Article ID: WMC003968 ISSN 2046-1690



# Urinary Tract Infections in Geriatric Patients

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**Article ID:** WMC003968

**Article Type:** Review articles

**Submitted on:**25-Jan-2013, 03:22:35 PM GMT **Published on:** 28-Jan-2013, 11:07:17 AM GMT

**Article URL:** http://www.webmedcentral.com/article_view/3968

**Subject Categories:**NEPHROLOGY

**Keywords:**Urinary infections, Microorganisms, Kidney diseases, Pathogens, Bacteriuria, Antimicrobial Therapy

**How to cite the article:**Staykova S . Urinary Tract Infections in Geriatric Patients . WebmedCentral NEPHROLOGY 2013;4(1):WMC003968



**Source(s) of Funding:**

None

**Competing Interests:**

None

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## Abstract

Infections of the urinary tract and asymptomatic bacteriuria become more frequent with age in both genders. The ascending path of infection dominates in elderly patients. Very important factor is the weakening of the protective mechanisms due to changes in the glomerules and the tubular interstitial system of the kidney. Typical symptoms of infection of the upper urinary tract may be missing. The clinical picture often is characterized by nausea, pain in the abdomen and difficulty breathing. E.coli remains the most common uropathogen in the elderly. However, it occurs less frequently than in the younger population. There are also increased rates of UTIs with other strains such as Proteus, Klebsiella, Enterobacter, Seratia, and Pseudomonas. In elderly patients Staphylococcus saprophyticus is not isolated. The frequency of urinary tract infections caused by Gram (+) microorganism is higher, especially in the male population.

## Introduction

Urinary tract infection (UTI) is one of the most common renal diseases seen in nephrology practice. There are some differences in the epidemiology, microbiology, pathogenesis, host defense mechanisms and therapy between the elderly and the younger adults. The differences in the geriatric population are the scope of the following review.

## Epidemiology

The incidence and prevalence of both UTI and asymptomatic bacteriuria (ASB) increase with advanced age. Among young to middle-aged women the incidence of bacteriuria found on a single survey is about 2-5% and further rise occurs up to 10-20% in the age interval 65-80 years. Becteriuria, whether asymptomatic or clinically overt, is relatively uncommon in males (0, 1-1, and 0%) until the age of 60, after which it rises up to 5-10% in the next two decades (7, 8, 9, and 10).

Longitudinal studies (two or more performed surveys; time intervals 0, 5-5 years) in elderly demonstrate an increased cumulative positive incidence, ranged 38-44% in women and 15-28% in men. These studies document also that the geriatric population with bacteriuria is not a homogeneous group, and individuals with negative urine culture initially can be infected during examination and vice versa. Only about 5% of all observed elderly demonstrate persistent bacteriuria every time (4, 8).

The place of residence is an important factor related to the prevalence of bacteriuria in the elderly. Both nursing home residents and those hospitalized demonstrate an increased rate of bacteriuria in comparison to the elderly who are well and are community residents. This can be related to the fact that institutionalized elderly are more prone to have other medical risk factors for the development of UTI such as cerebrovascular disease, dementia, more debilitated state with perineal soiling, less complete bladder emptying, bladder catheterization, and more often antibiotic prescription. It is well known that hospitalization may lead to dissemination of bacteria by means of instruments, bet pans and personnel (1, 10).

E.colli and Staphylococcus saprophyticus are responsible for about 80-90% of all uncomplicated UTIs in young and middle-aged people. E.coli remains the most common uropathogen in the elderly, but occurs with less frequency than in the younger population. An increased rate of UTIs with other strains such as Proteus, Klebsiella, Enterobacter, Seratia, Pseudomonas etc. is noted. S. saprophyticus is not isolated in the elderly. Gram positive microorganisms occur more frequently among old men, but the reason for this event remains unclear. Therapeutic management for uncomplicated infection has been compromised by increasing antimicrobial resistance, particularly global dissemination of the CTXM-15 extended spectrum ?-lactamase (ESBL) producing Escherichia coli ST-131 strain. Prevention strategies exploring non-antimicrobial approaches continue to show limited promise, and approaches to limit empiric antimicrobials are now being explored. For complicated urinary tract infection, increasing antimicrobial resistance limits therapeutic options for many patients. In addition to ESBL producing E. coli, NDM-1 E. coli, Klebsiella pneumoniae and other resistant Gram negatives, such as Acinetobacter species, are being isolated more frequently. There has been renewed interest in catheter-acquired urinary

