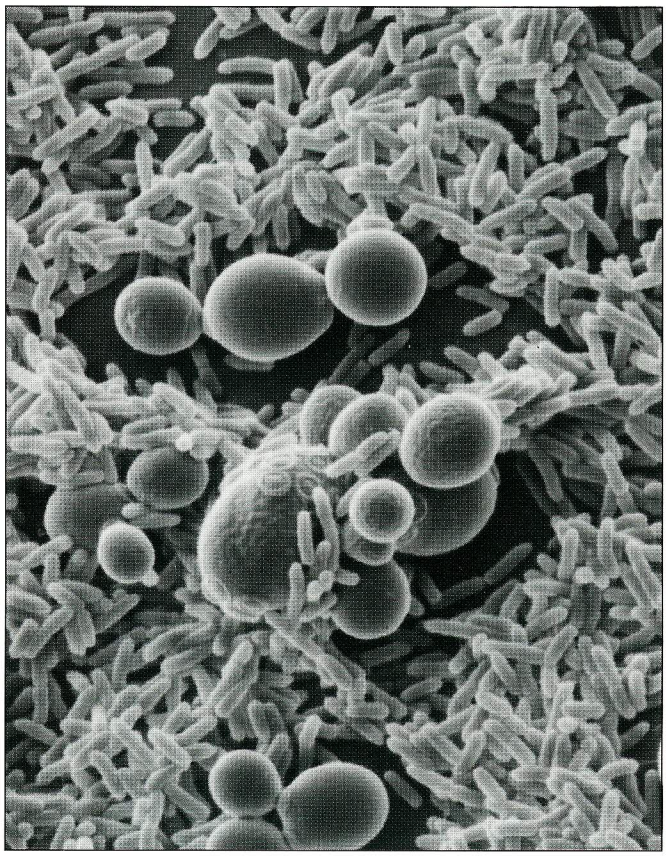
Uncovering Urinary Tract Infections

A Look at Bacterial Adherence & Biofilms



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Cover Photograph: Mixed biofilm of the yeast-like fungus *Candida albicans* and the Gram negative bacterium *Serratia marcescens* on an All-Silicone Catheter

Abstract

Urinary tract infections (UTIs), which show a strong correlation with catheterization, are the most common hospital-acquired infections in the United States. UTIs markedly increase patient costs and mortality. The prevention or even the delay of the symptoms of UTIs offer significant health and economic benefits. The Bardex® I.C. Catheter, with unique antimicrobial properties, markedly resists bacterial attachment *in vitro*. *In vivo* studies show that the Bardex I.C. Catheter is associated with a reduced incidence of UTIs and a delay in the onset of UTI symptoms.

Urinary Tract Infections

Microbial colonization of indwelling and implantable medical devices may lead to serious and often fatal infections. Most commonly, urethral catheterization contributes to a high incidence of nosocomial urinary tract infections (UTIs) estimated to exceed 500,000 cases per year. Complications related to catheter-associated UTIs have caused an increased incidence of bacteremia[5] and a three-fold increase in mortality.

Significant bacteriuria

Urine is normally sterile. It passes from the kidney and the bladder free of microorganisms. Bacteriuria is the presence of microorganisms in the urine regardless of the source. "Significant bacteriuria" indicates that bacteria are multiplying in the urine. Passed urine that was sterile in the bladder will contain fewer than 10,000 colony forming units (CFU) of bacteria per ml. Classically, "significant bacteriuria" is characterized arbitrarily by CFU greater than 100,000/ml. Bacterial counts in the urine of infected and noninfected patients develop in the range between 10^3-10^5/CFU/ml. This is caused by:

a) differences in growth rate between different bacterial species

b) the use of antibiotics and/or antimicrobial agents which affect bacterial growth rate

c) the pH of the urine, its flow rate and its chemical composition

d) the time of incubation in the bladder

e) occasional obliteration of the flow of urine from an affected kidney

Bacterial counts as low as 10^2/CFU/ml in urine obtained aseptically from a catheter may be "significant," because the microorganisms cannot be unquestionably attributed to contamination. Eventually, such low densities, (a beginning of cryptic infections) may rise to 100,000 CFU/ml in less than 24 h. The most common causes of urinary tract infections are presented in Table 1.

