Review Article

Prevention of urinary tract infection in patients with spinal cord injury – a microbiological review

A Galloway

Public Health Laboratory, Institute of Pathology, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne NE4 6BE, England, UK

The importance of urinary tract infection (UTI) in patients with spinal cord injury cannot be understated. Many patients with significant bacteriuria are considered to be colonised rather than infected, and treatment should be reserved for those with clinical symptoms or other signs of infection.¹ Published research on the prevention and management of UTI in patients with spinal cord injury often has limitations due to differences in definitions of UTI, studies on groups using different urinary drainage appliances, the mixture of newly injured and longstanding injured patients and studies being carried out predominantly on male patients.² The complications due to UTI and the difficulties in treating established infection mean that prevention is essential. Close urological follow-up is crucial in ensuring that adequate bladder drainage is achieved avoiding the use of long term indwelling urinary catheters if at all possible.³ For those patients who require long term urinary appliances patient education and strict attention to hygiene and catheter care policies is important. The role of antiseptic/antibiotics is strictly limited in preventing UTI in patients with spinal cord injury and may even be harmful. Further study into which groups of patients may benefit from the use of antiseptics or antibiotics is urgently required. Continued research into different methods of prevention eg by vaccination, immunotherapy, the use of receptor analogues and bladder interference should also be encouraged.

Keywords: spinal cord injury; urinary tract infection; prevention

Introduction

Urinary tract infection remains a major cause of morbidity in patients with spinal cord injury⁴ although with improved management mortality from urinary sepsis is reducing.⁵ The normal human bladder is inherently resistant to infection through a number of defence mechanisms and the development of UTI therefore depends upon the balance between bacterial virulence and host defences.⁶ Host defences include the mechanical effect of flushing the urine; cell mediated immunity; local production of immunoglobulin in the bladder wall and the mucous lining of the bladder also offers a protective effect. When host defences are seriously compromised by defective bladder emptying or by the presence of a urinary catheter, vesicoureteric reflux or stones then the individual is likely to be susceptible to virtually any organisms that can invade the urinary tract, irrespective of the presence or absence of any bacterial virulence factors.⁶ The formation of bacterial biofilms containing aggregates of micro-organisms in the bladders of spinal cord injured patients who require catheterisation may explain why infection, once established, is often persistent and apparently resistant to antibiotics.⁷ The

presence or absence of symptoms may be a poor guide to the damaging effect of bacteriuria on the bladder epithelium.⁸ UTI most commonly results from ascending transurethral invasion of the bladder by pathogenic organisms normally present in the gut. Ascending infection is preceded by colonisation of the introitus or periurethral area or migration of bacteria within the urinary collection system.

Bladder drainage

Correct management of the bladder in the early stages following spinal cord injury is particularly important. Preservation of renal function is the ultimate goal and the choice of bladder drainage is particularly important in reducing the incidence of UTI.^{9,10} Ideally the patient is appliance free but the use of indwelling catheterisation may be necessary. The incidence of bacteriuria in the patient with a longterm indwelling catheter (ie >28 days) is high and has been reported as approximately 98%^{11,12} and mixed populations of bacteria are frequently isolated.¹³ Bacteriuria is associated with both acute and chronic

complications including bacteraemia, acute pyelonephritis, bladder and renal stones, vesicoureteric reflux, chronic interstitial nephritis, renal failure and death.^{12,14} Indwelling catheters should therefore be used for as short a time as possible and consideration should be given to the use of intermittent or fine bore supra-pubic catheterisation or condom drainage as these methods appear to be associated with lower rates of bacteriuria¹⁵⁻¹⁷ and fewer complications.¹⁸ Other procedures which facilitate adequate bladder emptying may be used eg surgery to relieve urinary outflow obstruction, the use of electrostimulation, reflex voiding or pharmacological agents acting on the bladder or its sphincters. Low residual volumes are associated with lower rates of UTI.¹⁹ Close urological follow-up at a specialist centre is essential to maintain satisfactory bladder and renal function and prevent complications.^{20,21}

Catheter care and infection control

The importance of hygienic catheter care using a closed drainage system,²² hand hygiene, staff and patient education has been well recognised as being important in preventing UTI.²³ In addition the team approach to bladder management has been highlighted.²⁴ Table 1 summarises the recommendations for prevention of catheter-associated UTI.

