RECONSTRUCTIVE UROLOGIC SURGERY

Pediatric and Adult

John A. Libertino
Leonard Zinman

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Preface

During the past 25 years, the reconstructive aspects of urologic surgery have emerged and become a major component of our surgical specialty. In this period of time, the ileal conduit, renovascular reconstruction, renal transplantation, and many pediatric reconstructive procedures have been added to our surgical armamentarium.

The purpose of this book is to present the major pediatric and adult reconstructive surgical procedures available today. The technical aspects of reconstructive urologic surgery will be the major focus of this heavily illustrated volume. Since no one individual can be an authority on every aspect of reconstructive urologic surgery, recognized authorities from this country and abroad have enthusiastically collaborated to produce this textbook, which is the outgrowth of a postgraduate symposium held at the Lahey Clinic Foundation.

We hope this book will provide the experienced practitioner of urology and the resident in training with techniques that can be incorporated into their surgical practice. Hopefully it will also act as a catalyst for further surgical innovation and ultimately render this work obsolete.

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Chapter ONE

Treatment of Bacterial Urinary Tract Infections Associated with Urologic Surgery

Edward J. McGuire, M.D.

Bacterial colonization of the urinary tract is frequently found in patients undergoing major urologic surgical procedures. In such patients, bacteriuria may be chronic before operation or may occur in relation to the operative procedure. The significance of bacteriuria varies with the clinical circumstances in which it occurs; in some patients the risk may be small, but in others urinary infection may pose a threat to a successful surgical procedure or even a hazard to life. Ideally, antimicrobial treatment should result in permanent eradication of bacteriuria, and, in some patients, surgical correction of an anatomic or functional urinary disorder may enable this result. However, in others, treatment goals may more realistically be limited to the prevention of bacterial tissue or vascular invasion. While host factors are important, a working knowledge of the bacteriology of the organisms commonly associated with urinary tract infection and of the antimicrobial agents employed in their treatment is helpful in attaining a satisfactory clinical result.

BACTERIOLOGY OF URINARY TRACT INFECTIONS

Organisms, which commonly infect the urinary tract, can arbitrarily be grouped by antibacterial sensitivity patterns and by the clinical settings which favor colonization by a particular organism or group of organisms. Most urinary infections acquired outside the hospital are caused by three organisms: Escherichia coli, Proteus mirabilis, and the enterococci. They are generally penicillin sensitive, although E coli infections acquired in the hospital are less likely to respond to therapy than those encountered in domiciliary practice (76% of 855 Yale-New Haven Hospital isolates in the first quarter of 1975). Proteus mirabilis, a urease-producing organism, is frequently associated with struvite calculi. In the presence of these calculi, persistent bacteriuria may occur with essentially

static antibacterial sensitivity patterns despite multiple courses of antimicrobial therapy (28). The enterococci, gram-variable organisms, show important differences in response to the usual urinary antimicrobial agents; they are sensitive to the penicillins and occasionally to erythromycin and furadantin but frequently resistant to carbenicillin, gentamicin, nalidixic acid, and the cephalosporins. Common antimicrobial sensitivity patterns for this group of organisms are given in Table 1.1.

The second group of urinary tract organisms occur largely in hospitalized patients, in patients with structural or functional urinary tract abnormalities, or in patients previously treated with antimicrobial agents. Klebsiella, Enterobacteriaceae, indole-positive Proteus species (morganii, vulgris, and rettgeri), and occasionally other organisms, some of which were previously grouped as the "Paracolons," comprise this group. Some strains of Klebsiella are urea splitting and are also associated with formation of struvite calculi. Klebsiella is frequently associated with superinfections in hospitalized patients previously treated with antimicrobial agents (31). The organism is often sensitive to the cephalosporins. Enterobacteriaceae is generally not sensitive either to penicillin or the cephalosporins. Typical antimicrobial sensitivity patterns for this group of organisms are given in Table 1.2.