Table 1. – **Urinary Tract Infections in the United States** [a]

Microorganisms	Uncomplicated UTIs and colonization		Complicated UTIs
	Males	Females	
Escherichia coli	80 [b]	72	26
Enterococci spp.	4	<1	17
Pseudomonas aeruginosa	<1	<1	12
Candida albicans	<1	2-4	7
Klebsiella spp.	6	4	<5
Proteus spp.	7	6	<5
Staphylococcus saprophyticus	<1	15	<1
Enterobacter cloacae and *Citrobacter freudii*	2	<1	<1

[a] Compilation of data from references on probable etiologic agents associated with UTI among hospitalized patients; 1983-1990.

[b] Incidence (%) among hospitalized patients (adapted from Kunin, 1987; Stamm, et al. 1991).

There has been a great interest in studying the epidemiological characteristics of UTIs in various populations. Male infants compose about 75% of all UTI patients in the first 3 months of life; thereafter females takeover. *Escherichia coli* accounts for nearly 90% of the infections of newborns and infants. Symptomatic UTIs (infections accompanied with clinical signs like fever, irritability, vomiting, and diarrhea) in preschool children (1-5 years of age) are from 10-20 times more common in girls than in boys. Gram-positive cocci are the more prevalent causative microorganisms among the preschool group. Among the elderly, about 60% of the cases of bacteriuria are caused by Gram-negative microorganisms, especially *E. coli.* UTIs are more common in adult women than any other groups. Factors that affect the frequency of UTIs in females include pregnancy and sexual activity.

A variety of syndromes among hospitalized patients that are associated with UTI, are listed in Table 2. Catheterization is the single most important factor.

Although indwelling catheters predispose patients to UTIs, catheterization is necessary for a variety of syndromes and diagnostic procedures. These include measurement of urine output, collection of urine during surgery, and urinary retention. The catheter allows the bacteria to gain entry to the urinary tract in several ways:

Table 2. – **Patient Populations at high risk of developing Urinary Tract Infections** [a]

Populations	Percent (%) of Hospitalized Patients
Indwelling catheter over 48 hours (open drainage)	98
Hydronephrosis, nephrolithiasis	85
Congenital urologic disease	57
Women with cystocoele	23
Diabetes mellitus	20
Hypertension	14
Pregnancy term	10
Routine medical OPD	5
After single catheterization	2

[a] Adapted from: Kunin, 1987.

1) bacteria may be carried into the urethra during the insertion of the catheter,