In spinal cord injury centres there is often widespread contamination of the environment with gram

negative bacilli which are often multi-resistant. Sanderson and Rawal found extensive contamination of the patients environment with the same organism which had previously been isolated from the patients' urine.²⁵ Environmental contamination was found in face cloths, clothing, wheelchairs and on bedside lockers. Contamination of the hands of staff and patients can therefore readily occur and lead to cross-infection.^{26,27} The importance of hand-washing as a primary infection control measure in preventing cross-infection has been emphasised and re-emphasised by several workers in the last century.²⁸

Choice of catheter

There has been recent interest in the development of catheter materials which would prevent encrustation and the formation of biofilms. However Ramsey and colleagues reported encrustation and the development of biofilms on all types of catheter materials routinely used including plastic, latex, teflon-coated latex and silicone.²⁹ Roberts *et al* in an *in vitro* study reported that bacterial adherence to hydrophilic coated latex catheters did not occur and recommended their use.³⁰ Other types of catheters which have also been investigated include a lubricating catheter (into which a mixture of methyl cellulose and polymixin B is inserted); vented catheters; silver oxide-coated catheters and catheters impregnated with antiseptics or antibiotics.³¹ None of these have been adopted for routine use although research continues into the different catheter designs.

The use of topical antiseptics

Patients with spinal cord injury soon develop colonisation with gram negative bacilli. Fawcett *et al* showed that the perineum, groins, penile shafts and urethras were heavily colonised by a range of multiply resistant gram negative bacilli which started to colonise 2-3 days after admission.³² They also found that the same species of bacteria could be demonstrated colonising the skin prior to the development of UTI. It is desirable therefore to attempt to ensure that the external meatus around the catheter is kept clean and free from encrustation.³³

The use of topical antiseptics (eg chlorhexidine or silver sulphadiazine) applied to the perineal area and/or urethra prior to catheterisation has proved disappointing in preventing bacteriuria, although widely practised.^{34,35} Equally the use of medicated soap,^{32,36} and antiperspirants³⁷ has been unsuccessful in preventing bacterial colonisation. It would be reasonable however to promote cleanliness and local hygiene by daily perineal washing with soap and water. The removal of an external urinary collection system at night time has been shown to reduce urethral colonisation with *Pseudomonas* but not with *Klebsiella* but has no effect on the incidence of bacteriuria.³⁸

Table 1 Summary of the major recommendations for prevention of catheter-associated urinary tract infection (Wong & Hooton, 1981)²²

Category I. Strongly recommended for Adoption

Educate personnel in correct techniques of catheter insertion and care

Catheterise only when necessary

Emphasise hand washing

Insert catheter using aseptic technique and sterile equipment

Secure catheter properly

Maintain closed sterile drainage

When irrigation is necessary, use intermittent method

Obtain urine samples aseptically

Category II. Moderately Recommended for Adoption

Periodically re-educate personnel in catheter care

Use smallest suitable bore catheter

Do not perform continuous irrigation as a routine infection-control measure

Refrain from daily meatal care

Do not change catheters at arbitrarily fixed intervals

Category III. Weakly Recommended for Adoption

Consider alternative techniques of urinary drainage before using an indwelling urethral catheter

Replace the collecting system when sterile closed drainage has been violated

Spatially separate infected and uninfected patients with indwelling catheters

Avoid routine bacteriological monitoring.

Antiseptic solution in drainage bags

The use of antiseptics in catheter drainage bags to prevent bacteriuria has also been reported. *In vitro* studies have indicated that a formaldehyde preparation may be effective.³⁹ *In vivo* studies with chlorhexidine have however proved disappointing.⁴⁰

Hydrogen peroxide seems of benefit in those requiring short term drainage only.⁴¹ Giroux and Perkas, however, found hydrogen peroxide unsatisfactory when used for leg bags in patients with spinal cord injury as the gas released (as a result of the breakdown of the hydrogen peroxide) caused inflation of the drainage bag with subsequent impairment of drainage.⁴² In addition they reported that povidone-iodine although apparently effective *in vitro* was not successful *in vivo* in preventing bacteriuria. Also some patients developed iodine allergy and the discolouration of the drainage bag made it difficult to make a visual assessment of the state of the urine. They recommended the use of 0.06% sodium hypochlorite for the surface disinfection of the urinary drainage bag and 6% household bleach to clean re-usable bags (followed by thorough rinsing with water).⁹

Bladder washouts or instillations

The use of bladder washouts or instillations with a variety of substances has also been recommended to prevent the formation of debris and stones and to prevent and control infections. Suby-G solution (containing citric acid 3.25%) twice weekly has been advocated by some workers to help prevent encrustation of the catheter especially in the early weeks following spinal cord injury when hypercalciuria may occur.⁴³