tract infection, the most common health-care associated infection, with several recent evidence-based guidelines for infection prevention available. However, technologic progress in the development of adherence-resistant catheter materials remains disappointing.

A possible explanation for decreased E.coli-UTIs among geriatric population can be the increased rate of hospitalization. Uropathogen strains such as Proteus, Klebsiella, Serratia and Pseudomonas are more often isolated from patients in hospital compared to community population. Another reason responsible for the altered microbiological pattern in the elderly can be the increased frequency of urinary tract obstructions (due to prostatic hypertrophy in men, prolapsed bladder in women, and neurogenic bladder in both sexes) associated often with instrumentation and catheterization. Antimicrobial therapy administrated more frequently in the geriatric population can lead to selective growth of antibiotic-resistant strains (10, 11).

Of clinical importance is the fact of increased isolation of Providencia stuartii among institutionalized elderly. UTIs due to Providencia are typically nosocomial infections characterized by multiple antimicrobial resistance (2, 8).

The presence of polymicrobial bacteriuria (i. e. isolation of more than one species from a single urine specimen; mixed flora) is a common finding in elderly hospitalized patients often in association with long-term catheterization (3, 9). Providencia stuartii and Morganella morgani are the most frequently isolated uropathogens in long-term catheterized patients with polymicrobial bacteriuria. Clinical observations point out that other microorganisms such Pseudomonas, Proteus and Klebsiella tend to occur more frequently in mixed cultures, whereas E.coli is more common in monomicrobial infections. The clinical significance of polymicrobial UTIs is related to the increased rate of urosepsis, enhanced antimicrobial resistance and increased mortality among the patients (6, 7).

# Pathogenesis

**Frequency and distribution pattern of urinary tract infection pathogens:**

The ascending route of infection remains the most common manner of invasion in the elderly. Colonization of the periurethral area and in the female, the vaginal vestibule, by uropathogens is believed to be the first crucial step in the pathogenesis of UTI. The microorganisms then ascend through the urethra into the bladder and, at the end, can reach the kidney parenchyma via the ureters. The barriers against uropathogens invasion and growth inside the bladder include: the presence of normal perineal flora (lactobacilli), anatomic integrity of the urinary system, micturition, antibacterial properties of urine and intact phagocitic function. One or more problems in these defense mechanisms can exist in the elderly.

Hormonally associated changes in the vaginal flora during and especially after menopause are thought to be an important factor in the pathogenesis of UTIs in older women. In premenopausal females circulating estrogen stimulates vaginal colonization by lactobacilli, the latter producing lactic acid from glycogen and thus maintaining a low vaginal pH, which inhibits the growth of most uropathogens. It is known that low vaginal pH is the main preventing factor against colonization by enteric bacterial flora. After menopause the attenuated ovarian function leads to estrogen deficiency and thus to disappearance of lactobacilli, increased vaginal pH and augmented colonization of the vagina by microorganisms, predominantly fecal E.coli. The existence of such colonization by enteric bacteria can be responsible in part for the increased frequency of UTIs in older women.

Antimicrobial therapy, administrated more often in the elderly, also alters normal periurethral flora (lactobacilli, streptococci, coagulase-negative streptococci) and favors colonization with potential urinary pathogens such as Enterobacteriaceae and Pseudomonas (5, 11).

