

Urinary Tract Infection

Introduction

Urinary tract infection (UTI), the most common of all bacterial infections, affects humans throughout their life span. Twenty percent to 35% of all women experience at least one episode of UTI sometime in their lives. UTI occurs in all populations, from the neonate to the geriatric patient, but has a particular impact on females of all ages, males at the two extremes of life, kidney transplant patients, and anyone with functional or structural abnormalities of the urinary excretory system. Because of the wide range of individuals affected and because UTI is frequently superimposed on other medical problems, physicians in virtually all specialties are called on to deal with this clinical problem.

Not only is UTI common, but the range of clinical effects it can produce is exceptionally broad, from acute pyelonephritis with gram-negative sepsis to asymptomatic bacteriuria and even so-called symptomatic abacteriuria.

It is clinically important to classify UTIs by type of infection, presence or absence of symptoms, tendency to recur, and presence or absence of complicating factors (Table 1). Recurrent infections can be subdivided into reinfections caused by new bacterial strains and relapses caused by the same strains that caused the preceding infections. Complicating factors are host factors facilitating establishment and maintenance of bacteriuria or worsening the prognosis of UTIs engaging the kidneys.

Table 1. Classification of urinary tract infection

Classification by	Types of UTIs
Type of UTI	Cystitis Pyelonephritis Asymptomatic bacteriuria
Symptoms	Symptomatic Asymptomatic
Recurrences	Sporadic Recurrent Relapse Reinfection
Complicating factors	Uncomplicated

Complicated

Epidemiology

It has been calculated that worldwide there are at least 150 million cases of symptomatic UTIs each year. Because many UTI patients have recurrent infections, the number of individuals who have UTIs each year is lower than the number of cases.

In an unselected material, 90% of the patients will have cystitis and 10% pyelonephritis. The infections will be sporadic in about 75% of the patients and recurrent in 25%. About 2% will have complicated infections due to factors that increase the risk of establishment and maintenance of bacteraemia. These patients typically have frequently recurring UTIs. If factors that may increase the severity of a renal infection are included, the frequency of complicated infections is about 8%.

During life, UTIs are somewhat more common in very young boys than in very young girls, that is due to the higher frequency of urethral malformations in boys. Later in childhood, symptomatic UTI is more common in girls, who also more frequently have asymptomatic bacteriuria. This is in most cases due to the short urethra but may also be the result of sexual abuse. Symptomatic UTIs are by far most common in sexually active women. In young men, bacterial UTIs are rare and often the result of underlying infections of the prostate. In the elderly, both symptomatic UTIs and asymptomatic bacteriuria are common. In women, that is often the result of atrophic vaginal mucosa, and in men, to prostate hyperplasia or prostate cancer.

UTI is the most common type of hospital-acquired infection, because of the frequent use of bladder catheters.

Etiology

The microbiologic etiology of a UTI depends on several factors. Table 2 summarizes the most common findings. In all types of UTI, *E. coli* is the dominating bacterial species causing up to 85% of all symptomatic UTIs in women with community-acquired, sporadic, uncomplicated infections. In most countries, the second most common species causing such infections is *Staphylococcus saprophyticus* (sometimes called micrococci). In patients with recurrent infections, species such as *Enterococcus faecalis*, *Enterococcus faecium*, *Klebsiella* spp., *Proteus* spp., *Providencia stuartii*, and *Morganella morganii* become more common. In

patients with very frequent recurrences and/or bladder catheters, especially in hospital and nursing home settings where antibiotics are frequently used, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Serratia marcescens*, and *Stenotrophomonas maltophilia* are important organisms. In such patients, *E.coli* accounts for less than 50% of the infections. Findings of *Proteus mirabilis* or other *Proteus* spp. may indicate that the patient has renal calculi or a tumor, because these organisms grow in an alkaline environment. Calculi in the renal pelvis, the ureter, or the bladder may also be formed as a result of growth of ammonia-producing organisms such as *Proteus* spp.. Because *Proteus* spp. are common in the male preputial flora, the finding of such organisms in a voided urine sample from uncircumcised men or young boys should be interpreted with caution.