A number of antiseptic and antibiotic solutions have been suggested for instillation into the bladder after intermittent catheterisation. Haldorson and colleagues however, reported no benefit in using neomycin instillations as they did not reduce the incidence of bacteriuria.⁴⁴ Pearman *et al.* later suggested that Trisdine (chlorhexidine 0.01% with EDTA) was preferable to use than kanamycin/colistin as it was more stable at room temperature, less likely to select antibiotic resistant bacteria and less expensive.⁴⁵ There has been some success reported with the prophylactic use of chlorhexidine bladder washouts in patients undergoing short term catheterisation. However many workers have reported chlorhexidine resistance in bacteria isolated from the urine of catheterised patients.⁴⁶ There has also been little success in using antiseptic bladder washouts in treating established infection in patients requiring long-term indwelling catheterisation.^{47,48}

Stickler and co-workers studied antiseptic resistance in their Unit. They found noxythiolin to have poor clinical activity and approximately 10% of their urinary isolates showed resistance to cationic antiseptics (chlorhexidine, cetrimide and benzalkonium

chloride).^{48,49} Their more recent work using a bladder model suggested that mandelic acid (1%) may be useful as a bladder washout.⁵⁰

The use of bladder washouts or instillations is not without problems. There is an increased risk of infection from frequently breaking the closed drainage system; the problem of bacterial resistance; chemical cystitis may occur and mechanical damage to the bladder (from disruption of the mucosal cells and damage to the protecting mucous layer) may facilitate bacterial invasion into deeper mucosal layers.⁵¹ For those patients with long-term indwelling catheters it is likely that the physical effects of a washout may be more important than the action of any local antiseptic especially in controlling the formation of debris.

Oral antiseptic, acidifying and alkalinising agents

Oral antiseptic, acidifying or alkalinising agents are often used in patients with spinal cord injury. Methenamine salts (mandelate and hippurate) are antiseptics which have been widely used. They act by releasing formaldehyde in an acid urine. This has theoretical advantages as bacterial resistance to formaldehyde does not develop, there is no effect on the bowel flora and it is relatively inexpensive.^{52,53} Kevorkian *et al.* reported that methenamine mandelate (given with ammonium chloride for acidification) was an effective prophylactic agent and significantly reduced the incidence of UTI in patients with neurogenic bladders.⁵⁴ Krebs and co-workers found oral methenamine with bladder instillations of hemiacridin (to acidify the urine) were effective in reducing the incidence of bacteriuria in patients undergoing intermittent catheterisation.⁵²

There is no consensus of opinion on the use of ascorbic acid as an acidifying agent.⁵⁵ McDonald and Murphy reported that ascorbic acid was superior to methionine in acidifying the urine of catheterised patients.⁵⁶ Nickey studied the effect of giving subjects cranberry juice and ascorbic acid (alone or in combination), on urinary pH.⁵⁷ He found that essentially the same degree of mean lowering of pH occurred when these were used alone or in combination. Others however, have reported that ascorbic acid was not an effective urinary acidifier⁵⁸ or effective in preventing UTI.⁵⁹ Pearman and England equally did not find ascorbic acid useful and recommended ammonium chloride or methionine as acidifying agents for their patients.⁵³ Grundy and Russell recommended the use of ascorbic acid or hexamine (methenamine hippurate) for use in patients with spinal injury with recurrent urinary tract infections.⁶⁰

Alkalinising agents eg sodium bicarbonate, oral citrate, and acetazolamide have also been used. The activity of aminoglycoside antibiotics (eg gentamicin) is increased in alkaline urine and these agents have been recommended for patients receiving treatment. Unfortunately, the use of alkalinising agents is likely to predispose to the formation of debris or urinary

stones and is contraindicated in patients with poor renal function. The effectiveness of acidifying or alkalinising agents is, however, influenced by diet and needs to be taken into consideration when managing the individual patient.⁶¹

Prophylactic antibiotics

In the catheterised patient the prophylactic use of antibiotics reduces the incidence of bacteriuria initially and success has been reported using trimethoprim, sulphamethoxazole or nitrofurantoin;⁶² ampicillin;⁶³ norfloxacin⁶⁴ and ciprofloxacin.⁶⁵ Studies on the long term efficacy of prophylactic antibiotics have, however, shown no benefit either in reducing the rate of bacteriuria,⁶⁶ or symptoms.^{67,68} Their use in a patient with an indwelling catheter is, therefore, not generally recommended.^{10,35,69}