Normally, urine possesses some antimicrobial activity. Urinary defense mechanisms include: low pH value, extremes of osmolality, high urea content, increased organic acid concentration and the antibacterial properties of prostatic secret in men. All of the above mentioned protective mechanisms can alter during the senescence and thus enhance the susceptibility to UTIs.

Loss of prostatic bactericidal secretions during senescence per se or after prostatectomy can also play a role in the increased incidence of UTIs among older men.

On the other hand, chronic bacterial prostatitis is not uncommon in elderly men but the clinical features are often asymptomatic. Definitive eradication of bacteria from prostatic tissue is often impossible and thus prostate contributes to the increased rate of UTIs, especially of relapsing UTIs, in older men (9, 11).

Diabetes mellitus, a medical condition which is more common in the elderly, is generally accepted as an

increased risk for development of UTI. The enhanced risk in diabetic patients can be associated with metabolic and mechanical disturbances such as poor control of blood glucose, diabetic neuropathy with neurogenic bladder and chronic urine retention, more frequent instrumentation and catheterization of the urinary tract, recurrent vulvo-vaginitis in females, diabetic micro- and macroangiopathy. Conversely, UTIs can lead more often to diabetic complications such as ketoacidosis (3, 8).

Micturition with complete emptying of the bladder "wash-out effect" is one of the most important defense mechanisms preventing the attachment of uropathogens and colonization of the bladder. Obstruction at the level of the urinary bladder due to prostatic diseases in men, prolapsed bladder in women and neurogenic bladder in both sexes are more frequent in the geriatric population. The increased volume of residual urine raises the number of bacteria remaining in the bladder after voiding. Vital bacteria are able to ascent against urine flow of 25 ml/min and the existence of urinary stasis may facilitate bacterial adhesion and invasion (3, 4). On the other hand, bladder distention decreases the surface area of the mucosa relative to the total volume of the bladder and thus leads to diminishing of the effect of mucosal bactericidal factors. In addition, some experimental data suggest that bladder-wall distention is associated with decrease of blood flow to the bladder mucosa, and thus the delivery of leukocytes and antibacterial factors is reduced too. It is suggested as well, that in the presence of bladder-wall ischemia due to obstruction or atonia, bacteria can penetrate the bladder lining, usually resistant to the microbial entry (7, 10).

Bacterial attachment by means of fimbriae (pili) to the bladder mucosa receptors occurs prior to colonization and is the main event mediating the onset of UTI. Usually bladder urothelium is coated with mucopolysaccharide (uromucoid), which is believed to be an essential defense mechanism because it is able to bind and cover bacterial type I pili and thus to attenuate the adherence capacity of uropathogens to the cells. Uromucoid excretion is decreased in elderly women and this can explain, in part, the heightened susceptibility to UTI in females with advancing age. An established enhanced adherence capacity of E.coli to the urothelium in elderly men is proposed as responsible occasionally for the increased rate of bacteriuria in older males (3, 4, and 10).

Phagocyte cells do not appear to have a role in preventing bacterial attachment to the bladder cells. Their main function remains ingestion and killing of the microorganisms. The process of bacterial killing is associated with generation of reactive oxygen radicals (ROS) which conversely, are highly cytotoxic for the surrounding tissues (8, 10). Phagocyte ROS production (assessed by chemiluminescence on whole blood) is markedly elevated in elderly people and it is suggested that this overproduction of cytotoxic ROS could be responsible, in part, for the tissue damage and lymphocyte function impairment in advancing age (9, 11).

Impaired immunological mechanisms in the elderly are associated with altered antibody production and may predispose to UTI in both sexes (6).