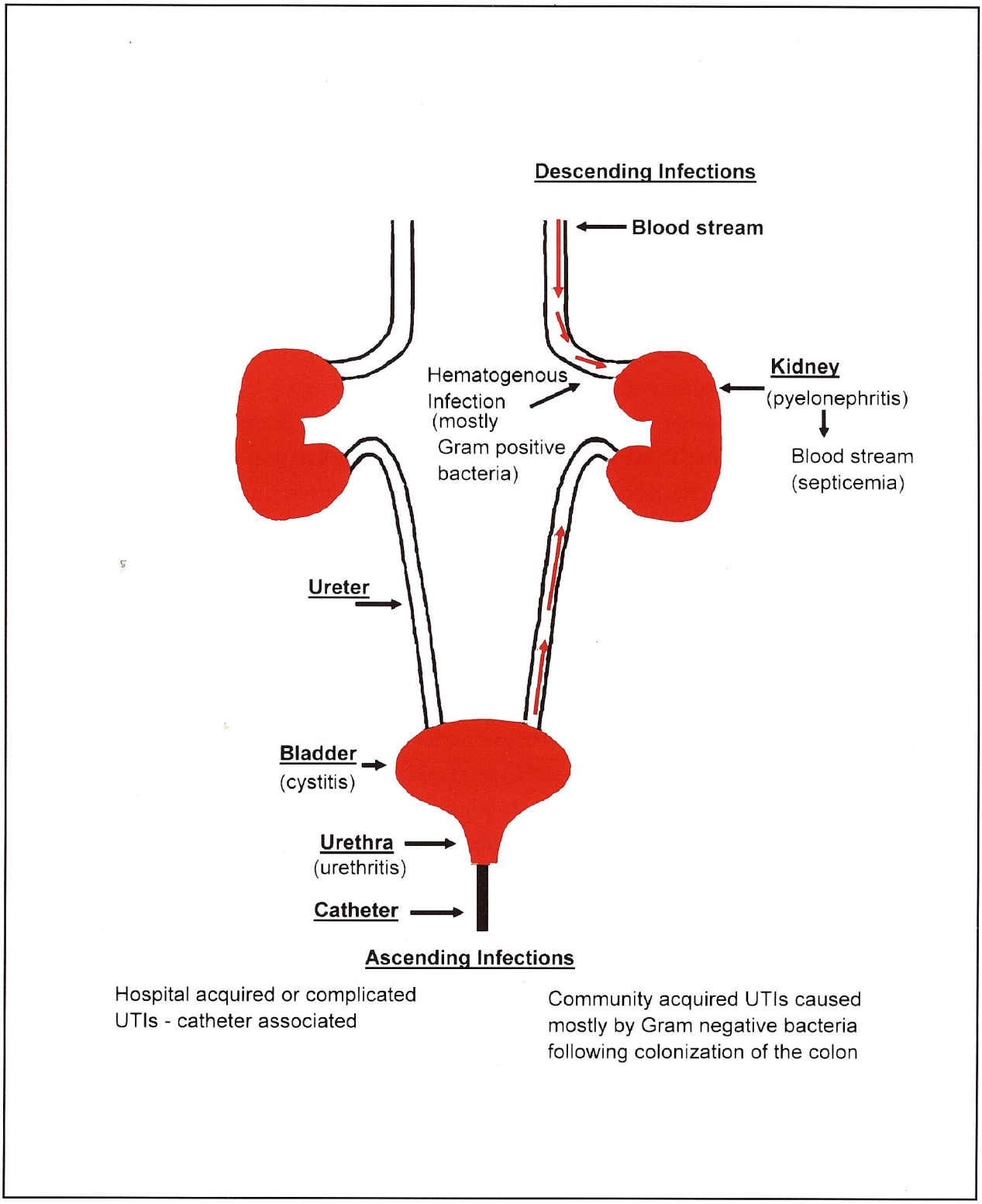
2) bacteria may circulate up to the upper part of the urethra or travel intraluminally to the bladder from the inside of the collecting bags,

3) bacteria may gain access to the bladder externally from the urethral meatus.

Four factors have been seen repeatedly to be a major risk factor for UTI: female, duration of catheterization, absence of systemic antibiotics, and catheter care violations.

Numerous studies have demonstrated the access of bacteria to the bladder extraluminally through a thin fluid space between the catheter and the urethral mucosa. Also contamination of the drainage spout or disconnection of the catheter-drainage tube junction of the open drainage system has been implicated in the intraluminal migration of the organisms to the bladder. Patients catheterized with an open drainage system often develop UTIs after about 3-4 days. Even with the use of preventive measures including the administration of systemic antibiotics, the application of local antibiotics either in the form of lubricants or impregnation into the catheter, and the irrigation of the bladder with antimicrobial solutions, the development of UTIs still occurs. Closed drainage systems appear superior to open systems in regard to the prevention of catheter associated infections. Nevertheless, closed sterile drainage systems that ideally permit maintenance of sterile urine for up to 10-14 days still are associated with an incidence of infection of about 5%-10% per patient-day.

Figure 1. – **Structures and Associated Diseases of the Urinary Tract** [a]



[a] Adapted from Salyers and Whitt, 1994.

Biofilms

Marshall (1992) reported that most bacteria can exist in two distinct physical environments:

1) the planktonic (floating) state, whereby cells function as individuals, and

2) the sessile (adherent) state, whereby they attach to surfaces, form biofilms, and function as a closely integrated community.

Individual cells that attach to catheters (primary adherence) eventually become coalesced and embedded in a slime or glycocalyx. Insertion of prosthetic devices into the human body often leads to the formation of biofilms on the surface of the devices. Biofilms on biomaterials provide foci of infection for other parts of the body via bacterial detachment and biofilm sloughing. The development of a bacterial biofilm confers a degree of antimicrobial resistance to bacteria, including bacteria adhering to Foley catheters *in vivo* and *in vitro*. The biofilm forms a matrix that concentrates nutrients and possibly protective enzymes (penicillinase) near the cells, but tends to exclude predators (macrophages) and antibacterial agents (antibodies and antibiotics).