Table 2. Microbial etiology of urinary tract infection

Organisms	Clinical Characteristics
Gram-negative bacteria	
<i>Escherichia coli</i>	Typical
<i>Klebsiella pneumoniae</i>	Often reinfection
<i>Enterobacter</i> spp.	Often reinfection and/or nosocomial infection
<i>Proteus</i> spp.	May indicate tumor or calculi
<i>Providencia stuartii</i>	Often reinfection and/or nosocomial infection
<i>Morganella morganii</i>	Often reinfection and/or nosocomial infection
<i>Serratia marcescens</i>	Often nosocomial infection
<i>Acinetobacter baumannii</i>	Often nosocomial infection
<i>Burkholderia</i> spp.	Often nosocomial infection
<i>Pseudomonas aeruginosa</i>	Often nosocomial infection
<i>Stenotrophomonas maltophilia</i>	Often nosocomial infection
Gram-positive bacteria	
<i>Staphylococcus saprophyticus</i>	Most common during summer
<i>Staphylococcus aureus</i>	May indicate focus outside the genitourinary
<i>Enterococcus</i> spp.	Often reinfection
Other Gram-positive bacteria	In most cases contaminants
Fungi	
<i>Candida</i> spp.	May indicate focus outside the genitourinary

Pathogenesis

Possible routes of infection

The first consideration in discussing the pathogenesis of UTI is the route by which microorganisms, especially bacteria, reach the urinary tract in general and the kidney in particular. Four potential routes have been proposed: the ascending route, from the urethra to the bladder, then by the ureters to the kidneys; the hematogenous route, with seeding of the kidney during the course of bacteremia; intestine to kidney by way of lymphatics; and direct infection.

Ascending Infection

There is considerable clinical evidence that most infections of the kidney result from ascension of fecally derived organisms from the urethra and periurethral tissues into the bladder and then by the ureter to the renal pelvis, with subsequent invasion of the renal medullae at this site. In discussing the pathogenesis of ascending infection, it is useful to examine the various steps necessary for the spread of organisms from the periurethral region to the kidney.

Hematogenous Infection

In humans, blood-borne infection of the kidneys and urinary tract accounts for less than 3% of the cases of UTI and pyelonephritis. When one considers the organisms that are capable of causing pyelonephritis by the hematogenous route, a list different from that outlined in Table 32-1 is compiled. Whereas *E. coli*, the other Enterobacteriaceae, *S. saprophyticus*, and *E. faecalis* account for approximately 95% of UTIs, the major causes of hematogenous infection are *S. aureus*, *Salmonella* species, *P. aeruginosa*, and *Candida* species. Because the kidneys receive 20% to 25% of the cardiac output, any microorganism that reaches the bloodstream can be delivered to the kidneys.

Lymphatic route

Direct infection.

Bacterial Virulence Factors Influencing Infection

One of the most striking characteristics of UTI is that a single species of bacteria, *E. coli*, not only accounts for the great majority of UTIs but also can cause a wide range of clinical disease, from asymptomatic bacteriuria to cystitis to full-blown pyelonephritis. This observation by itself raises a series of important questions: Are there differences between the *E. coli* strains that cause these different clinical forms of UTI? In particular, are there "nephritogenic" strains of *E. coli*, that is, strains that

possess the ability to adhere, ascend, and invade the anatomically normal urinary tract? Conversely, are nonvirulent strains able to adhere, ascend, and invade the anatomically abnormal urinary tract? Is there a difference between the characteristics of the *E. coli* strains causing the acute inflammatory condition that we recognize as acute pyelonephritis and those causing chronic renal scarring and progressive loss of renal function?

On the basis of a series of landmark studies done in the past two decades that have combined clinical epidemiology with molecular biology and well-designed animal models, it is now possible to say that the answer to all of these questions is clearly yes; that is, strains of *E. coli* that invade the urinary tract are not merely the most prevalent components of the fecal flora. Rather, they are specific clones that possess a variety of virulence characteristics that facilitate intestinal carriage, persistence in the vagina, and then ascension and invasion of the anatomically normal urinary tract. In the presence of foreign bodies, VUR, or obstruction, these events can occur in the absence of such characteristics, which emphasizes that host characteristics are as important as the nature of the invading organism in determining the outcome of the infection.

The first evidence that *E. coli* strains causing pyelonephritis were different from other isolates came from serotyping studies, in which the O (somatic or surface cell wall) antigen, H (flagellar) antigen, and K (capsular) antigen of isolates from well-defined clinical populations were determined. Whereas the serotypes associated with asymptomatic bacteriuria do not differ from those present in the fecal reservoir, strains from symptomatic patients are significantly different both when serotyping is carried out and when molecular genetic analyses are performed. Thus, *E. coli* strains bearing eight of the approximately 170 different O antigens (O1, O2, O4, O6, O7, O16, O18, and O75) account for approximately 80% of the cases of pyelonephritis caused by this species, with a small number of K antigens (K1, K2, K5, K12, and K13 or K51) being identifiable on more than 70% of the pyelonephritis isolates. In contrast, the H antigens appear not to be independently associated with virulence.