# Laboratory diagnosis

Usually the same laboratory criteria are used for confirmation of UTIs both in the elderly and in the younger population. The mead-stream specimen of urine (MSU) remains the "gold standard" for obtaining a urine specimen for microbiological examination. The elderly residents who are well are usually able to give adequate amount of voided urine for microbiological culture. In the impaired institutionalized elderly, particularly those with dementia and/or incontinence, obtaining adequate urine specimen may be difficult. Urine incontinence leads to perineal soiling and is often associated with unpleasant odor, which often serves as reason enough for antimicrobial treatment. At present, it is not clear whether antibiotic therapy is the best method for odor elimination. A more preferred method resolving this unpleasant problem is the improved hygiene (9). For women with virtually total incontinence it may be practically impossible to obtain urine specimen without any contamination. Urine for culture should be obtained from catheterized men by aspiration from the catheter with a needle after the catheter is disinfected and the glans penis has been cleaned beforehand (7).

After the generally accepted work of Kass, $10^5$ colony-forming units (CFU) of a single microorganism per ml in a MSU became accepted as "significant" bacteriuria. Contrary to this classic standard, another school of thought proposes that because of the greater likelihood of contaminated specimens in the elderly, $10^6$, or more CFU/ml could be a better standard of bacteriuria in geriatric patients (3, 5). Currently the accepted thresholds remain $10^5$ CFU/ml in two consecutive cultures for individuals with ASB, $10^2$ or more CFU/ml with a known uropathogen in acutely symptomatic women, $10^3$ or more CFU/ml of any microorganism in men. Clinical symptoms and $10^2$ or more CFU/ml in a specimen obtained by suprapubic

aspiration indicates UTI. The above mentioned criteria have specificity of about 85% and if precise new techniques are used sensitivities of about 95% (1, 3).

Contemporary criteria for diagnosis of polymicrobial bacteriuria include: 1) Isolation of the same combination of microorganisms from urine and blood, especially in cases with urosepsis; 2) Isolation of the same combination of microorganisms from follow-up urine cultures; 3) Isolation of the microbial combination from urine obtained by suprapubic aspiration or urethral catheterization, and 4) Yield of each isolate in high concentration (?$10^4$ CFU/ml); the cutoff may be under $10^4$ CFU/ml when the same microorganisms is present in the blood (1, 3, 11).

Pyuria is the other cardinal symptom reflecting the host response to an infecting organism. The presence of 10 or more leukocytes per $mm^3$ of urine, measured by haemocytometer, is associated with cultures growing $10^5$ or more CFU/ml, irrespective of symptoms. The presence of pyuria in the absence of bacteriuria supports an infection with Chlamydia thrachomatis (6, 7).

In elderly asymptomatic women, a level of 20 leukocytes or more $mm^3$ has a positive predictive value of 80% for upper UTI: leukocyte counts less than this number are uncommon (negative predictive value of 88%) in upper UTI (9, 11)

Because of the many false-positive and false-negative results, the test for antibody-coated bacteria in urine has not played an important role in the diagnoses of UTI in elderly (4, 10).

# Treatment

Asymptomatic bacteriuria (ASB) is generally accepted as a benign condition in the elderly and is not an indication for antibiotic therapy. At present, antimicrobial treatment of ASB has not been shown to alter morbidity and mortality, improve renal function or to be cost effective. Such therapy may lead to development of resistant micro flora (10, 11). Antibiotic therapy of ASB is advocated in elderly individuals prior to cystoscopy because of the high risk of bacteremia and shock following the procedure (7, 12). In elderly women, ASB after short-term catheter use (up to 30 days) frequently becomes symptomatic and for this reason it should be treated. Single-dose therapy with trimethoprin-sulfamethoxazole (TMP-SMX) may be the treatment of choice for women under 65 years of age and it is as effective as 10 days of therapy; in older females (>65 years) both types of therapy are less effective and the optimal regimen (more than 10 days) remains a controversial question (9).

