on device success and patient quality of life.

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Future Developments in Prosthetic Surgery

20

Fanourios Georgiades and Maarten Albersen

Abstract

Recent technological advances have allowed developments in a range of medical specialities including urology. Regenerative medicine is a promising, attractive, interdisciplinary field, which will provide solutions for a number of urological conditions in the future, including urinary incontinence and erectile dysfunction. Applications of regenerative medicine in urology range from cell-based therapies to customised autologous or synthetic tissue transplantation. In this chapter we discuss how different approaches within the field of regenerative medicine have been applied or are in the process of being applied in clinical practice, to provide newer resources and options for patients with diseased or damaged tissues.

Keywords

Urinary incontinence • Erectile Dysfunction • Penile Prosthesis • Testicular Prosthesis • Regenerative Medicine • Stem Cells

Introduction

The majority of current applications using prosthetic materials in the field of urology focus mostly on replacing volume without a strong emphasis on the functional preservation of the tissues. Current trends in all aspects of surgery focus on functional preservation of the existing tissues with additional support from external material when needed. Due to a shortage in donor tissues/organs, in comparison to the high demand for replacing damaged or lost tissues/organs, researchers have concentrated on identifying new materials, resources and technologies to address this issue [1]. The field of regenerative medicine was established to combine knowledge from various disciplines to achieve this goal (Fig. 20.1).

Regenerative medicine refers to the interdisciplinary field of research and clinical applications that focuses on the functional and structural

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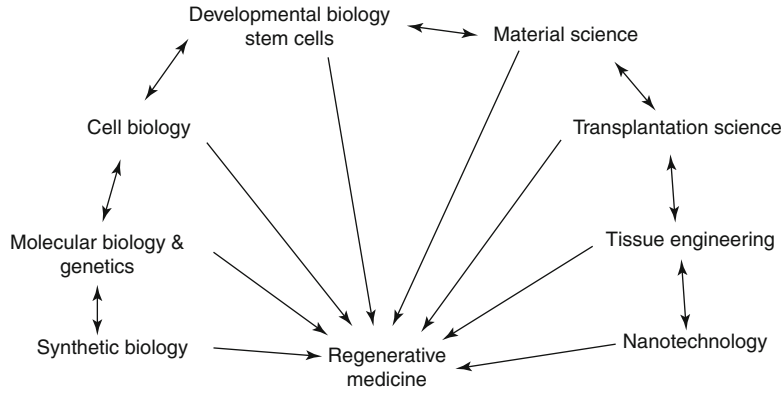

Fig. 20.1 Clinical disciplines and life science fields that contribute to regenerative medicine and also contribute to each other for the advancement of their own respective fields

restoration of damaged or diseased tissues and cells, by replacement or by using the endogenous tissues' regenerative potential [2, 3]. Several fields currently contribute to regenerative medicine, including older traditional fields, such as genetics, cell biology and also new and emerging fields such as nanotechnology and synthetic biology [3].

Applications of regenerative medicine in urology ranges from cell-based therapies to customised autologous or synthetic tissue transplantation. In this chapter, we discuss several exciting and promising approaches currently being investigated as part of regenerative medicine, focusing on applications related to urology. More emphasis is given to cell-based therapies and tissue engineering approaches as these areas have more relevant examples for clinical applications in urology.

Cell-Based Therapies

Since the invention of the microscope by Anthony Leeuwenhoek (1632–1723), man has been interested in cellular biology. The microscope allowed for direct visualization of cells, and cell propagation and differentiation were witnessed for the first time [4]. These technical developments led to the recognition of cells as being the building blocks of life, capable of giving rise to other cells and complete tissues. It was not until early in the twentieth century that researchers realized that various types of blood cells all came from one particular type of 'stem cell' in the bone marrow, which in turn encouraged physicians to administer bone marrow by mouth to patients with anemia or leukemia. A breakthrough in the discovery of stem cells followed in 1963, when it was discovered by Ernest A. McCulloch and James E. Till that normal mouse blood-forming tissue contains a class of cells which, on being transplanted into heavily irradiated mice, can proliferate and form macroscopic colonies in the spleen [5, 6]. They noted that within a given colony, differentiation occurred along three lines, into cells of the erythrocytic, granulocytic and megakaryocytic series, respectively. Later, it was shown that mice with defective marrow could be restored to health with infusions into the blood stream of marrow taken from other mice. Since that time, patients receiving chemotherapy or irradiation have undergone bone marrow transplants, in fact the first form of stem cell therapy. It took until 1998 when James Thompson first successfully removed cells from spare embryos at fertility clinics and grew them in the laboratory [7]. He thereby established the world's first human embryonic stem cell line, which still exists today. This discovery launched stem cell research into the limelight and ever since, a plethora of evidence has emerged to illustrate that these embryonic stem cells can differentiate in any cell type in the body, thus potentially having the capability to replace or regenerate any diseased, injured or purposefully removed cells and tissues.

Stem cells are defined by their capability for self-renewal and differentiation into more specialized cell types [4]. The self-renewal trait means offspring from repeated division remain undifferentiated, and thus sustains a stem cell pool at the

niche where these stem cells are derived from. In 'asymmetric division' a parent cell divides into an exact copy and one more differentiated daughter cell. In 'stochastic differentiation' one father cell divides into two differentiated cells, while another father cell divides into two exact copies of itself in order to maintain the population of stem cells [8]. Differentiation into more specialized cell types, e.g. smooth muscle cell, endothelial cell, or neuron was initially thought to serve as a replacement of defected or apoptotic cells in stem cell therapy (the "building block theory"). Stem cells are classified by their developmental capacity as totipotent, pluripotent, multipotent, progenitor and precursor cells. Totipotent cells in zygote and morula develop into completely differentiated organisms, and in extra-embryonic tissues such as the placenta. Pluripotent cells divide into all three germinal layers (ectoderm, mesoderm and endoderm) but do not produce extra embryonic tissue. The classical and most well known examples of pluripotent cells are embryonic SCs (ESC) although research has been limited as a result of ethical concerns as it requires the destruction of embryos. To cope with these concerns, researchers have investigated and succeeded in reprogramming terminally differentiated cells from adults to become pluripotent [9, 10]. For this discovery, John B. Gurdon and Shinya Yamanaka received the 2012 Nobel Prize in physiology and medicine [11].