The amount of K antigen expressed appears to be especially important, because strains of *E. coli* particularly rich in K antigen appear to be more successful both in reaching the bladder and in ascending to and invading the kidney than are strains with low amounts of K antigen.

Host Factors Influencing Infection

Factors predisposing to pyelonephritis

Several factors are important clinically in predisposing the kidney to infection.

Urinary Tract Obstruction. Reference has already been made to the role of obstruction in hematogenous and ascending pyelonephritis. Clinically, renal infections are associated with a variety of obstructive lesions. Obstruction at the level of the urinary bladder interferes with the mechanisms by which the normal bladder eradicates bacteria in at least three ways: first, the increase in residual urine volume raises the number of bacteria remaining in the bladder after voiding; second, bladder distention decreases the surface area of the mucosa relative to the total volume of the bladder and thus decreases the effect of the postulated mucosal bactericidal factors; and finally, there is some experimental evidence that bladder wall distention diminishes flow of blood to the bladder mucosa and hence the delivery of leukocytes and antibacterial factors. The net result is that even "nonuropathogenic" strains can cause ascending infection and bacteremic pyelonephritis.

Whereas complete ureteral obstruction markedly increases the susceptibility of the kidney to infection and also results in reactivation of healing lesions, gradual or partial ureteral obstruction induced either surgically or by irradiation of ureters affects renal susceptibility to hematogenous infection to only a slight degree. It is probable, therefore, that the association between partial obstruction and pyelonephritis in humans is due to an effect on the ascending mechanism of infection, either by interfering with ureteral urodynamics or by accentuating the effect of VUR.

Congenital abnormalities such as polycystic kidney disease, vesicoureteral reflux.

Instrumentation of the Urinary Tract. Any instrumentation of the urinary tract increases the possibility of infection. The following risk factors have been shown to play a role in the pathogenesis of catheter-associated infection: duration of catheterization, absence of use of a urinometer, microbial colonization of the drainage bag, diabetes mellitus, absence of antibiotic use, female patient, complex urologic problem (i.e., a requirement for a catheter other than to passively drain the urine perioperatively or to monitor urine output), abnormal renal function, and errors in catheter care. Once a urethral catheter is in place, even with closed drainage systems, the daily frequency of bacteriuria is 3% to 10%, with the great majority of patients becoming bacteriuric by the end of 1 month.

Female urethra The female urethra is short and allows transport of bacteria to

the bladder also in healthy individuals. With many uropathogens such transport is facilitated by adherence of the bacteria to urethral epithelial cells.

Pregnancy.

Disturbance of immune capacity such as diabetes, anemia, chronic hepatic disease, chronic kidney disease, tumor and so on. Patients with diabetes mellitus have an increased risk for development of symptomatic UTI, including pyelonephritis. The postulated causative factors for this increased frequency of upper UTI are that the metabolic derangements in diabetes lead to increased urinary glucose concentrations; a defect in leukocyte function; and the propensity for obesity, vulvovaginitis, neuropathy, and angiopathy.

Pathology

Acute Pyelonephritis

The acute lesions can vary considerably in severity from some that affect only the pelvic mucosa (pyelitis) to others that involve entire lobules of the medulla and cortex.

On macroscopic examination, kidneys from patients with severe acute pyelonephritis are enlarged and contain a variable number of abscesses on the capsular surface and on cut sections of the cortex and medulla. Tissue between infected areas appears normal. Occasionally, areas of inflammation extend from the cortex into the medulla in the shape of a wedge. In the presence of obstruction, the calyces are enlarged, the papillae are blunted, and the pelvic mucosa is sometimes congested and thickened. The papillae may be completely normal in some cases or may show outright papillary necrosis in others.

Histologic changes are characterized by involvement of the tubules and interstitium. The interstitium is edematous and infiltrated by a variety of inflammatory cells, predominantly neutrophils. Within abscesses, the tubules show necrosis, and many tubules contain polymorphonuclear leukocytes. The patchiness of the inflammation is particularly striking. Thus, completely normal tubules and interstitium may lie adjacent to a large necrotizing renal abscess. Even in areas of the most severe inflammation, normal glomeruli can be seen, and indeed, intraglomerular inflammation is rare except in some forms of monial glomerulonephritis. In the presence of total ureteral obstruction, the inflammatory reaction sometimes affects the entire kidney.