The use of prophylactic antibiotics for patients receiving intermittent catheterisation is controversial. Thorsteinsson and Keys reported no success in preventing infection for patients receiving trimethoprim-sulphamethoxazole.⁷⁰ Similarly Kuhlemeier *et al.* found no benefit in the use of trimethoprim-sulphamethoxazole, nalidixic acid, methenamine hippurate or nitrofurantoin.⁵⁹ Others have found that irrespective of the method of bladder drainage prophylactic trimethoprim-sulphamethoxazole does not reduce the incidence of symptomatic UTI but does increase the incidence of resistant isolates in asymptomatic patients.^{71,72} Reid *et al.* reported that prophylactic trimethoprim-sulphamethoxazole was not effective in preventing UTI but found that ciprofloxacin was particularly able to penetrate adherent biofilms and suggested it may be an appropriate agent to use.⁷ Biering-Sorenson and colleagues also found ciprofloxacin to be a useful prophylactic agent.⁷³ Some workers have found nitrofurantoin useful in preventing UTI.^{74–76} Linden and Joiner however, considered *Pseudomonas aeruginosa* as a coloniser and not a 'uropathogen' and dismissed its significance.⁷⁵ *Pseudomonas aeruginosa* cannot however always be assumed to be harmless as in one study it was found to be the commonest organism associated with symptomatic UTI in patients with spinal cord injury.⁷⁷

In certain circumstances the use of prophylactic antibiotics needs to be considered. It has been suggested for those who have recurrent UTIs and a dilated upper urinary tract. Three months prophylaxis has been recommended if infection persists after treatment of any established infection and other conditions which would promote recurrent infections eg calculi or bladder outflow obstruction.⁷⁸ The threat of emerging resistant bacteria, risk of unwanted side effects of antibiotics, unnecessary expense and the potential risk to other patients from cross-infection with multiply resistant bacteria are all good reasons why the use of antibiotics should be used with extreme caution in patients with spinal cord injury.⁷⁹

Experimental methods of prevention

A number of other approaches to the prevention of recurrent UTIs have also been explored. There are a variety of ways by which bacterial adherence may be inhibited. First, the use of vaccination. The results in humans generally appear to be disappointing as there is wide antigenic variation among gram negative bacilli causing recurrent infection.⁸⁰ Research, however, continues and recent work with animal models suggests there may be some success in using a vaccine containing *Proteus* outer membrane protein⁸¹ or a polyvalent vaccine containing the bacteria most frequently causing UTI – 'SolcoUrovac'.⁸² Secondly, there has also been limited success in using receptor analogues with galactose α 1-galactose β containing structures in preventing adhesion as the potential efficacy depends on the frequency of gal α 1-gal β recognising bacteria in the population studied.^{80,83} Thirdly, the instillation of a mucopolysaccharide into the bladder (similar to the naturally occurring glycosaminoglycan which normally protects the uroepithelium) has been suggested.⁷⁶

The use of bacterial interference has gained interest recently. There has been some success in treating women with recurrent UTIs by using vaginal pessaries of lactobacilli in an attempt to colonise the perineum and urethra with normal flora.⁸⁴ Hagberg and colleagues have had some success with instillations of *E. coli* showing no recognised virulence factors (isolated from a patient with asymptomatic bacteriuria), in preventing symptomatic infection with patho-

Table 2 Prevention of urinary tract infection in patients with spinal cord injury

-
I. Essential
1. Choice of drainage system
2. Treatment of complicating factors
-outflow obstruction
-stones
3. Infection control
-hygienic catheter care
-staff and patient education
4. Urological follow-up
II. Probably beneficial
1. Choice of indwelling catheter
2. Oral antiseptics, acidifying agents
3. Bladder washout-to control debris
4. Prophylactic antibiotics for recurrent infections (if no indwelling catheter)
III. Potentially harmful
1. Liberal use of antiseptics for skin cleansing, bladder washouts or in catheter drainage bags.
2. Prophylactic antibiotics for patients with indwelling catheter.
IV. Experimental
1. Vaccination
2. Receptor analogues
3. Bacterial interference
4. Immunotherapy
-

genic bacteria. *E. coli* bacteriuria persisted for up to 4 months without causing any symptoms or signs of infection.⁸⁵ Immunotherapy with orally administered extracts from *E. coli* has also been reported to be effective in reducing the incidence of urinary tract infections in paraplegic patients.⁸⁶