Multipotent SCs include hematopoietic and mesenchymal/stromal SCs, which can essentially differentiate into any daughter cell within their own germinal layer. Unipotent cells are progenitor or precursor cells with limited proliferation potential and are able to differentiate into one or several specific cell types. While these divisions have been classically used in the categorization of stem cells, researchers have shown that in the right experimental circumstances, multipotent cells can be transdifferentiated *ex vivo* to cells belonging to another germ layer [12]. *In vivo* however, there is still debate as to whether these cells transdifferentiate after engraftment (provided engraft in the tissue takes place) into functional cells fitting into the host tissue environment. Beside their ability to differentiate into various daughter cells, recent research has shown that various types of stem cells can influence the environment into which they are transplanted in a paracrine fashion (the "paracrine theory"), and the principle of engraftment and differentiation has been questioned [13]. In addition, a large body of literature utilizing animal models has demonstrated the ability of MSCs to migrate to injured tissues in several disease models including cardiac injury, renal failure, and skin wounds. These processes are likely to be mediated by chemokines, small signalling molecules of which it has been shown that stem cells follow a concentration gradient in their environment to "home" or to be recruited to the site of injury or inflammation, where these chemokines are released (the "homing theory") [14]. Various stem cell subtypes have been shown to express receptors for these chemokines which upon binding, prepare these cells for attachment to the endothelium and transendothelial migration at the site of injury/inflammation [15, 16].

It has been postulated that stem cells may play a role in the replacement of prosthetics in urology by preserving functional tissue or reversing disease processes to render tissues in their pre-disease, healthy status [3, 17]. Whereas artificial sphincters are currently used to treat intrinsic sphincter deficiency and penile prostheses are used to treat end-stage erectile dysfunction due to cavernosal smooth muscle dysfunction, in the future we may be able to use stem cells to regenerate functional urethral sphincter muscle and to regain lost function of the erectile tissue in patients with severe diabetes, after radical prostatectomy or in Peyronie's disease.

Stem Cells for the Treatment of Erectile Dysfunction

The most widely studied model in stem cell application for erectile dysfunction (ED) is the cavernous nerve injury model, mimicking ED following radical prostatectomy [18, 19]. This model is heavily investigated as it reflects a typically difficult-to-treat group of patients who do not respond to PDE5-inhibitors and therefore

present a medical need for further development in ED treatment. In 2004, the first experimental study investigating the injection of embryological stem cells into the corpus cavernosum and major pelvic ganglion was published by Bochinski and colleagues who found improved erectile function, while the stem cells had not engrafted in either the corpus cavernosum or the ganglia [20]. Later trials where conducted with adult stem cells such as adipose tissue-derived stem cells (ADSC) or bone marrow-derived stem cells (BMSC), and consistently showed improved erectile function in the absence of stem cell engraftment [21–23]. Even though most of the investigators injected cells into the corpus cavernosum, no cells could be detected several weeks after the injection. It was further demonstrated that these adult stem cells had effects on multiple tissues after intracavernosal injection. Stem cells where able to reverse denervation-induced loss of smooth muscle cells by prevention of apoptosis, and to reduce the deposition of collagen in the corpora cavernosa and thereby limit the fibrosis as well as preserve the elasticity of the tissue needed for an intact function of the veno-occlusive system [4]. Strikingly, while the cells were at most instances injected into the corpora, increased nerve regeneration of the cavernous nerves and increase levels of nitric oxide synthase where observed shortly after stem cell injection [16].

The latter finding stimulated researchers to investigate the fate of the injected cells. As the corpus cavernosum is a highly vascularized organ, it is likely that cells are flushed rapidly from the corpora and end up in the systemic circulation [24]. Fandel and colleagues described for the first time that these circulating cells were recruited to the major pelvic ganglia, where the cell bodies of the cavernous nerves are located, which was later confirmed by Qiu and colleagues in a pelvic irradiation model [16, 25]. It was shown that during the inflammatory response to nerve injury, chemokines are released which not only draw inflammatory cells to the injury site, but also (both endogenous and exogenous) stem cells [14]. These findings stimulated a paradigm shift from the building block theory to the paracrine theory to be applicable in this disease model. This shift in thinking was confirmed by Albersen and colleagues, and later Sun and colleagues, who obtained similar functional results after injection of either stem cell lysate, or conditioned stem cell culture medium, thereby exposing the diseased tissue to soluble bioactive factors contained in stem cells, while precluding engraftment from taking place [21, 26, 27].

While the cavernous nerve injury model is an acute injury model and results in the release of chemokines at the injury site, in chronic disease models linked to ED such as aging, diabetes and metabolic syndrome, it remains debatable whether stem cells exert their beneficial effects on erectile function by engraftment and differentiation or by recruitment and release of bioactive signalling molecules into their surroundings. Nonetheless, in ED models in chronic disease, stem cell injection has consistently shown beneficial effects on rescuing erectile function [4] These issues are discussed in more detail by Albersen et al. [4] and Alwaal et al. [28], where a more complete review of the field of cellular therapy for ED is provided.

The study of the application of both BMSCs and ADSCs have ample preclinical data, nevertheless several crucial issues must be addressed prior to the therapeutic application of stem cells. Firstly, identifying the type of stem cell which would be most appropriate considering factors such as cost, ethical issues, ease of isolation, culturing, effectiveness and source. Secondly, migration and survival of cells in the host tissue after administration as well as mode of action still requires further investigation. Thirdly, surveillance is needed for possible adverse effects of SC transplantation both potential cell growth as well as the effects of the secretome on possible concomitant subclinical pathology.

