

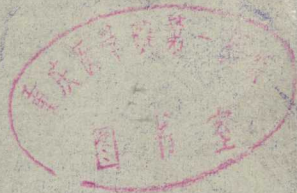
The Management of Infectious Diseases  
in Clinical Practice

Edited by

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## Preface

Few areas of clinical practice have witnessed an accelerated growth of useful information during the past several years comparable to that seen in the field of infectious diseases. "New" etiologic agents and syndromes have been recognized, such as Legionnaires' disease, a variety of chlamydial infections, campylobacter enteritis, *Clostridium difficile* toxin-induced pseudomembranous colitis, and staphylococcal toxic shock syndrome. New guidelines for the management of "old" problems have been proposed—for example, shorter course treatment for tuberculosis and urinary tract infections. New insights have emerged into the mechanisms of host defense and of those infections that threaten the lives of our immunocompromised patients. In virology, important breakthroughs have occurred, and there has been a productive reawakening of interest in parasitology. Finally, new diagnostic methods have been introduced into practice, and there has been an almost explosive development of new antimicrobial agents.

Given the pace and complexity of many of these developments, it has become increasingly difficult for the clinical practitioner to keep abreast of those aspects that should have direct application to patient care. The main goal of this book is to facilitate this process. In this volume, an outstanding group of infectious disease specialists have summarized current approaches to the management of infections of greatest clinical importance. This book should be useful to virtually all primary care physicians—to the generalist, family practitioner, pediatrician, internist, and surgeon.

The book is organized into three subject areas: (1) infections of specific organ systems, (2) different types of pathogens, and (3) specific problem areas and general diagnostic and therapeutic considerations. The pathogenesis of each infectious disease is briefly reviewed; the main emphasis, however, is on a practical approach to diagnosis and treatment. For quick reference, there has been a liberal use of tables.

A "camera ready" form of manuscript preparation has been employed because it requires significantly shorter production time, and hence, facilitates the rapid availability and currency of the information covered.

The editors are deeply indebted to each of the authors of this book, to Jane Anderson for her assistance in its preparation, and to the staff of Academic Press for their encouragement and help in producing a timely publication.

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TABLE 1. Bacterial Urinary Infection Syndromes

Definitions and Presenting Features

PART I

GENITOURINARY TRACT INFECTIONS

URINARY TRACT INFECTIONS:

PRACTICAL APPROACHES TO DIAGNOSIS AND MANAGEMENT

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I. THE DISEASE ENTITY

Symptoms arising from infection of the urinary tract is a common problem in medical practice and experienced by most women at some time throughout life. Several studies have suggested that as many as 20% of women experience dysuria during the course of a year. One half of these women consult a physician about these symptoms for approximately 90 physician visits for dysuria per 1000 women per year (1). Urinary infection occurs frequently in female children (1-2 infections/year/100 schoolage girls) and in elderly men.

Table 1 summarizes definitions and presenting features useful as diagnostic entities in urinary infection. Unfortunately, no clinical presentation is uniquely associated with bacterial urinary infection and the diagnosis depends on careful microbiologic investigation of a clean voided urine with a quantitative culture.

Aerobic gram negative rods cause almost 90% of all urinary infections with Escherichia coli responsible for about 80% of community acquired infections. Coagulase negative Staphylococcus sp account for about 10% of infections. Infections acquired in hospital are more often due to P. aeruginosa, Proteus sp and Klebsiella sp.

The acute urethral syndrome is a diagnosis given to patients who have symptoms usually confined to the urethra

TABLE 1. Bacterial Urinary Infection Syndromes

## Definitions and Presenting Features

Acute cystitis - Dysuria or painful urination with frequency, urgency, and a variable incidence of hematuria, malodorous urine, bladder spasms. Fever not more than 38°C. Pyuria and bacteriuria (usually more than 100,000 organisms per ml urine).

Acute urethral syndrome - Dysuria with variable bladder symptoms and "no growth" or low counts in urine cultures. Sometimes accompanied by vaginitis. May be due to bacteria or Chlamydia trachomatis.

Acute pyelonephritis - Fever and chills, flank pain, often accompanied by bladder and urethral symptoms. Bacteriuria with pyuria; sometimes with white cell casts. Usually unilateral. Bacteremia common.

Acute prostatitis - Severe perineal, rectal or penile pain with fever and chills. Bacteria in initial voided urine. Bacteremia common.

Chronic urinary infection - A diagnosis that defies a useful definition but implies recurrent bacterial urinary infection.

Chronic prostatitis - Recurrent usually low grade perineal discomfort, sometimes with intermittent episodes of bacterial cystitis or pyelonephritis. Etiology of non-bacterial prostatitis uncertain.

Chronic pyelonephritis - Roentgenologic diagnosis based on pyelographic evidence of renal scarring and calyceal destruction with loss of fine details of calyceal structure. May be accompanied by recurrent renal symptoms, bacteriuria, and pyuria. Renal impairment may be present often with an inability to concentrate urine normally after fluid deprivation.

Asymptomatic bacteriuria - Bacteriuria sometimes accompanied by pyuria. May be confined to the bladder or involve in addition one or both upper tracts. Of uncertain significance in most populations. Should be treated if present during pregnancy or if complicated by intermittent symptoms or evidence of destructive changes in the upper tracts.

(continued Table 1)

Reinfecting recurrent urinary infections - New organism from outside the urinary tract ascending the urethra and establishing infection at a variable interval after eradication of a prior infection.