Conclusions

There are a number of approaches to prevention of UTI in patients with spinal cord injury. Expert urological management is essential. Following this microbiological preventive methods start to play a role (Table 2). Antiseptics and antibiotics can be used in a variety of ways but should be used with caution as resistance can readily develop, making serious infections difficult to treat.⁵⁵ Research into different methods of prevention of UTI needs to continue.⁸⁷ In particular it would be useful to look into greater detail as to which patients would benefit from antiseptics, antibiotics or immunotherapy. The use of multi-centre trials would allow sufficient numbers of patients to be readily evaluated. Other approaches to prevention also need to be explored and should be encouraged. In terms of the microbiological aspects of prevention of UTI plenty has been done but there is still a lot more that can be achieved.²⁴

Acknowledgements

I would like to thank Mr BP Gardner for his helpful comments. Also Dr HT Green, Mr KR Krishnan and the staff of the Regional Spinal Injuries Centre, Southport for their support during my research.

References

- Cardenas DD, Hooton TM. Urinary tract infection in persons with spinal cord injury. *Arch Phys Med Rehabil* 1995; **76**: 272–280.
- Anonymous. The prevention and management of urinary tract infections among people with spinal cord injuries. *National Institute on Disability and Rehabilitation Research Consensus Statement*. January 27–29. *J Am Paraplegia Soc* 1992; **15**: 194–204.
- Gupta S, Chawla JC. Review of urinary tract abnormalities in 100 patients with spinal cord paralysis. *Paraplegia* 1994; **32**: 531–539.
- Van Kerrebroeck PEV, Koldewijn EL, Scherpenhuizen S, Debruyne FMJ. The morbidity due to lower urinary tract function in spinal cord injury patients. *Paraplegia* 1993; **31**: 320–329.
- Whiteneck GG *et al.* Mortality, morbidity, and psychosocial outcomes of persons spinal cord injured more than 20 years ago. *Paraplegia* 1992; **30**: 617–630.
- Stamm WE *et al.* Urinary tract infections: from pathogenesis to treatment. *J Infect Dis* 1989; **159**: 400–406.
- Reid G *et al.* Use of adhesion counts to help predict symptomatic infection and the ability of fluoroquinolones to penetrate bacterial biofilms on the bladder cells of spinal cord injured patients. *Paraplegia* 1994; **32**: 468–472.
- Reid G *et al.* Bacterial biofilm formation on the bladder epithelium of spinal cord injured patients. II. Toxic outcome on cell viability. *Paraplegia* 1993; **31**: 494–499.
- Perkash I. Long-term urologic management of the patient with spinal cord injury. *Urol Clin North Am* 1993; **20**: 423–434.
- Stover SL, Lloyd LK, Waites KB, Jackson AB. Neurogenic urinary tract infection. *Neurol Clin* 1991; **9**: 741–755.
- Newman E, Price M. Bacteriuria in patients with spinal cord lesions: its relationship to urinary drainage appliances. *Arch Phys Med Rehabil* 1977; **58**: 427–430.
- Warren JW *et al.* A prospective microbiologic study of bacteriuria in patients with chronic indwelling urethral catheters. *J Infect Dis* 1982; **146**: 719–723.
- Clayton CL, Chawla JC, Stickler DJ. Some observations on urinary tract infections in patients undergoing long-term bladder catheterization. *J Hosp Infect* 1982; **3**: 39–47.
- Warren JW, Muncie HL, Bergquist EJ, Hoopes JM. Sequelae and management of urinary infection in the patient requiring chronic catheterization. *J Urol* 1981; **125**: 1–8.
- Erickson RP, Merritt JL, Opitz JL, Ilstrup DM. Bacteriuria during follow-up in patients with spinal cord injury: 1. Rates of bacteriuria in various bladder-emptying methods. *Arch Phys Med Rehabil* 1982; **63**: 409–412.
- Grundy DJ *et al.* A comparison of fine-bore suprapubic and intermittent urethral catheterisation regimes after spinal cord injury. *Paraplegia* 1983; **21**: 227–232.
- Perrouin-Verbe B *et al.* Clean intermittent catheterisation from the acute period in spinal cord injury patients. Long term evaluation of urethral and genital tolerance. *Paraplegia* 1995; **33**: 619–624.
- Morita H, Sazawa A, Kanno T, Koyanagi T. Long term urinary prognosis of cervical cord injury patients. *Paraplegia* 1994; **32**: 30–35.
- Merritt JL. Residual urine volume: correlate of urinary tract infection in patients with spinal cord injury. *Arch Phys Med Rehabil* 1981; **62**: 558–561.
- Pearman JW. Infection hazards in patients with neuropathic bladder dysfunction. *J Hosp Infect* 1984; **5**: 355–358.
- Killorin W, Gray M, Bennett JK, Green BG. The value of urodynamics and bladder management in predicting upper urinary tract complications in male spinal cord injury patients. *Paraplegia* 1992; **30**: 437–441.
- Wong ES, Hooton TM. Guidelines for prevention of catheter associated urinary tract infections. *Infect Control* 1981; **2**: 125–130.
- Waites KB, Canupp KC, De Vivo MJ. Epidemiology and risk factors for urinary tract infection following spinal cord injury. *Arch Phys Med Rehabil* 1993; **74**: 691–695.
- Wyndaele JJ. Development and evaluation of the management of the neuropathic bladder. *Paraplegia* 1995; **33**: 305–307.
- Sanderson PJ, Rawal P. Contamination of the environment of spinal cord injured patients by organisms causing urinary tract infection. *J Hosp Infect* 1987; **10**: 173–178.
- Sanderson PJ, Weissler S. Recovery of coliforms from the hands of nurses and patients: activities leading to contamination. *J Hosp Infect* 1992; **21**: 85–93.
- Barnes DG *et al.* Correlation of bacteriological flora of the urethra, glans and perineum with organisms causing urinary tract infection in the spinal cord injured male patient. *Paraplegia* 1992; **30**: 851–854.
- Goldmann D, Larson E. Hand-washing and nosocomial infections. *N Engl J Med* 1992; **327**: 120–122.
- Ramsay JWA *et al.* Biofilms, bacteria and bladder catheters. A clinical study. *Br J Urol* 1989; **64**: 395–398.
- Roberts JA, Kaack MB, Fussell EN. Adherence to urethral catheters by bacteria causing nosocomial infections. *Urology* 1993; **41**: 338–342.
- Wille JC, Blusse van Oud Alblas A, Thewessen EAPM. Nosocomial catheter associated bacteriuria: a clinical trial comparing two closed urinary drainage systems. *J Hosp Infect* 1993; **25**: 191–198.
- Fawcett C, Chawla JC, Quoraishi A, Stickler DJ. A study of the skin flora of spinal cord injured patients. *J Hosp Infect* 1986; **8**: 149–158.
- Falkner FR. The insertion and management of indwelling urethral catheters - minimizing the risk of infection. *J Hosp Infect* 1993; **25**: 79–90.