Pseudomonas and Serratia urinary infections occur in patients with structural or functional abnormalities of the urinary tract, long-term catheter drainage, ileal conduit urinary diversions, and in patients with infected calculi, as both organisms may be urease producing. These organisms are distinguished by an insensitivity to most antimicrobial agents without dose-related toxicity. However, carbenicillin may be useful for both Pseudomonas and Serratia infections (80% of Yale-New Haven Hospital Serratia isolates in the first quarter of 1975) and oxytetracycline may be effective in Pseudomonas infections (35). Some evidence has shown that bacteremia resulting from this highly resistant group of organisms is more difficult to treat successfully than similar conditions resulting from E coli infections (15) (Table 1.3).

TABLE 1.1
Percent of Group 1 Isolates Sensitive to Various Antimicrobials*

	E coli	Proteus Mirabilis	Entero-cocci
Number of isolates	855	212	575
Ampicillin	76	98	100
Cephalosporin	80	96	N**
Sulfamethoxazole-Trimethoprim	86	84	N**
Kanamycin	98	96	...
Gentamicin	100	98	...
Carbenicillin	80	98	...
Nalidixic acid	99	99	...
Tetracycline	70	N**	...
Nitrofurantoin	90	80	...

* Kirby-Bauer method.
** N = 30% or less.

ANTIMICROBIAL AGENTS AND SENSITIVITY TESTING

The content of an antimicrobial agent in commercially available sensitivity disks is such that diffusion of the material onto the agar plate results in a concentration of antibiotic which approximates an ideal level in the serum except in the case of nalidixic acid or nitrofurantoin. Considerable evidence exists that concentrations in urine, and not in serum, are of critical importance in the ultimate response of urinary tract infections to antimicrobial agents (22, 34). This suggests that disk sensitivity testing may underestimate efficacy of antimicrobial agents with greater concentration in urine than in serum and is particularly true with the cephalosporins and ampicillin. Conversely, chloromycetin is approximately 80% detoxified in the liver, and a significant percent is excreted in the urine as an inactive metabolite, which reduces its efficacy in urinary tract infections particularly in patients with impaired renal function. Moreover, since the concentration of antibiotic in the urine is critical to the ultimate prognosis of curing urinary infection, inadequate renal function may limit the effectiveness of treatment with any antimicrobial agent. Cure of urinary tract infection in an anephric patient or a patient with vir-

TABLE 1.2
Percent of Group 2 Isolates Sensitive to Various Antimicrobials*

	Enterobacter	Klebsiella	Proteus (Indole +)	Citrobacter
Number of isolates	200	318	75	50
Ampicillin	N**	N**	N**	N**
Cephalosporin	N**	88	N**	N**
Sulfamethoxazole-Trimethoprim	26	N**	N**	N**
Kanamycin	95	95	100	90
Gentamicin	99	100	100	100
Carbenicillin	86	N**	E†	N**
Nalidixic acid	95	95	100	100
Tetracycline	92	93	E†	90
Nitrofurantoin	30	28	N**	88

* Kirby-Bauer method.
** N = 30% or less.
† E = 30 to 50%.

TABLE 1.3
Percent of Group 3 Isolates Sensitive to Various Antimicrobials*

	Pseudomonas	Serratia
Number of isolates	217	41
Tetracycline	N**	N**
Kanamycin	N**	88
Gentamicin	97	100
Nalidixic acid	N**	95
Carbenicillin	92	90

* Kirby-Bauer method.
** N = 30% or less.

tually no renal function may be impossible except by direct instillation of an antimicrobial agent into the urinary tract.

ANTIMICROBIAL AGENTS

Oral Agents with No Useful Serum Activity

Sulfonamides. These agents are useful in infections acquired outside the hospital but are of limited use in surgical patients. Sulfonamide administration is associated with rapid changes in the intestinal flora, presumably the pool of organisms from which superinfections occur. Most infections acquired in the hospital are not reliably susceptible to these agents.