It is obvious that a prevention of microbial adherence or even a single day's delay in the development of a biofilm can be of major benefit to the catheterized patient. To this effect Bard Medical Division has introduced the BARDEX I.C. Catheter. The BARDEX I.C. Catheter, with its unique silver process, reduces the primary adherence of the most common cause of UTI, *E. Coli*, by 25% to 99%. After attachment, other Gram-negative bacteria such as *P. aeruginosa* have shown significant cell damage and death (Gabriel et al., 1996). The silver in the BARDEX I.C. Catheter does not readily ionize. Silver metal is applied to the latex in an approximate monolayer thickness through a proprietary process (Ahearn et al., 1995). In contrast to silver oxide-coated materials which readily release silver ions, the BARDEX I.C. Catheter material gives negligible zones of inhibition for bacteria in agar diffusion studies. In a recent hospital study (Carlton, 1996), no catheter associated UTIs occurred during a three-month study period with a silver/hydrogel catheter (BARDEX I.C. Catheter), whereas in four proceeding three-month periods, catheter-associated UTIs ranged from 7 to 32. However, statistically significant differences on the basis of UTIs per 1000 device-days were not observed. The preliminary report of Lee and Hernandez (1996) noted that with the exclusive use of a hydrogel / silver coated catheter (BARDEX I.C. Catheter), the number of catheter-associated UTIs decreased from 46 per 659 patients for a six-month period to 29 per 665 patients for the following six months. The decrease of 37% in UTIs strongly supports the value of further studies on the antimicrobial properties of the BARDEX I.C. Catheter. These *in vivo* reports indicate that the BARDEX I.C. Catheter is associated with a reduction in the incidence of UTIs, or at least, a delay in the onset of symptoms.