As expected after a consecutive series of successful preclinical and translational studies, human data on stem cell therapy is emerging some 10 years after the first reports on animal models. Bahk et al. in a pilot-study implanted umbilical cord stem cells in the penis of seven men with diabetes-related ED [29]. This study reported an improvement in erectile dysfunction,

with 6/7 patients regaining spontaneous morning erections after the treatment. Furthermore, blood glucose levels improved in all patients treated with stem cells, however, these results did not seem to be long-lived. Various cellular products including mesenchymal stem cells (both BMSC and ADSC), and adipose stromal vascular fraction (which contains the perivascular niche in which stem cells reside) are currently being studied in clinical trials. Recently, Yiou et al. reported a phase 1/2 trial of intracavernous bone marrow mononuclear cells (BM-MNCs) in post radical prostatectomy erectile dysfunction [30]. This study enrolled 12 subjects with penile arterial insufficiency and/or veno-occlusive dysfunction at 6 months to 3 years following treatment for localized prostate cancer. There were no significant adverse reactions and no signs of cancer recurrence. At 6 months, increased erectile function measured by the erectile hardness score (EHS) and Doppler ultrasound parameters were more pronounced in combination with pharmacotherapy. It is evident that the promising results from these early phase clinical trials need to be confirmed in larger scale clinical trials before any definitive conclusions can be drawn on the effectiveness of stem cell therapy for ED. Currently 10 clinical trials are actively recruiting patients investigating stem cell therapy for ED [31].

Stem Cells for the Treatment of Peyronie's Disease

Since previous preclinical studies in the field of ED and fibrosis had confirmed possible effects of stem cell application in fibrotic diseases, researchers postulated that the antifibrotic and immunomodulatory effects of mesenchymal stem cells may be of benefit in Peyronie's disease [32–36]. Current treatments for the chronic, stable phase of Peyronie's disease include surgical correction, with or without a graft and penile prosthesis implantation with straightening of the curvature, furthermore, collagenase injections into the Peyronie's disease plaque have resulted in curvature improvement. In the active phase however, there is very limited evidence-based therapies that can be applied to limit the progression of the disease or even halt the development of a Peyronie's disease plaque. Castiglione et al. postulated that mesenchymal stem cells, in this case ADSC where used, can modulate the host inflammatory and fibrotic response to a pro-inflammatory or pro-fibrotic insult such as injury [36]. To test this hypothesis, they injected stem cells in a rat model for Peyronie's disease in which plaques were induced by the injection of TGFβ into the tunica albuginea of rats. One day after fibrosis induction, stem cells where injected at the site of injury. They showed that stem cell treated rats did not develop fibrosis and elastosis and the erectile function of the stem cell treated cohort was preserved. Later, Gokce and colleagues confirmed that stem cells exerted their antifibrotic actions in Peyronie's disease by decreasing the expression of tissue inhibitors of metalloproteinases (TIMPs), and stimulating expression and activity of matrix metalloproteinases (MMPs) [33]. Furthermore, upregulation of interferon in these injected stem cells resulted in more pronounced effects [32]. So far the only human trial conducted so far investigating stem cell therapy for Peyronie's disease consisted of five patients without a control group [37]. The authors reported reduction of the plaque or complete disappearance in 7/10 investigated plaques. These results need to be validated in larger studies with a control cohort.

Stem Cells for Urinary Incontinence

The application of regenerative medicine for stress urinary incontinence (SUI) has been dominantly focusing on cell therapy in order to restore the natural continence mechanism in models for intrinsic sphincter deficiency [17]. The rationale behind this is that surgical correction with slings or artificial sphincters is characterized by complications such as erosion, obstructive voiding, urinary retention, and relatively high retreatment rates. The aim of (stem) cell therapy would be to replace these surgical procedures, which treat the

symptom of SUI but not the underlying disease. For intrinsic sphincter deficiency, the aim of true regenerative treatment options would be to restore the sphincter muscle to its pre-disease functional and structural status [17, 38–41]. Animal models that have been used to study stress incontinence are either birth-trauma models, consisting of vaginal balloon distention, pudendal nerve crush injury, or a combination of both, or models with direct sphincter injury, such as (electro) cauterization [42].

As the main aim of these studies is sphincter regeneration and thus formation of skeletal muscle, much attention has been given to various cells committed to the muscle lineage, which have been called variously as myoblasts, satellite cells, muscle progenitor cells, and muscle-derived stem cells (skeletal muscle derived precursor cells; skMPC), but also complete isolated or regenerated myofibres [41]. It should be noted that the actual cell preparations might differ considerably from one study to another as a result of different protocols for harvesting and culturing these cell preparations. The first study to examine whether autologous muscle precursor cells were able to assist in sphincter regeneration was performed by Yiou et al. in 2002, who injected skMPC from limb skeletal muscle to the urethral sphincter 2 days after injecting Notexin, a myotoxic substance [43]. They observed that injection of skMPC resulted in histological outcomes hinting at enhanced sphincter regeneration and the injected cells remained in these sphincters for up to 1 month. Similar results where obtained with a variety of different cells derived from muscle, in different rodent models including vaginal distention, pudendal nerve injury, and direct sphincter injury. In addition to the data from Yiou et al. later studies showed improved leak point pressure (the intraluminal bladder pressure at which the passive resistance of the urethra is overcome and leak occurs), engraftment of skeletal muscle precursor cells in the urethral sphincter, and in some cases expression of skeletal muscle markers by the engrafted cells [41]. It thus appears that when autologous and muscle-specific cell sources are used, engraftment (building block theory) does seem to be a mechanism of action of cell therapy for urinary incontinence.