- 34 Sanderson PJ, Weissler S. A comparison of the effect of chlorhexidine antiseptics, soap and antibiotics on bacteriuria, perineal colonization and environmental contamination in spinally injured patients. *J Hosp Infect* 1990; **15**: 235–243.
- 35 Sanderson PJ. Prophylaxis for catheter related urinary infection. *J Hosp Infect* 1991; **18**: 1–3.
- 36 Gilmore DS *et al.* Effects of bathing on *Pseudomonas* and *Klebsiella* colonisation in patients with spinal cord injuries. *J Clin Microbiol* 1981; **14**: 404–407.
- 37 Montgomerie JZ, Gilmore DS, Graham IE, Schick DG. The effects of antiperspirant on the perineal skin flora of patients with spinal cord injury. *J Hosp Infect* 1988; **12**: 43–49.
- 38 Gilmore DS, Schick DG, Young MN, Montgomerie JZ. Effect of external urinary collection system on colonization and urinary tract infections with *Pseudomonas* and *Klebsiella* in men with spinal cord injury. *J Am Paraplegia Soc* 1992; **15**: 155–157.
- 39 Yum S *et al.* A disinfectant delivery system for control of micro-organisms in urine collection bags. *J Hosp Infect* 1988; **11**: 176–182.
- 40 Gillespie WA *et al.* Does the addition of disinfectant to urine drainage bags prevent infection in catheterised patients? *Lancet* 1983; **i**: 1037–1039.
- 41 Maizels M, Schaeffer AJ. Decreased incidence of bacteriuria associated with periodic instillations of hydrogen peroxide into the urethral catheter drainage bag. *J Urol* 1980; **123**: 841–845.
- 42 Giroux J, Perkash I. In vitro evaluation of current disinfectants for leg bags. *J Am Paraplegia Soc* 1985; **8**: 13–15.
- 43 Grundy D, Swain A, Russell J. ABC of spinal cord injury. Early management and complications - II. *BMJ* 1986; **292**: 123–125.
- 44 Haldorson AM, Keys TF, Maker MD, Opitz JL. Nonvalue of neomycin instillation after intermittent urinary catheterization. *Antimicrob Agents Chemother* 1978; **14**: 368–370.
- 45 Pearman JW, Bailey M, Harper WES. Comparison of the efficacy of "Trisdine" and kanamycin-colistin bladder instillations in reducing bacteriuria during intermittent catheterisation of patients with acute spinal cord trauma. *Br J Urol* 1988; **62**: 140–144.
- 46 Baillie L. Chlorhexidine resistance among bacteria isolated from urine of catheterized patients. *J Hosp Infect* 1987; **10**: 83–86.
- 47 Brocklehurst JC, Brocklehurst S. The management of indwelling catheters. *Br J Urol* 1978; **50**: 102–105.
- 48 Stickler DJ, Plant S, Bunni NH, Chawla JC. Some observations on the activity of three antiseptics used as bladder irrigants in the treatment of urinary tract infections in patients with indwelling catheters. *Paraplegia* 1981; **19**: 325–333.
- 49 Stickler DJ, Thomas B, Chawla JC. Antiseptic and antibiotic resistance in gram-negative bacteria causing urinary tract infections in spinal cord injured patients. *Paraplegia* 1981; **19**: 50–58.
- 50 King JB, Stickler DJ. An assessment of antiseptic bladder washout solutions using a physical model of the catheterized bladder. *J Hosp Infect* 1991; **18**: 179–190.
- 51 Elliott TSJ *et al.* Bladder irrigation or irritation? *Br J Urol* 1989; **64**: 391–394.
- 52 Krebs M, Halvorsen RB, Fishman IJ, Santos-Mendoza N. Prevention of urinary tract infection during intermittent catheterization. *J Urol* 1984; **131**: 82–85.
- 53 Pearman JW, England EJ. *The Urological management of the patient following spinal cord injury*. Springfield, Illinois: Charles C Thomas, 1973.
- 54 Kevorkian CG, Merritt JL, Ilstrup DM. Methenamine mandelate with acidification: An effective urinary antiseptic in patients with neurogenic bladder. *Mayo Clin Proc* 1984; **59**: 523–529.
- 55 Stickler DJ, Chawla JC. An appraisal of antibiotic policies for urinary tract infections in patients with spinal cord injuries undergoing long-term intermittent catheterisation. *Paraplegia* 1988; **26**: 215–225.
- 56 McDonald DF, Murphy GP. Bacteriostatic and acidifying effects of methionine, hydrolyzed casein and ascorbic acid on the urine. *N Engl J Med* 1959; **261**: 803–805.
- 57 Nickey KE. Urinary pH: Effect of prescribed regimes of cranberry juice and ascorbic acid. *Arch Phys Med Rehabil* 1975; **56**: 556.