Symptomatic UTI should be treated in the elderly. Because senescence is accompanied by reducing number of nephrons as well as vestibular and cochlear androgen sensory cells, the elderly are at a greater risk for aminoglycoside-induced nephro- and ototoxicity. Therefore, aminoglycosides should be avoided in the elderly people if at all possible (1, 5). Nitrofurantion also should be prescribed with caution in geriatric patients because it is ineffective in individuals with glomerular filtration rate below 50 ml/min, and in turn, when used in the face of reduced renal function there is a risk of a partially reversible peripheral neuropathy. Because the new generations of fluoroquinolons act very effective against wide spectrum of uropathogens, including Pseudomonas and are available orally, they often serve as first line therapy (2, 4).

Initial antibiotic treatment in the elderly with acute pyelonephritis (or exacerbated chronic pyelonephritis) is more often empiric and should be started with an ureidopenicillin (mezlocillin or piperacillin) or a third-generation cephalosporin given parenteraly.

Once there is clinical response, patients can be switched from parenteral to oral therapy. A two week regimen of treatment seems appropriative in such cases but the optimal duration of the active treatment remains still an open question (8, 9).

Failure to obtain an adequate clinical response 72 hours after initiation of treatment suggests the possibility of urinary tract obstruction, intrarenal or perinephric abscess. The perinephric abscess requires surgical intervention, but the intrarenal abscess usually can be treated with long-term antibiotic therapy. Urether obstruction due to calculus associated with acute (exacerbate) pyelonephritis is a clinical indication for percutaneous nephrostomy. Obstruction at the level of the urinary bladder due to prostatic diseases in men with acute pyelonephritis requires catheterization (5, 6).

Elderly women with typical signs of lower UTI should be treated at least 3 to 7 days. The preferred first-line therapy antibiotics are norfloxacin, ciprofloxacin, or TMP-SMX. If symptoms reappear when the treatment is stopped, it can suggest renal involvement and these patients should be restarted again on a 14 day course of antimicrobial therapy (10, 12).

For symptomatic men, short-term treatment is unreliable and therefore such patients should receive 7 to 10 (14) days of therapy. One common reason for relapse of UTI in elderly men is the presence of chronic bacterial prostatitis. It is frequently

asymptomatic or the symptoms may be mistaken for UTI. Chronic bacterial prostatitis requires long-term (4 to 12 weeks) treatment (TMP-SMX, or quinolones, or erythromycin) to penetrate tissues adequately (7, 12).

Recent studies point out the possibility of using intravaginal estriol cream in elderly women with recurrent UTIs. Estrogen replacement therapy reduces the incidence of UTI; this desired positive effect is associated with a significant decrease in vaginal pH value due to reappearance of Lactobacilli and a decrease in the rate of vaginal colonization with Enterobacteriaceae (9, 11, and 12). Topical estrogen administration can serve as an alternative to the use of long-term low-dose antibiotics in elderly postmenopausal women with recurrent UTIs. Preventing UTI relapses in the elderly in the last years is by administering in the spring-autumn period of immunological stimulators: Uro-Vaxon, Immunobor, Urostim, and Biozin. The treatment is long, takes 2-3 months, once daily, in combination with other antimicrobial therapy or as a single agent.

One interesting issue is the use of cranberry juice (300 ml per day) for the purpose of reduction of the frequency of bacteriuria and pyuria in elderly women. This salutary effect could be associated with two compounds in cranberry juice that inhibit the adherence of E.coli to the uroepithelial cells. The first of them is fructose (common to many other fruit juices) and the second is a nondialyzable polymeric substance, isolated only from cranberry and blueberry juices (3, 10).

# Conclusion

The large variety of microbiological agents causing UTIs in geriatric patients is a challenge for the medical community. Infections caused by poliresistant pathogens, some of them acquired in hospital setting or during instrumental procedures, make that even more difficult and the use of combination of antibiotics, vaccines, immune modulators and herbs is often used. Contemporary 21 century medicine requires an intelligent approach considering the age of the patients, most common causes, co-morbidities, and side effects of treatment as well as the prevention of microbiological contamination during medical procedures.