Chronic Pyelonephritis

Gross pathology

The most characteristic changes are seen on gross rather than microscopic examination. The most common morphologic appearance of chronic pyelonephritis is that referred to as coarse renal scarring or focal scarring, consisting of corticopapillary scars overlying dilated, blunted, or deformed calyces. The remarkable pelvocalyceal deformity is not easy to visualize grossly on pathologic examination but is particularly obvious in tracings of the calyces made on excretory urograms. The kidneys are usually smaller than normal, and extreme reductions in size of one of the two kidneys are not unusual. Involvement can be bilateral or unilateral, depending on whether reflux or obstruction has occurred on one or both sides; with bilateral involvement, the kidneys are usually asymmetrically scarred. The scars vary in size but are usually broad, involve a whole lobe, are rather shallow, and have a flatter surface than do healed infarcts. The areas between scars may be smooth but are usually finely granular, reflecting hypertrophic changes. Although any part of the kidney may be involved, the large majority of scars are in the upper and lower poles, consistent with the frequency of intrarenal reflux in these areas. The medulla is distorted, and affected papillae are flattened. In cases with obstruction, the pelvis and calyces are distinctly dilated, but they may be of normal caliber in the absence of obstruction (in late cases) or after obstruction has been relieved. The pelvic and calyceal mucosa can be thickened and granular, particularly in cases of chronic reflux.

Microscopic findings

The histologic appearance is one of tubule damage and interstitial inflammation and scarring, and it varies according to the evolutionary stage of the lesion. Old, extensive scars can be composed almost entirely of atrophic or dilated tubules, separated by fibrous tissue, with remaining large blood vessels. More recent scars show variable amounts of interstitial mononuclear inflammation, tubule atrophy and necrosis, increase in interstitial fibrous tissue, and periglomerular fibrosis. Many tubules are dilated, lined by flattened epithelium, and filled with colloid casts (thyroidization). The inflammatory infiltrate is variable. Lymphocytes and monocytes predominate, but occasionally one can see large foci of plasma cells; in the presence of active inflammation, neutrophils can be plentiful. Pus casts are also frequently present, particularly when there is active infection. However, pus casts can also be present in the absence of bacteriuria, presumably owing to ischemic damage.

Vascular changes within the scars can be either mild or more severe. Both

arteries and arterioles may show medial and intimal thickening; the intimal thickening is of the fine, concentric cellular type. In some cases, there is clear-cut elastic reduplication. Vascular changes within the scarred areas are present even in patients who are not hypertensive, although they become more severe in the presence of hypertension. In the nonscarred areas, hyaline arteriolar changes are limited to those patients with secondary hypertension.

The pelvis and calyces are universally affected. Usually there is infiltration of the subendothelial connective tissue by inflammatory cells, which often form large masses or lymphoid follicles. Neutrophils, eosinophils, and occasionally giant cells may also be present. The mucosal epithelium may be severely thickened and infiltrated with inflammatory cells. The amount of collagen in the underlying connective tissue is usually also increased.

Although glomeruli may be entirely normal or show only periglomerular fibrosis, a variety of glomerular changes may be present. Ischemic changes, consisting of solidification of glomerular tufts and deposition of collagen within Bowman space, are frequent, as are small shrunken glomeruli. Focal or diffuse proliferation and necrosis can also be present; these have been considered secondary to hypertension.

Clinical presentations

Acute uncomplicated cystitis

By far the most common clinical symptoms associated with UTI that brings patients to medical attention are those referable to the lower urinary tract: dysuria (burning or discomfort on urination), frequency, nocturia, and suprapubic discomfort. Approximately 10% of women of reproductive age come to medical attention each year with these symptoms. Of these, two thirds have significant bacteriuria, whereas one third (those with the acute urethral syndrome) do not. Of the patients with significant bacteriuria, 50% to 70% have infection restricted to the bladder, but fully 30% to 50% will have covert infection of the upper urinary tract as well. The differentiation between patients with and without covert renal involvement cannot be done on clinical grounds alone. This lack of sensitivity of clinical evaluation in delineating the anatomic site of UTI has led to two practices: the treatment of most forms of UTI with identical therapeutic regimens, and an intensive effort by many investigators to develop noninvasive techniques for localizing the anatomic site of infection. However, as described subsequently, such techniques have proved to be too insensitive to be useful in the clinical management of the individual patient. Therefore,

management of the patient with the dysuria-frequency syndrome has to be based on the recognition of the possibility that infection more serious than simple cystitis may be present.