- 58 Weingarden SI, Parker WD, Hetey SK, Johnson EW. Ascorbic acid: It's usefulness in acidifying the urine. *Arch Phys Med Rehabil* 1978; **59**: 521.
- 59 Kuhlemeier KV, Stover SL, Lloyd LK. Prophylactic antibacterial therapy for preventing urinary tract infections in spinal cord injury patients. *J Urol* 1985; **134**: 514–517.
- 60 Grundy D, Russell J. ABC of spinal cord injury. Urological management. *BMJ* 1986; **292**: 249–253.
- 61 Burr RG, Nuseibeh IM. Blockage of indwelling urinary catheters: the roles of urinary composition, the catheter, medication and diet. *Paraplegia* 1993; **31**: 234–241.
- 62 Merritt JL, Erickson RP, Opitz JL. Bacteriuria during follow-up in patients with spinal cord injury; II. Efficacy of antimicrobial suppressants. *Arch Phys Med Rehabil* 1982; **63**: 413–415.
- 63 Mountokalakis T, Skounakis M, Tselentis J. Short-term versus prolonged systemic antibiotic prophylaxis in patients treated with indwelling catheters. *J Urol* 1985; **134**: 506–508.
- 64 Vollaard EJ *et al.* Prevention of catheter-associated gram-negative bacilluria with norfloxacin by selective decontamination of the bowel and high urinary concentration. *J Antimicrob Chemother* 1989; **23**: 915–922.
- 65 van der Wall E *et al.* Prophylactic ciprofloxacin for catheter-associated urinary tract infection. *Lancet* 1992; **339**: 946–951.
- 66 Nyren P *et al.* Prophylactic methenamine hippurate or nitrofurantoin in patients with indwelling urinary catheter. *Ann Clin Res* 1981; **13**: 16–21.
- 67 Maynard FM, Diokno AC. Urinary infection and complications during clean intermittent catheterisation following spinal cord injury. *J Urol* 1984; **132**: 943–946.
- 68 Mohler JL, Cowen DL, Flanagan RC. Suppression and treatment of urinary tract infection in patients with an intermittently catheterized neurogenic bladder. *J Urol* 1987; **138**: 336–340.
- 69 Merritt JL. Urinary tract infections, causes and management, with particular reference to the patients with spinal cord injury: A review. *Arch Phys Med Rehabil* 1976; **57**: 365–373.
- 70 Thorsteinsson G, Keys T. The frequency and type of urinary tract infections in patients on intermittent catheterization by self and by catheterization team. *Arch Phys Med Rehabil* 1983; **64**: 519–521.
- 71 Gribble MJ, Puterman ML. Prophylaxis of urinary tract infection in persons with recent spinal cord injury: a prospective, randomised, double-blind, placebo-controlled study of trimethoprim-sulfamethoxazole. *Am J Med* 1993; **95**: 141–152.
- 72 Sandock DS, Gothe BG, Bodner DR. Trimethoprim-sulfamethoxazole prophylaxis against urinary tract infection in chronic spinal cord injury patients. *Paraplegia* 1995; **33**: 156–160.
- 73 Biering-Sorensen F *et al.* Ciprofloxacin as prophylaxis for urinary tract infection: prospective, randomized, cross-over, placebo controlled study in patients with spinal cord lesion. *J Urol* 1994; **151**: 105–108.
- 74 Duffy L, Smith AD. Nitrofurantoin macrocrystals prevent bacteriuria in intermittent self-catheterization. *Urology* 1982; **20**: 47–49.
- 75 Lindan R, Joiner E. A prospective study of the efficacy of the low dose nitrofurantoin in preventing urinary tract infections in spinal cord injury patients, with comments on the role of pseudomonads. *Paraplegia* 1984; **22**: 61–65.
- 76 Anderson RU. Urinary tract infection in spinal cord injury. *J Am Paraplegia Soc* 1985; **8**: 18–19.
- 77 Galloway A *et al.* Antibody coated bacteria in urine of patients with recent spinal injury. *J Clin Path* 1990; **43**: 953–956.
- 78 Gardner BP *et al.* The urological management of spinal cord damaged patients: a clinical algorithm. *Paraplegia* 1986; **24**: 138–147.
- 79 Waites KB, Canupp KC, De Vivo MJ. Eradication of urinary tract infection following spinal cord injury. *Paraplegia* 1993; **31**: 645–652.
- 80 Svanborg Eden C, de Man P, Linder H, Lomberg H. Natural vs. induced resistance to urinary tract infection. In: Kass EH, Svanborg Eden C, editors. *Host parasite interactions in urinary tract infections*. Chicago: University of Chicago Press, 1989: 249–257.