Relapsing recurrent urinary infection - Persistence of the organism within the urinary tract (usually in a focus in the prostate or kidney) with emergence (regrowth) after therapy.

## II. ITS NATURAL HISTORY

In the absence of treatment, the natural history of various urinary infection syndromes is uncertain. Patients with acute cystitis and occasionally even patients with acute pyelonephritis experience symptomatic improvement despite continuing bacteriuria. In one series, asymptomatic women with bacteriuria were followed for one year. One third spontaneously resolved during the year, one third became symptomatic and one third continued to have asymptomatic bacteriuria (3).

without a positive urine culture ( $< 100,000$  organisms/ml). Recent studies have shown that these patients can be categorized by the presence of inflammatory cells. Patients with pyuria usually have either "low count" bacteriuria or Chlamydia trachomatis urethritis. A ten day course of doxycycline has been found effective for most patients (2). Patients without pyuria do not respond to antimicrobial agents and the etiology of their symptoms remains uncertain.

Most urinary pathogens gain access to the bladder and kidneys by ascending against the urinary stream. Only S. aureus and Candida albicans reach the kidney in most instances via the hematogenous route. In women, the propensity to frequent re-infections appears to be due to a biologic defect that permits heavy prolonged colonization of the perineum with gram negative rods. Probably this is due to increased adherence of E. coli to uroepithelial cells. In a recent study, we have shown that sexual intercourse is an important antecedent event in women with recurrent infection. About 80% of infections in sexually active young women occur on a postintercourse day. Voiding patterns and residual urine are presumably also important factors in urinary infection pathogenesis.

Bacteria can readily ascend to the kidneys if vesicoureteral reflux is present. However, only 20% of patients with acute bacterial cystitis and 40% of patients with asymptomatic bacteriuria, have organisms in the upper tracts. The presence of renal calculi or of unilateral renal disease, permit organisms to persist in the upper tract despite antimicrobial therapy.

The antimicrobial coated bacteria test has been used to localize the site of infection in patients who are either asymptomatic or have symptoms confined to their lower urinary tract. Organisms emanating from the kidneys are coated with antibody to the osomatic antigen. This antibody is produced within renal tissue in response to invasive infection. Bacteria that originate from the bladder are not coated with antibody. Unfortunately, this test as presently carried out, is only useful for epidemiologic and therapeutic investigation and is not reliable for the treatment of the individual patient.

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TABLE 2: Prognostic Factors in Urinary Infection

Source of infection	Usually More Difficult to Treat and Prone to Recur
Presenting symptoms	Institutionally acquired Acute pyelonephritis Acute prostatitis Asymptomatic infection
Etiology	Resistant organisms, such as <u>P. aeruginosa</u>
Site of infection (localization by ACB or single dose therapy)	Asymptomatic or recurrent infection localized to the kidney or prostate
Underlying disease	Infection complicated by obstruction, calculi, congenital anomalies, neurologic disease
Pattern of recurrence	Relapse after previous courses of treatment
Renal function	Impaired
Sex	Males
	Usually More Simple to Treat
	Community acquired
	Acute cystitis
	Susceptible organisms, such as <u>E. coli</u>
	Infection confined to the bladder
	None
	Reinfections after previous curative regimens
	Normal
	Females



### III. MANAGEMENT OF EPISODIC INFECTION

The response to therapy is variable but can be predicted by several prognostic factors. Several of these are outlined in table 2.

Single dose treatment has been popularized during the past five years through at least eight studies, each of which have shown that a single dose of an antimicrobial agent can cure more than 90% of women and girls with acute cystitis or asymptomatic infection localized to the bladder (4,5). Single dose therapy is inexpensive, rarely associated with side effects, and does not predispose to the acquisition of resistant pathogens. Those patients who have failed single dose therapy have not recurred with symptoms or signs of renal infection within the initial weeks of follow-up. However, all patients treated with single dose therapy must have a follow-up to identify those patients who will recur.

The identification of patients with renal infection who require more prolonged intensive therapy and additional investigation, is the most important advantage of single dose therapy. Studies with single dose therapy that have used localization techniques, have determined that failure of single dose therapy in females is an excellent indicator of renal infection (specificity of over 90%) and failure of single dose therapy will detect all patients who have urologic or anatomic abnormalities in their urinary tract.

No single dose studies have yet been reported in males. Many males with symptoms confined to their lower urinary tract also have concomitant prostatic infection. Two weeks or more of therapy is required, usually with an agent such as trimethoprim/sulfamethoxazole, that enters prostatic tissue (6).

Patients with upper tract symptoms are usually ill with symptoms and signs of acute pyelonephritis. They should be treated with wide spectrum parenteral antimicrobial therapy until a clinical response occurs and the susceptibility of the infecting organisms is known. An aminoglycoside such as gentamicin or tobramycin together with ampicillin is appropriate initial therapy. Some patients with renal infection are not acutely ill and can be treated without hospital admission with an oral well absorbed wide spectrum antimicrobial agent such as cephalexin or trimethoprim/sulfamethoxazole. The prevalence of ampicillin resistant organisms in most community acquired urinary infection studies, makes ampicillin or amoxicillin a less effective choice for the initial treatment of acute upper tract infection prior to susceptibility testing.

Patients with hospital acquired infection particularly associated with catheterization who develop invasive renal