Acute pyelonephritis

The clinical findings associated with full-blown acute pyelonephritis are familiar: recurrent rigors and fever, back and loin pain (with exquisite tenderness on percussion of the costovertebral angle), often with colicky abdominal pain, nausea and vomiting, dysuria, frequency, and nocturia. Although bacteremia may complicate the course of symptomatic pyelonephritis in any patient, such bacteremias are seldom associated with the more serious sequelae of gram-negative sepsis, that is, the triggering of the complement, clotting, and kinin systems, which may lead to septic shock, disseminated intravascular coagulation, or both. When shock or disseminated intravascular coagulation occurs in the setting of pyelonephritis, the possibility of complicating obstruction must be ruled out. In one particularly important form of obstructive uropathy, which is associated with acute papillary necrosis, the sloughed papilla may obstruct the ureter. This form should be particularly suspected in diabetic patients with severe pyelonephritis and high-grade bacteremia, especially if the response to therapy is delayed.

Chronic Pyelonephritis

Unlike the dramatic clinical presentation of many patients with acute pyelonephritis, chronic disease typically has a more insidious course. Clinical signs and symptoms may be divided into two categories: those related directly to infection and those related to the degree and location of injury within the kidney. Surprisingly, the infectious aspects of the disease may be minor. Although intermittent episodes of full-blown pyelonephritis may occur, these are the exception. More common is asymptomatic bacteriuria, symptoms referable to the lower urinary tract (dysuria and frequency), vague complaints of flank or abdominal discomfort, and intermittent low-grade fevers.

Much more striking than the infectious or inflammatory symptoms are the physiologic derangements that result from the long-standing tubulointerstitial injury. These derangements include hypertension, inability to conserve Na^+ , a decreased concentrating ability, and a tendency to the development of hyperkalemia and acidosis. Although all of these are seen to a greater or lesser extent in all forms of renal disease, in patients with tubulointerstitial nephropathy such as this, the degree of physiologic

derangement is out of proportion to the degree of renal failure (or serum creatinine elevation). Thus, in other forms of renal disease, physiologic derangements are minimal at serum creatinine levels of 2 to 3 mg/dL; in the patient with chronic pyelonephritis and reflux nephropathy with serum creatinine at this level, polyuria, nocturia, hyperkalemia, and acidosis may all be observed.

Diagnostic evaluation

History and Physical Examination

Despite the incomplete relationship between clinical symptoms and the presence of infection at various sites in the urinary tract, useful information can be gained from a skillfully obtained history. When a patient with a single acute episode of symptomatic UTI is examined, the first consideration is whether there are signs or symptoms suggesting the presence or imminent development of systemic sepsis: spiking fevers, rigors, tachypnea, colicky abdominal pain, and exquisite loin pain. Such patients require immediate attention and probably parenteral therapy within a hospital setting. If the patient is not acutely septic, attention turns to such concerns as previous history of UTIs, renal disease, or such conditions as diabetes mellitus, multiple sclerosis, other neurologic conditions, history of renal stones, or previous genitourinary tract manipulation conditions that could predispose to UTI and affect the efficacy of therapy. A careful neurologic examination can be particularly important in suggesting the possibility of a neurogenic bladder.

When the patient with possible chronic pyelonephritis and reflux nephropathy is examined, two types of information should be sought: the history of UTI in childhood and during pregnancy; and the possible presence of such pathophysiologic consequences as hypertension, proteinuria, polyuria, nocturia, and frequency.

Urinary Findings

Gram's stain is the simplest method for detecting significant bacteriuria is to examine the urine under the microscope. If bacteria are found using the oil immersion objective, there are likely to be more than 10⁵ bacteria/ml of urine.

The most reliable result is obtained if the sample is taken via suprapubic aspiration, a technique frequently used in infants but rarely in older children and adults. It is superior to sampling by bladder catheterization, which carries a risk of about 2% for introduction of bacteria into the bladder and subsequent iatrogenic bacteriuria. The normal procedure for quantitative cultures is to collect a midstream urine sample. This requires that the patient is well informed about the sampling

procedures. During voiding, the first and the last parts of the urine should not be sampled. After sampling, the urine should be chilled (but not frozen) to prevent growth during transportation to the laboratory. At the laboratory, the sample is streaked onto agar plates using a loop, which delivers a known amount of urine. The result is obtained after incubation overnight and allows determination of the bacterial species present in the sample and the number of organisms per milliliter of urine. The presence of more than one species in a sample is a strong indication of defective sampling procedures and contamination.