One translational issue with the use of many of these skMPC, is that they require either large muscle biopsies to obtain sufficient quantities, or extensive *in vitro* upscaling prolonging the time in culture, which may harbour some risks including changes in the cellular phenotype and contamination of the culture [44, 45]. A suggested approach overcoming the issue of low cell yield may be (trans)differentiated myoblasts from other sources of stem cells such as ADSC, or the direct injection of uncommitted stem cells such as ADSC or BMSC. Injection of uncommitted mesenchymal stem cells could potentially result in *in vivo* transdifferentiation into differentiated muscle cells and fibres (building block theory), or to stimulate the host tissue to regrow by bioactive signalling (paracrine theory). Lin et al. were the first to inject autologous undifferentiated ADSC, either locally or IV, in rats after balloon distention of the vagina and they showed that ADSC homed to the affected segment of the urethra and bladder neck and where detectable there until 4 weeks after injection [46]. Later that year, myoblasts differentiated from ADSC yielded similar results and increased leak point pressures up to 3 months after injection [47]. Several later studies using both ADSC and BMSC have at multiple instances confirmed these results. For a detailed and complete overview of stem cell studies in urinary incontinence, the reader is referred to Lin et al. [41] and Klein et al. [40].

In contrast to studies in ED, the research into cellular therapy for stress urinary incontinence has rapidly progressed to larger animal models and clinical translation is well underway with several clinical trials ongoing. In 2007–08, a series of 5 clinical trials investigating both male and female patients treated with skMPC (some with co-injection of fibroblasts) showed astonishingly high cure rates of up to 90 %. However, at least two of these studies where later retracted on reasons of "critical deficiencies in the way patients' consent was obtained and source data were documented", according to an Austrian government report. In 2008, Carr and co-workers published the first human trial conducted in the USA reporting

improvement in SUI in five out of eight women who were followed-up for 1 year, with one of these women reporting total continence [48]. They later expanded their work to compare low and high-dose injections of skMPC in 33 women and reported that a higher percentage of those in the high dose versus the low dose group experienced a 50% or greater reduction in pad weight, had a 50% or greater reduction in diary reported stress leaks, and had 0–1 leaks during 3 days [49] In a pooled analysis of their phase 1 and 2 trials, the same group of authors reported that in total 80 women where investigated, and higher dose groups tended to have greater percentages of patients with at least a 50% reduction in stress leaks and pad weight at 12-months follow-up [50]. All dose groups had a statistically significant improvement in patient reported outcomes in two different questionnaires at 12-month follow-up compared to baseline. Currently, the company behind these trials is actively recruiting participants for phase 3 trials in Europe and North-America [51]

Tissue Engineering Approaches

Tissue engineering refers to the field of developing biological substitutes capable of replacing and restoring function in a damaged tissue or organ. This objective necessitates the combination of knowledge from the disciplines of material science, bioengineering, transplantation, cell and molecular biology [52]. The development of this field stemmed from the rapidly evolving field of transplantation and the lack of donor tissue. With initial concepts developing as early as the 1970s, the field grew exponentially during the 80s and 90s, following the isolation and culture of embryonic stem cells from mice and human embryos, respectively [53]. Initial work in the field showed immense promise with many successful pre-clinical animal applications involving skin replacement, and with the advancement of technology the field was able to reach clinical application in the mid 1990s [53, 54].

In general, the field involves the *ex vivo* development of constructions from biomaterials, termed "scaffolds" or "matrices", with the intention to reproduce the natural extracellular matrix (ECM) of specific tissues. These can either be transplanted and promote tissue growth *in vivo* or be expanded *ex vivo* under controlled conditions before transplantation. Matrices can be classified according to the substrate biomaterial or the origin of the tissue used for their construction. Scaffolds can be derived from the patient himself (autologous), from donors (heterologous/allogeneic), from other species (xenogenic) or synthetic materials and can also be used in combination with cells to enhance the regenerative potential. Within this section of the chapter we will discuss different approaches used in tissue engineering concerning their clinical applications in Urology.

Natural Acellular Matrices and Decellularised Scaffolds

Initial biomaterial selection focused around natural polypeptides from existing donor tissues. The concept revolves around the idea of preserving peptide domains and amino acid sequences that will retain the ability of binding cell membrane receptors, ensuing cell-ECM interactions and facilitating cell-cell interactions. This essentially will drive tissue growth and population of the matrix from cells, post-transplantation or *ex vivo* using different cell types; but also, will aid in directing differentiation of naive stem cells towards a specific cell lineage. Moreover, the use of natural materials allows the safe degradation in a normal metabolic rate, incorporating the prosthetic material in a way that mimics the natural healing process [52, 55].

Collagen has played a key role in this concept, as it is the most abundant protein in the ECM of all tissues that can be readily extracted and purified from human or animal tissues [56]. In combination to its low immunogenicity and greater pliability [57], it is an ideal biomaterial, therefore was one of the first biomaterials to be used both in animal and clinical studies. Other naturally occurring polypeptides used in the literature include the structural protein laminin [58] and the seaweed-derived polysaccharide alginate [59].

The same materials have been shown to be compatible with inkjet printer technologies [60, 61] and can also be used in combination with cells and other macromolecules to drive differentiation towards a specific cell lineage [62]. Moreover, advancements in the field of printer technologies have allowed the commercial availability of three-dimensional printing and the integration of this technology to tissue engineering applications for two-dimensional tissues (e.g. skin, cartilage), hollow tube tissues (e.g. bronchi, vasculature) and even solid organs (e.g. kidneys) [63, 64]. The major challenge of this approach is to produce a matrix that reproduces the ECM micro-architecture to a functional degree. For tissues that are part of the urinary tract, this can range from the simpler tubular structures (e.g. urethra, ureters) to extremely complex tissue patterns (e.g. kidneys).