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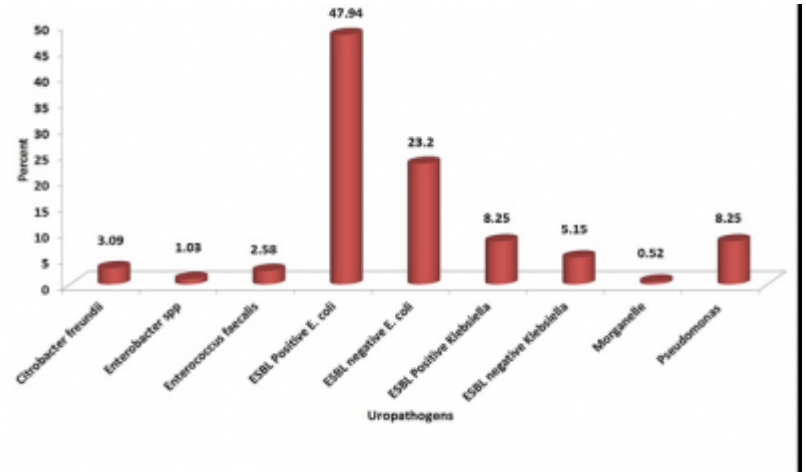
# Illustrations

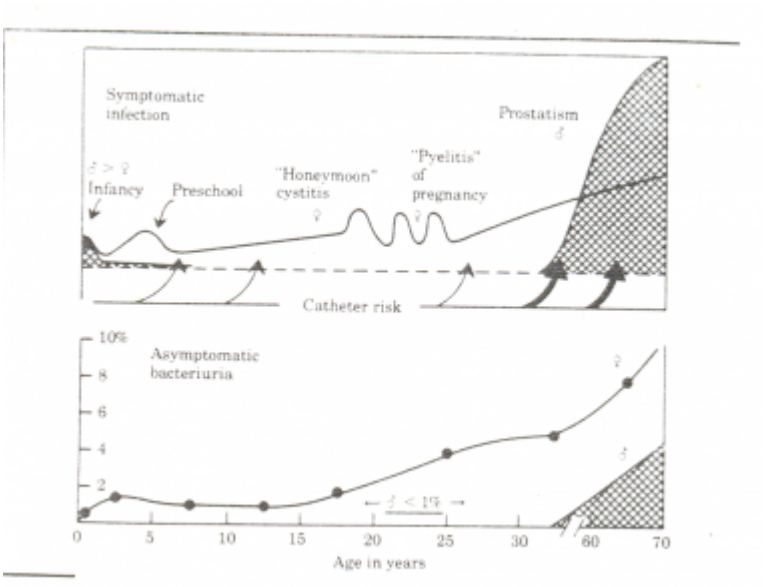
## Illustration 1

Frequency and distribution pattern of urinary tract infection pathogens



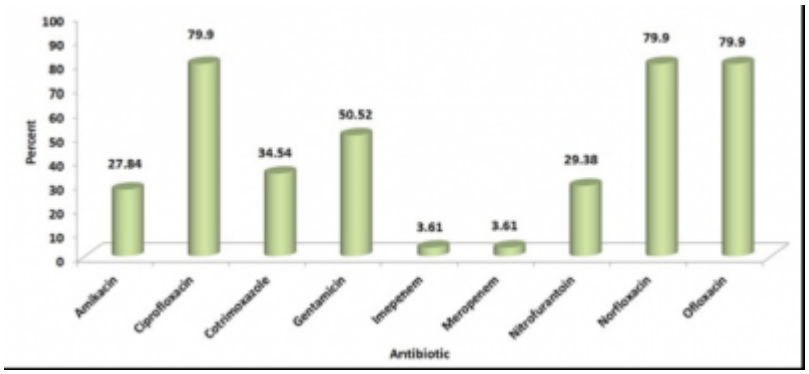

## Illustration 2

Rate of ASB and Catheter risk from childhood to adult age



# Illustration 3

Effectiveness in antibiotic treatment



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