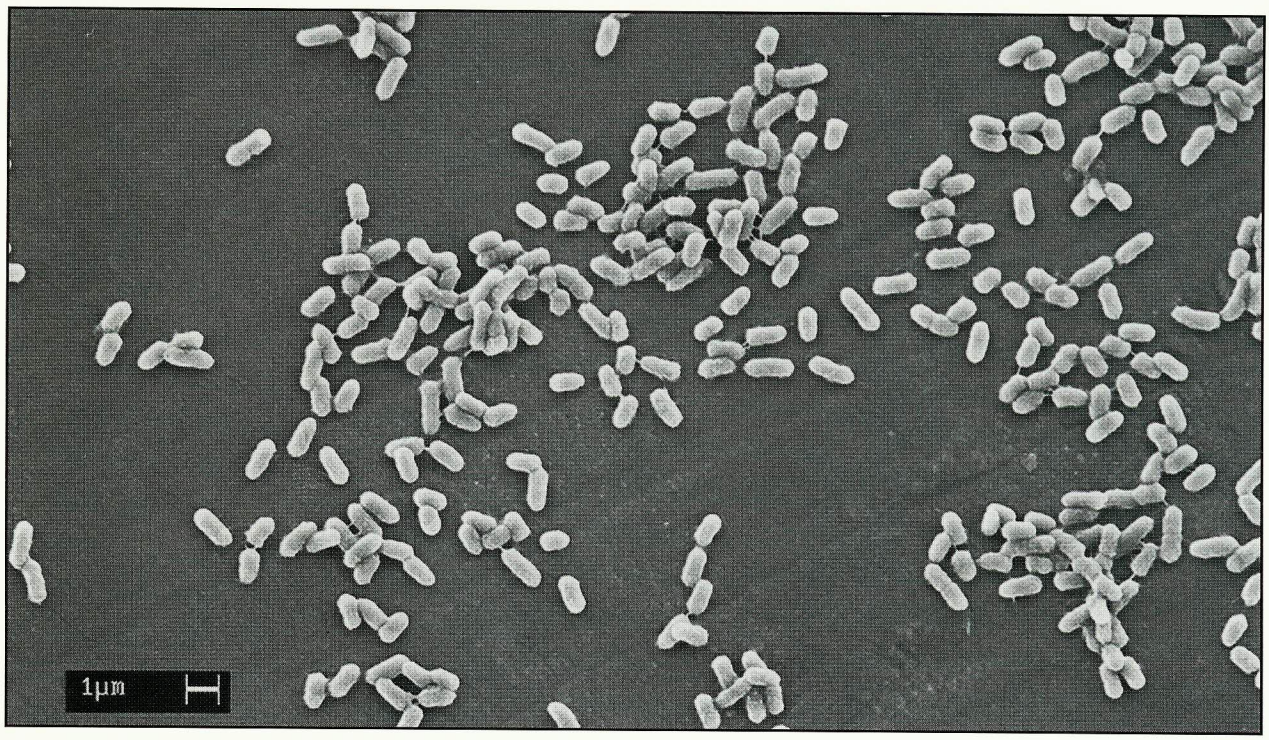


Figure 2a.

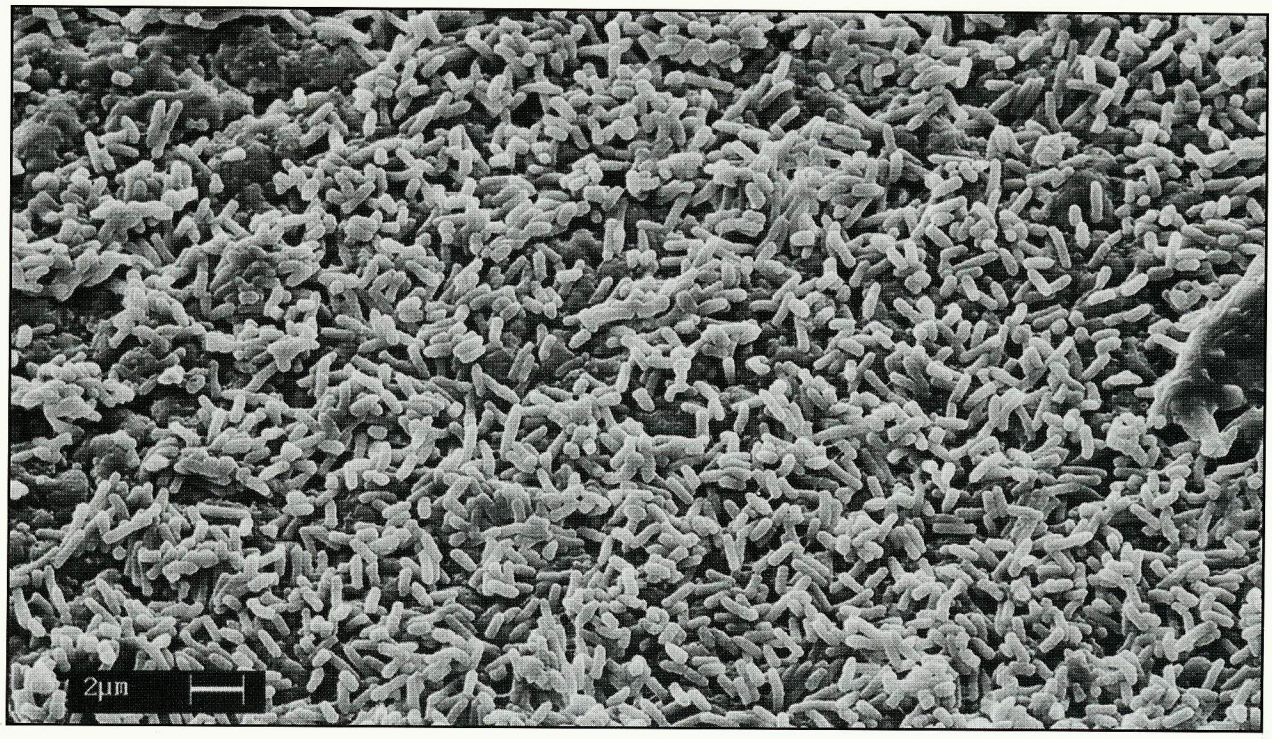


Figure 2b.

Primary adherence of the Gram negative bacterium *Pseudomonas aeruginosa* (**a**) after 2 hours on an All-Silicone catheter surface compared with a biofilm (**b**) produced by 18 hours.

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