A potential solution to this issue was the development of scaffolds obtained from donor tissues, the subsequent removal of the cellular components by mechanical, enzymatic and/or chemical means, resulting in a "decellularised" ECM that is capable of retaining the composition and microarchitecture to some extent of the original tissue [65]. Several organs have been studied using this methodology, including lungs [66], liver [67], heart [68], kidneys [69], small intestine [70], oesophagus [71], urinary bladder [72] and tissues such as the urethra [73], the trachea [74] and blood vessels and heart valves [75]. The vast majority of the above studies demonstrate that the micro-architecture of the ECM can be preserved facilitating the incorporation of cells into the matrices. Moreover, the preservation of additional ECM components, such as elastin, glycosaminoglycans (GAGs) and growth factors, additionally support the attachment, migration and proliferation of added cells. However, decellularisation treatments could potentially affect the degradation rate of the produced matrix *in vivo*, as specific polypeptide sequences susceptible to enzymatic degradation are exposed due to the treatment with decellularisation agents [65]. Despite the combination of decellularisation treatments, it is very unlikely to remove completely all cellular material from the source tissue, negligible immunogenicity has been observed post-transplantation at pre-clinical level animal studies [67, 76] and in clinical applications [77]. Notable clinical applications using this methodology have been in the field of transplantation of tissue engineered airway [78] and bladder augmentation in patients requiring cystoplasty [79]. Specifically in urology, natural acellular and decellularised scaffolds have been used for the reconstruction of the urethra, bladder and penile structures, such as the tunica albuginea and the corpora cavernosa [80].

Experimental animal studies involving reconstruction of the penile urethra using collagen based-acellular matrices on rabbits has found that in large defects the matrix contracts and can create stenoses or strictures. Dorin et al. concluded that with tubularised acellular matrices the regeneration capacity of the adjacent epithelium appears to be limited by the length of the graft and was found to be at 0.5 cm [81]. In contrast, when these acellular scaffolds are applied in an onlay fashion for urethral reconstruction, the scaffolds appear to be beneficial in patients with abnormal urethral conditions such as urethral strictures [82] and in patients with hypospadias who had undergone a previous repair [83]. A more recent study from Brazil comprising 44 patients with long and complex urethral strictures who received cadaveric urethral acellular matrix onlay grafts and were followed up for a median of 42 months; end points showed that 88 % (39/44 patients) successfully voided after catheter removal with improved peak flow rates, there was a 5 % graft infection rate and 20 % of patients required urethral dilatations with 5 out of 44 patients having a complete restenosis and requiring reoperation [84].

To overcome this issue, studies have focused on a combination of matrices with autologous cells from several sources including autologous bladder epithelial cells, bone marrow mesenchymal stem cells, lingual keratinocytes and buccal musosa cells [85, 86]. It was recently demonstrated by De Filippo et al. that tubularised acellular scaffolds obtained from decellularised bladder in combination with autologous epithelial and smooth muscle cells from the bladder can be used successfully in long segment reconstruction of the urethra [87].

Despite the complex and unique architecture of the phallus, natural acellular scaffolds have been investigated for their use in reconstructing the corpora cavernosa. Initial approaches included segmental replacement with decellularised rabbit corpora seeded with human corporal endothelial and smooth muscle cells, which were incorporated successfully in nude mice retaining the ability to contract [88]. Due to the dynamic function of the corporal tissues, the reduced cellular component of the prepared grafts was found to be limiting the functionality of the engineered corpora. A solution to this problem was given by the incorporation of a "bioreactor", a specialised automated culture incubator which can mimic the biochemical and biomechanical function of the tissue to be expanded *ex vivo* offering dynamic cell seeding [89]. The bioreactor applied to tissue engineered corpora by Eberli et al. led to improvements in the cellular content and functionality of the corporal tissue [90]. The same group, with a more comprehensive study were able to demonstrate that the entire pendulous penile corpora can be engineered in rabbits using decellularised donor corpora seeded with autologous corporal endothelial and smooth muscle cells, showing structural and functional outcomes analogous to native tissues [91]. Recipient rabbits were able to impregnate females demonstrating an immense potential for patients in need of penile reconstruction.

A potential application of this technology could benefit patients with penile deformities, particularly those with Peyronie's disease. The current surgical management often involves excision of the tunica albuginea on the contralateral side or incision of the plaque combined with grafting of autologous or cadaveric materials including small intestinal submucosa, pericardium, dura and fascia lata with variable outcomes [92]. Schultheiss et al. have demonstrated in a porcine model using acellular collagen matrices seeded in a bioreactor with porcine fibroblasts that a homogeneous multi-layered tissue engineered graft, which can withstand axial strain in a specific direction can be produced [93]. Similarly Joo et al. demonstrated that bladder decellularised matrices can be used as grafts in rabbits for tunical defects with excellent healing without contracture and complete fusion of the graft at 6 months post-implantation which is indistinguishable histologically from the native tunica [94].

The bladder is an organ often prone to reconstructive surgery. Diseases affecting the bladder render it fibrotic and contracted, which can affect the patients quality of life and often requires surgical intervention to augment its capacity and relieve pressure in the upper urinary tract. Since the development of the first free tissue grafts in 1917 by Neuhof [95], several approaches were developed employing different materials such as small intestine submucosa, pericardium, dura and placenta [85]. The commonest material currently used is a segment of small bowel, complete with its vasculature, in a procedure called "enterocystoplasty" which is still associated with complications, including electrolyte abnormalities, infection, stone formation and an increased long-term risk of cancer, as the intestinal mucosa appears not to be compatible with continuous urine exposure [96].