Nalidixic Acid. Commercially available nalidixic acid disks for sensitivity tests result in concentrations on the agar plate which approximate those achievable in the urine. Reports (6) of the rapid emergence of resistant organisms during treatment have recently been disputed. A 10-year study of the sensitivity of urinary pathogens to nalidixic acid in a pyelonephritic unit showed essentially identical results at the beginning and termination of the study. Fecal excretion is minimal, and the intestinal flora remains fairly stable during long-term treatment (2). However, clinical response to the agent may vary, and its applicability in surgical patients should be limited to circumstances in which closed urinary drainage is achieved or can be achieved within a short period after the initiation of treatment, providing ideal conditions for antimicrobial therapy.

Methanamine Salts. Antibacterial activity of methanamine salts is dependent upon release of formaldehyde in the presence of an acid urine (pH, 5.5 or less). They are ineffective in the treatment of infections with urease-positive organisms because of the inability to achieve a truly acid urine. These include infections with certain Proteus species, Klebsiella species, Pseudomonas, and, occasionally, Serratia species. Applicability in surgical patients is limited.

Nitrofurantoin. Sensitivity patterns to nitrofurantoin have remained stable over a long period of time. There is no effective level of the antibiotic in serum, but the agent is concentrated in renal lymphatic tissue. In general, the range of sensitive bacteria is too small for widespread use in patients undergoing major surgical procedures with complicated urinary infections.

Sulfamethoxazole-Trimethoprim. This agent has recently been approved by the FDA for treatment of chronic urinary tract infections. Effective concentrations of trimethoprim in exocrine prostatic tissue are obtainable. Preliminary results in patients with chronic bacterial prostatitis are promising, but relapse of infection has occurred after three months of continuous therapy in 40% of a small series of patients (24). Enterobacteriaceae, the indole-positive Proteus species, Serratia, Pseudomonas, and the enterococci are commonly resistant. Effective urinary levels of trimethoprim in the urine may be achieved in patients with poor renal function who require dialysis (9).

Oral or Parenteral Agents with Serum Activity

Penicillin G and Ampicillin. Both of these agents achieve adequate concentrations in the urine and are effective against most E coli, Proteus mirabilis, and enterococci infections acquired outside the hospital. No dose-related toxicity exists, and commercially available disk sensitivities underestimate efficacy. The level of antibiotic in the serum with the usual oral dose of either agent is not generally effective (33). Penicillin G and ampicillin are the agents of choice for enterococci and Proteus mirabilis infections. Enterobacteriaceae species and Klebsiella species, which were sensitive when ampicillin was introduced, are now often resistant. Effective concentrations in the urine may be achieved in patients with uremia with parenteral administration (19).

The Tetracyclines. Renal clearance and excretion are highest with oxytetracycline. Longer acting agents achieve protracted serum concentrations at the expense of urinary excretion. The longer acting tetracyclines may be of value in bacterial prostatitis (12) and urethritis but are less effective in bacteriuric individuals. Many Pseudomonas strains acquired in the hospital are apparently sensitive to this agent. Tube dilution sensitivities are necessary to confirm sensitivity, but administration of this agent to volunteers showed effective urinary concentrations against 80% of 20 Pseudomonas isolates compared to 5% of Pseudomonas isolates when the same volunteers were given a longer acting tetracycline (11). Oxytetracycline is often effective against occasional and unusual organisms found in the urinary tract, for example, Achromobacter species, Citrobacter species, and Alcaligenes species. Doxycycline appears to be the most potent and least toxic tetracycline available and is especially suited for patients with azotemia because of its low incidence of nephrotoxicity.