- 81 Moayeri N, Collins CM, O'Hanley P. Efficacy of *Proteus mirabilis* outer membrane protein vaccine in preventing experimental proteus pyelonephritis in a BALB/c mouse. *Infect Immun* 1991; **59**: 3778–3786.
- 82 Kruze D, Holzebecher K, Andrial M, Bossart W. Urinary antibody response after immunisation with a vaccine against urinary tract infection. *Urol Res* 1989; **17**: 361–366.
- 83 Reid G, Sobel JD. Bacterial adherence in the pathogenesis of urinary tract infection. A review. *Rev Infect Dis* 1987; **9**: 470–487.
- 84 Reid G *et al.* Is there a role for lactobacilli in prevention of urogenital and intestinal infections? *Clin Microbiol Rev* 1990; **3**: 335–344.
- 85 Hagberg L *et al.* Colonisation of the urinary tract with bacteria from the normal fecal and urethral flora in patients with recurrent urinary tract infections. In: Kass EH, Svanborg Eden C, editors. *Host parasite interactions in urinary tract infections*. Chicago: University of Chicago Press, 1989; pp 194–197.
- 86 Hachen HJ. Oral immunotherapy in paraplegic patients with chronic urinary tract infections: a double-blind, placebo-controlled trial. *J Urol* 1990; **143**: 759–763.
- 87 Kamitsuka PF. The pathogenesis, prevention and management of urinary tract infection in patients with spinal cord injury. *Curr Clin Topics Infect Dis* 1993; **13**: 1–25.