Engineering the urinary bladder was fundamental in regenerative medicine as it was the first laboratory-grown organ to be transplanted into humans [79, 97]. The innovative method of using decellularised bladder submucosa collagen scaffolds seeded with autologous urothelial and smooth muscle cells, resulted in successful integration in patients with myelomeningocele [79]. Improvement of outcome was observed in patients whose augmentation also included covering with omentum to improve the vascularization of the scaffold. Following this study, other groups have used non-seeded small intestine submucosal (SIS) matrices in bladder extrophy patients [98], cloacal exstrophy repair [99], and those with spina bifida and spinal cord injury [100]. From these studies which used acellular collagen based scaffolds, bladder wall regeneration was achieved histologically, bladder capacity had increased in 17 out of the 19 patients in total. In terms of complications occurring in the 3 studies, 2 out of 19 patients had non-febrile urinary tract infection, 2 patients had struvite bladder stones formed and 1 patient suffered a bladder

rupture. All the groups have indicated the need for further studies concerning the use of acellular scaffolds for bladder augmentation; however, they all agree that with the current knowledge bladder augmentation using SIS acellular scaffolds cannot serve as a substitute for enterocystoplasty. Considering this data and data from pre-clinical animal studies [101], cell-seeded matrices could provide better results.

Biodegradable Synthetic Polymers

Synthetic biomatrices can be broadly divided into synthetic polymers, natural polymers (e.g. silk fibrin, glycosaminoglycans) and composites. Synthetic polymers can be further divided into polyesters of naturally occurring α-hydroxy acids, including polyglycolic acid (PGA), poly-lactic acid (PLA), and poly-co-glycolic acid (PLGA), polylactones, polyurethane (PU), poly(anhydrides) and poly(ortho-esters) [102]. The polymers are of immense interest in tissue engineering due to their numerous and long-standing clinical applications (e.g. absorbable sutures) and their biocompatibility [103]. Moreover, the potential for large scale production to custom controlled properties in terms of structure, durability and degradation rate, makes synthetic polymers attractive for tissue engineering strategies producing "off-the-shelf" matrices [80, 82].

As these polymers are held together by ester bonds, degradation occurs by non-enzymatic hydrolysis. For PGA, PLA and PLGA who are the most widely used polymers, degradation results in non-toxic natural metabolites such as lactic acid and glycolic acid, which can be further metabolised and excreted as carbon dioxide and water or by renal excretion in urine [104]. The rate of degradation is determined by the chemical structure, copolymer ratio, crystallinity, molecular weight, porosity and site of implantation [103]. The pliability of these materials, allows them to form three-dimensional scaffolds with the desirable microstructure, shape and dimension, depending on the fabrication method used. Several methods have been investigated including foaming, three-dimensional printing, phase separation, emulsion freeze-drying and electrospinning [105]. Biocompatibility has been assessed both *in vivo* and *in vitro* with most materials exhibiting no inflammatory response, but cell behaviour depends on the synthetic material used [106]. The major drawback of these materials is the lack of biologic recognition that may limit the regenerative potential of the engineered grafts [107].

The use of synthetic polymers for urethral reconstruction started as early as 1983 in animal pre-clinical studies, using a woven mesh from PGA (Dexon™ Mesh), with the authors reporting successful regeneration of urethral tissues indistinguishable from adjacent urothelium at 6 months post transplantation in 7 mongrel dogs [108]. PGA in combination with polyhydroxybutyric acid has also been shown to regenerate the urothelium, smooth muscle and vasculature following excision in dogs [109]. In 1992, Atala et al. were able to demonstrate that urothelial cells can be cultured on PGA non-woven mesh achieving spatial orientation and the mesh could be used for the culture of autologous urothelium and in reconstructive procedures involving the ureter, bladder and urethra [110]. Following that, several scaffolds from different synthetic materials and combinations have been used for seeding urothelial cells [111]. In one study, the composite thin film poly-L-lactide (PLLA) with electrospun polycaprolactone(PCL) was able to achieve better urothelial cell attachment, proliferation and differentiation when compared to small intestine submucosa or PLLA alone [112].

An interesting approach for phallic reconstruction was shown by Yoo et al. by incorporating bovine chondrocytes seeded onto PGA rods and implanted in mice, producing a durable, elastic cartilaginous structure that withstands high degrees of pressure [113]. The concept was applied to a rabbit model, by harvesting autologous chondrocytes from the ears and seeding them onto PLA coated PGA polymer rods and implanting them directly into the corpora of 10 rabbits. The scaffolds degraded by 2 months with mature chondrocytes incorporating into the corpora cavernosa, suggesting that this can serve as a model for the construction of autologous penile prostheses [114].

Synthetic polymer scaffolds have been used in five paediatric patients with posterior urethral strictures requiring urethral reconstruction using tubularised 50:50 PGA:PLGA composite scaffolds seeded with autologous urothelial and smooth muscle cells. The procedure was successful in 4 out of 5 patients at first attempt with one of the patients requiring a urethrotomy 4 weeks following surgery [115]. This was the first clinical observational study involving the use of tubularised urethral scaffolds in humans, with very encouraging results [111]. In addition, a composite collagen:PGA scaffold seeded with autologous cells with omental coverage was also used in 3 of the 7 patients in the pilot study of using tissue engineered bladders in paediatric patients with neurogenic bladder (myelomeningocele). According to the authors, all patients showed increased bladder capacity, compliance, decreased end-filling pressures and longer dry periods, but the ones receiving the composite engineered bladder had a better outcome than the ones receiving the decellularised collagen matrix [79].

Additionally, a phase II study with 10 patients with myelomeningocele (neurogenic bladder) who received a PGA matrix seeded with autologous urothelial and smooth muscle cells, was used to assess the safety and efficacy of the use of engineered bladder for augmentation purposes [116]. The patients were followed up at 12–36 months with the results revealing no significant improvement in the bladder capacity and bladder compliance, with all patients having at least one urinary tract infection during the trial, 3 patients developed bowel obstruction and 2 patients suffered a bladder rupture, requiring further surgical interventions. The authors concluded that no statistical or clinically significant improvement was observed and the severe adverse events associated with this trial "surpassed an acceptable safety standard". At the end of the trial, 2 patients had conventional augmentation (enterocystoplasty), 3 were scheduled for conventional augmentation, 2 decided not to have any additional surgery, 1 was stable and 2 had urodynamic studies scheduled with plans for augmentation [116]. A possible explanation of these results may be the quality of cells obtained from the patients, as it was shown that diseased bladder cells do not have the same regenerative capacity as healthy urothelium [117]. Thus, different sources of cells might be required for the successful reconstruction of the bladder in diseased states.