Cephalosporins. The oral agent, cephalexin, is virtually completely absorbed from the intestine. Studies by Cox (7) indicate that changes in fecal flora are minimal even during long-term treatment with cephalexin. All the cephalosporins are excreted in the urine at levels substantially higher than those achieved in the serum regardless of the route of administration. One of the newer cephalosporins, Cephazolin, has an identical spectrum to cephalothin but can be given in relatively low doses intramuscularly or intravenously without the potential nephrotoxicity of cephaloridine. The enterococci, Enterobacteriaceae species, and indole-positive Proteus species, Pseudomonas, and Serratia are commonly resistant (8).

Carbenicillin. The advantage of this agent is its effectiveness against many Pseudomonas and Serratia species. Klebsiella and the enterococci are relatively resistant. Sensitive strains are inhibited by concentrations of 50 to 100 μg per milliliter in the urine—a level easily achieved by parenteral administration but somewhat more difficult to obtain with oral administration. Recent reports (32) in the literature have noted the occurrence of a bleeding diathesis in patients receiving very large doses of carbenicillin.

Parenteral Agents

Aminoglycosides. Aminoglycosides are excreted almost completely in the urine. Toxicity is dose related and includes ototoxicity, nephrotoxicity, and neurotoxicity. Toxicity is particularly likely in patients with impairment of renal function. Kanamycin is not effective against most

Pseudomonas strains. Peak concentrations in the urine after administration of kanamycin are two to three times higher (15 to 20 μg per milliliter or more) than the levels found in serum, and most organisms are sensitive at or below 10 μg per milliliter, a level readily obtainable in urine (29).

Gentamicin inhibits 90% of Pseudomonas strains in concentrations of 10 μg per milliliter or less and inhibits a similar percent of Serratia species at somewhat lower concentrations (17). Peak levels in the urine are three to five times higher than peak levels in the serum. Except in rare instances, doses approaching maximal are not indicated in urinary tract infections without producing serious systemic symptoms. In patients treated with 2.4 mg per kilogram a day, peak levels reached 130 μg per milliliter, and mean levels ranged from 60 to 65 μg per milliliter (16). Toxicity of these agents is related to the concentration in serum, and the degree of toxicity is dependent on the amount of antibiotic given and the ability of the kidney to excrete the agent. Impaired renal excretion leads to increased concentrations in serum and may result in significant toxicity with continued administration. In patients with impaired renal function, adjustment of dosage schedules or adjustment in total dose or both is mandatory. Impaired efficacy in such circumstances may result from inability to achieve adequate concentration in the urine as well as from decreased total dose. A useful rule of thumb for adjustment of the dose is the rule of eights, that is, eight times the value for serum creatinine gives a number approximately equal to a safe interval in hours between doses (32). Use of this formula is possible only with a steady state of renal dysfunction.

Tobramycin (26), a new aminoglycoside antimicrobial agent which demonstrates increased activity against Pseudomonas species compared to gentamicin, has recently been approved by the FDA. Levels about 12 μg per milliliter in the serum are associated with toxicity. Doses range from 3 mg per kilogram a day to a maximal dose of 5 mg per kilogram a day for life-threatening infections. Peak levels of 6.5 μg per milliliter in the serum with peak levels of 90 to 500 μg per milliliter in the urine have been reported (18). Most sensitive organisms respond to the agent at levels substantially below these concentrations. Reduction in dose or prolongation of the interval between doses or both is necessary in patients with impaired renal function. In patients with a steady state of renal dysfunction, multiplication of the value for creatinine by six gives a number equaling the interval in hours between doses. Activity of the antibiotic in the urine falls below effective concentrations eight hours after the preceding dose in patients with normal renal function.

The Polymyxins. Polymyxin B and sodium colistimethate are active against most bacteria except the indole-positive Proteus species. These agents are less commonly employed now than in the past because the aminoglycoside antimicrobial agents are less toxic and somewhat easier to use. The polymyxins may be used in the treatment of Pseudomonas infections that are resistant to gentamicin. Colistimethate achieves effective levels in the urine more rapidly than polymyxin B, which may not achieve therapeutic urinary concentrations for 12 hours or more after intramuscular injection (13). Occurrence of paresthesias, a manifestation of neurotoxicity, is related to the concentration in the serum. Both polymyxin B and sodium colistimethate are potentially nephrotoxic agents.