3D Nano-Fibrous Scaffolds

Despite their common use, biodegradable synthetic materials have no effect on cell behaviour and cell spatial organisation, lacking the potential to guide differentiation of naive stem cells on their own. In addition, current processing techniques exhibit limitations in producing a microenvironment that is comparable to the native ECM, in terms of fibre alignment and dimension, with native ECM ranging from 50 to 500 nm and polymer fibres having a diameter of >10 μm [118]. Therefore, there is a failure to reproduce the geometry of ECM tissues to be engineered. A potential solution to this issue could be provided by the use of nanofibers that can be produced by self-assembly, thermally induced phase separation (TIPS) and electrospinning [118, 119].

Due to the simplicity of electrospinning, this technique has attracted interest in the field of tissue engineering and a wide variety of synthetic and natural materials have been used with this method to form nano-fibrous scaffolds. These include PLLA, PLGA, PCL, gelatin, collagen, silk protein and polyethelene oxide [119]. By means of an electrical field the polymer in a solution form is attracted through a slit into a collecting system, producing nanofibers of predefined diameter ranging from micrometres to nanometres [118]. The production of such scaffolds has been shown to be compatible with the *in vitro* culture of urothelial cells with further *in vivo* investigations on going [112]. Moreover, electrospun collagen, silk and composite collagen-silk scaffolds have been shown to accommodate human endometrial stem cells and assist in their differentiation towards a urothelium cell lineage, in terms of urothelial gene transcription, for potential use in bladder wall reconstruction [120].

The use of scaffolds produced by molecular self-assembly, a method where under specified

conditions biomolecules interact and self-organise to form functional architectures, is limited by the inability of this method to produce macropores for the accommodation of cells. TIPS on the other hand, which involves polymer dissolution, phase separation and gelation, solvent extraction, freezing and drying under vacuum, produces a nano-fibrous matrix in the range of the native ECM [119, 121] Another major advantage of TIPS is the combination with other processing methods for scaffolds including 3D printing for the construction of complex 3D structures with well-defined structures and pore morphology [63, 119] .

Another material of potential use in tissue engineering are the carbon nanotubes. These are nanometre-thick long (>100 nm) cylindrical carbon tubes with a wide range of electronic, thermal and structural properties. Their use in tissue engineering could be valuable in terms of cell tracking and labelling, in sensing cellular behaviour, modifying and influencing cellular behaviour (e.g. stem cell differentiation), and structural enhancement of matrices. However, several studies, have shown that carbon nanotubes may be cytotoxic and current research aims to develop ways to render this material safe for biomedical applications [122]

Xenogenic Extracellular Matrix

Xenogenic extracellular matrices have been in use for more than 25 years now, successfully treating conditions affecting the upper and lower urinary tract. Essentially by following the concept of decellularisation (described above), ECM from other mammals comprises the same constituents, enabling regeneration of seeded cells from human sources. Immune response against acellular xenografts has been studied extensively, exhibiting predominantly a T-helper 2 cell response, which aids in graft acceptance and effective tissue remodelling [123].

SIS and bladder submucosal matrix (BSM) both obtained from pigs, have been used in humans for several pathologies including urinary incontinence [124, 125], prevention of complications following partial nephrectomies [126, 127] and bladder augmentation [79]. Specifically, SIS use has been shown to benefit 22 patients who underwent partial nephrectomies where there is involvement of the collecting system, aiding in the closure of the pelvicalyceal system through angiogenesis, urothelial regeneration and organised ECM deposition [127]. The same conclusions were made by Simon et al. in a study of 53 patients who underwent nephron-sparing surgery where SIS was used to cover the tumour excision site with the additional benefit of better haemostasis [127].

In a study treating urinary stress incontinence, 142 out of 152 patients treated with a SIS pubovaginal sling reported complete resolution of symptoms was achieved without any postoperative complication [123]. However, a further study comparing the use of an acellular porcine dermis pubovaginal sling approach to the autologous rectus fascia sling, concluded that acellular porcine dermis should not be used due to significantly inferior long-term cure rates [125].

Scaffold-Free Grafts

The development of a temperature-responsive polymer, poly-N-isopropyl-acrylamide (PIPAAm) served as the medium for an exciting technology where cells could be cultured *in vitro* on the polymer and on changing the temperature, the cells detach from the polymer as a cell sheet [128]. This avoids the use of biomaterials avoiding foreign body responses and delayed tissue remodelling [129]. The technology was first used clinically in tissue engineering of the cornea using autologous oral mucosal epithelium, achieving transparent surfaces without complications during a mean 14 month follow-up [130]. The technology has also been used for the development of functional three dimensional liver systems using hepatocyte sheets [131].

This particular technology was recently used for the culture of rabbit bladder smooth muscle cells and the subsequent transplantation of the cell sheet onto rabbits who had a partial detrusorectomy. The grafted cells were fluorescently

labelled to identify their contribution to bladder wall regeneration. Histologically, from 4 weeks post-transplantation the muscle layer was well organised at the site of implantation [132]. From this study and from other examples of this exciting new technology, many other potential applications could be investigated in the field of urology. For instance, the use of fibroblast sheets in the treatment of Peyronie's disease, or the culture of urothelial cell sheets and tubularisation for the reconstruction of ureters or the urethra.

Additional Approaches

Penile Implants

Current treatment regimens for ED with PDE-5i have proven to be sufficient for a vast number of patients, with some others that are "non-responders" (pharmacologically refractory ED) seeking further treatment options, often involving invasive procedures [3]. Several mechanical and pharmacological non-surgical methods have been developed throughout the years, including vacuum erection devices, intracavernosal injections, intraurethral pellets and gels; however, penile prostheses are considered as the gold-standard therapy for end stage ED [133, 134]. Research on erectile technologies have investigated other non-surgical options including penile vibratory stimulation, low intensity extracorporeal shockwave, impulse magnetic field therapy. These methods are promising but further clinical studies are needed to assess effectiveness, ease of use, adverse effects and long term complications [134].