HOST FACTORS INFLUENCING TREATMENT OF URINARY INFECTION

Bacteriuria, the presence of a considerable number of microorganisms in the urine, is manifested by symptoms, fever, or bacteremia and implies a response to bacteriuria on the part of the host resulting from tissue or vascular invasion.

The four periods of risk related to significant urinary tract infection in patients undergoing urologic surgery are the preoperative, intraoperative, postoperative, and late postoperative periods. Preoperatively, risk is frequently encountered in patients whose condition necessitates diagnostic in-

strumentation or temporary catheter drainage, particularly if urinary tract obstruction or decompensation is present. On the other hand, patients with preexisting, long-standing bacteriuria are less likely to experience significant urinary tract infection unless superimposed acute decompensation has occurred (21, 23). Adequate surgical drainage may be a prerequisite in both groups of patients for antimicrobial therapy to be effective.

Significant infection may develop in patients with bacteriuria during the intraoperative and immediate postoperative periods. Positive blood cultures have been reported (3, 10) in a considerable number of patients with bacteriuria who have had a prostatectomy. However, despite this observation, significant infection intraoperatively or in the immediate postoperative period is uncommon. The factors which determine whether a given patient will experience gram-negative sepsis or even significant problems with infection after a transient episode of bacteremia related to an operative procedure have not been clearly established.

Significant infections are most commonly encountered within two to seven days after operation. The use of prophylactic antimicrobial therapy does not appear to influence the incidence of significant postoperative infection.

In the late postoperative period most patients are managed with closed urinary drainage. The occlusion or removal of a catheter may result in significant infection resulting from passage of infected material across an operative site. However, the period of risk is short, and conditions are favorable for successful antimicrobial therapy. Moreover, many patients with bacteriuria related to the presence of a catheter experience spontaneous clearing without treatment once the catheter is removed and satisfactory drainage is established.

Considerable controversy exists concerning the efficacy of antimicrobial prophylaxis in abacteriuric patients in preventing the development of significant infection. Prophylactic antibiotics in abacteriuric patients who require urinary drainage catheters at the time of operation may be effective in delaying the onset of bacterial colonization of the urinary tract, particularly if the agents are used in combination with closed urinary drainage (20). However, closed drainage may be difficult to maintain after operation, and, if the period of catheterization is long enough, bacteriuria will develop (5). Moreover, some workers (4) have not found retrograde intraluminal bacterial contamination to be a significant cause of urinary tract infections, and bacterial entry occurs around the catheter even in patients maintained on closed drainage. Prophylactic antimicrobial therapy may result in colonization of resistant hospital organisms (23). In abacteriuric patients, it is preferable to monitor the urine for the presence of bacteria and to determine the antimicrobial sensitivity pattern when growth occurs so that the appropriate antimicrobial agent may be instituted if a significant urinary tract infection develops. This also tends to obviate problems of superinfection.

Patients in whom bacteriuria develops as a result of preoperative instrumentation or catheterization for urinary obstruction and who experience a delay between admission and operation face an increased risk of significant infection. The overall rate of significant infection is about 20% in patients having prostatectomy. However, in one study (23), patients admitted with urinary retention in whom bacteriuria developed and who had a preoperative delay of five to nine days had a 70% rate of significant infection which was not influenced by prophylactic antimicrobial therapy. Short-term antimicrobial therapy using specific agents immediately before instrumentation or transurethral resection of the prostate has been found to be effective in preventing significant bacteriuric infection in the two groups of patients studied (25, 27). Other studies have disagreed with these findings because of differences in the duration of catheterization and the numbers of high-risk patients in each group (1, 14, 30, 36).

Patients with symptomatic urinary tract infection should be treated with an