Penile implants have been described in the literature as early as the 1500s, with initial approaches during the 1930s involving implantation of rib cartilage, acrylic and polyethylene; later in the 1960s the extensive use of silicone for implants, which were more biocompatible, and in the 1970s there was the introduction of the inflatable penile prosthesis [133, 135]. Use of penile prostheses has proven to be effective in the treatment of ED, however it includes significant risks such as infection and erosion that may demand removal of all prosthetic materials [80, 136]. Several enhancements have been developed to tackle weaknesses identified for each implant device, with current options including polyurethane coating, antibiotic prosthetic lining incorporation and hydrophilic coating, which are aimed at improving outcomes and reducing infection rates [133].. Selph and Carson, in 2011, have estimated that the infection rate for primary penile prostheses ranges between 1 and 3 %, with this increasing to 13.3 % for revision cases [137].

The most recent development, using a new approach to reduce infection rates in revision cases, was demonstrated by Swords et al. using a novel temporal intracorporal cast made of synthetic high purity calcium sulfate (SHP $CaSO_4$) which allows structural support and continuous delivery of antibiotics/antifungals post-penile prosthesis explantation [138]. The cast dissolves after 4–6 weeks and can be used for the period between the explantation of the infected material and the re-implantation of a new prosthesis, so as to reduce infection rates and maintain the intracoporal space which would otherwise undergo fibrosis and penile length loss [134, 138]. As this cast has only been used in two patients with satisfactory results, further investigations are still warranted prior to considering this as a routine option.

Other materials have also been investigated for the development of new penile implants with a nickel-titanium based shape memory alloy (SMA) being one of the most innovative approaches [134]. The SMA penile prosthesis, first described by Le et al. at the 2013 Annual Meeting of the American Urological Association, has the ability to change configuration between flaccid and erect with the application of heat, eliminating the need for a reservoir and scrotal pump [139]. The authors also showed comparable results when comparing the mechanical properties of the SMA to the current 3-piece devices and malleable prostheses [134, 139]. The SMA is a very attractive technology that could provide an additional treatment option for patients with ED and the lack of additional components would likely reduce the infection and mechanical failure rate.

Testicular Prostheses

Testicular prostheses were first used in 1941, in a 27 year old single man 3 years after his

orchiectomy as a result of trauma [140]. The material used was a combination of metals (vitallium; a non-ferrous alloy of chromium, cobalt and molybdenum), which resulted in the alleviation of the psychological symptoms but the testicular prosthesis was also colder and more solid than the other remaining testis. It was clear from this very first application of a testicular prosthesis that there was a demand for a more natural feeling prosthesis. Other materials have included glass marbles, plexiglass, dacron and polyethylene, without much success, until the use of silicone gel filled and silicone elastomer implants [141]. Due to safety concerns in the US following gel leaks from breast implants, saline-filled prostheses were developed to provide an alternative option for patients [141].

A recent study assessing patient satisfaction with testicular prostheses following testicular cancer revealed a high overall satisfaction in more than 80 % of the patients, but particular aspects were identified as problematic including the firmness/consistency of the implant (52.4 %), issues with the shape (15.4 %), size of the implant (23.8 %) and the high position of the implant in the scrotum (30.3 %) [142]. Therefore, newer materials are still required to achieve better satisfaction rates, with manufacturers currently developing newer implants such as hormone-releasing testicular prostheses for patients with congenital or acquired bilateral anorchia. Moreover, regenerative medicine can also play a role in testicular prosthesis development with a recent study showing the development of a cytocompatible decellularised testicular matrix, derived from cadaveric human tissue, which can potentially act as a scaffold for engineering a functional testis in the lab or be used for *in vitro* spermatogenesis [143]. In addition, other materials could be used for the development of hormone-releasing testicular prosthesis, as demonstrated by Raya-Rivera and colleagues in 2008, were bovine chondrocytes were isolated, expanded into a testicular shaped polymer scaffold using a bioreactor and converted into milky white cartilage testicular prostheses. Testosterone was added to the prepared prostheses and these were transplanted in mice with a sustained testosterone release [144]. Further investigations are required before these concepts reach pre-clinical and clinical applications.

The Future

While technology advances rapidly, the field of regenerative medicine gains additional knowledge from new and exciting technologies. One of these examples is highlighted by a recent animal study in which optogenetics, a combination of optics, genetics and cell biology and a branch of the new field of synthetic biology, were used to provide a solution for ED. Kim and colleagues, engineered an erectile optogenetic stimulator, a protein that can be induced by blue light to produce the secondary messenger cyclic guanosine monophosphate, an important signalling molecule for penile erection [145]. As this synthetic protein can be delivered directly into cavernosal cells, by means of transfection of DNA, it bypasses physiological control and the various causes of ED, inducing an erection on demand simply by the application of an external source of light [145]. This exciting new technology has a long way to go before it can be considered as a treatment option for patients with ED, but it highlights our progressive expansion in knowledge, but also the demand to find newer, simpler and effective solutions. With current clinical applications of regenerative medicine identifying potential issues with this approach, further studies are anticipated to provide solutions for the challenges ahead.

Conclusions

Regenerative medicine promises to provide solutions for a number of urological conditions in the future. A number of researchers have focused their attention on regenerative medicine, incorporating cell-based therapies, tissue engineering and many other technologies, to achieve a holistic solution for the functional replacement of damaged tissues/organs. With the publication of proof-of-concept studies, animal studies and a few clinical studies, the field has shown immense progress over the

last decade. However, further safety and efficacy assessments are warranted before the widespread use of these technologies for the treatment of patients. More studies generating new knowledge and combining approaches are awaited to overcome challenges identified thus far.

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