Infection-Localizing Tests

Although there may be great similarity in the clinical presentation of patients with upper and lower UTIs, there can be vast differences in the response to therapy and type of pathologic process. Bladder infection is a superficial mucosal infection at an anatomic site to which high concentrations of antibiotics can be easily delivered, whereas renal infection (and prostatic infection in men) is a deep parenchymal infection at a tissue site where natural host defenses are rendered less effective by a hostile physicochemical environment and to which antimicrobial delivery may be limited. One would predict that the type of antimicrobial therapy necessary to eradicate infection from the urinary tract would be different for these two anatomic sites, with renal infection (and prostatic infection) requiring a more intensive or prolonged course of therapy, or both, than bladder infection.

The problem has been to develop a means of assessing the anatomic site of infection, given the 30% to 50% frequency of covert renal infection in patients with symptoms referable only to the lower urinary tract. The only direct method of localizing the infection site is bilateral ureteral catheterization. Although too invasive for general use, it remains the standard with which all other methods of localization are compared. A less invasive procedure is the bladder washout procedure. In this procedure, a Foley catheter is introduced into the bladder, the bladder is irrigated with an antibiotic solution (usually neomycin or neomycin and polymyxin), and several urine samples are collected. Patients with lower UTI have sterile urine during the collection period after the washout, whereas patients with renal infection have bacteria in all of the samples after washout. The major drawback with this technique is its inability to distinguish between unilateral and bilateral renal infection. However, because it is easy to perform, safe, and inexpensive and does not require an expert cystoscopist, it has replaced the ureteral catheterization studies as the method with

which all noninvasive techniques are compared.

Three types of noninvasive techniques have been employed in an attempt to differentiate between renal and bladder infection: assay of renal medullary function by measurement of maximal urinary concentrating capacity; measurement of urinary enzymes as an index of tissue injury and inflammation; and measurements of the immunologic response to infection. The basis for each of these tests is the pathologic differences between upper and lower tract infections: renal medullary infection occurs at a site where critical aspects of urine formation are taking place, and where inflammatory and immunologic responses are brisk and extensive; bladder infection occurs in the superficial mucosa, where little is occurring functionally and where both inflammatory and immunologic responses are limited.

Radiologic and Urologic Evaluations

The primary objective of radiologic and urologic evaluations in UTI is to delineate abnormalities that would lead to changes in the medical or surgical management of the patient. Such studies are particularly useful in the evaluation of children and adult men. In women, there is more controversy regarding their appropriate deployment. The following guidelines would appear to be reasonable.

1. Either an excretory urogram or an ultrasound study is indicated to rule out obstruction in patients requiring hospital admission for bacteremic pyelonephritis, particularly if the infection is slow to respond to appropriate therapy. Patients with septic shock in this setting require such procedures on an emergency basis, because such patients often cannot be effectively resuscitated unless their "pus under pressure" is relieved by some form of drainage procedure that bypasses the obstruction.

2. Children with first or second UTIs, particularly those younger than 5 years, merit both excretory urography and voiding cystourethrography for detection of obstruction, VUR, and renal scarring. Dimercaptosuccinic acid scanning may be used in lieu of intravenous pyelography to detect scars but will not delineate anomalies in the pyelocalyceal system or the ureters. This effort is aimed at identifying not only those who might benefit from surgical correction but also those with lesser degrees of scarring and VUR who would benefit from prolonged antimicrobial prophylaxis. Because active infection by itself can produce VUR, it is usually recommended that the radiologic procedures be delayed until 4 to 8 weeks after the eradication of infection.

3. Most men with bacterial UTI have some anatomic abnormality of the urinary

tract, most commonly bladder neck obstruction secondary to prostatic enlargement. Therefore, anatomic investigation, starting with a good prostatic examination and then proceeding to excretory urography or urinary tract ultrasound studies with postvoiding views, should be seriously considered in all male patients with UTI.

4. Although there is general agreement that first UTIs in women do not merit radiologic or urologic study, the management of recurrent infection is more controversial. In such women, the once routine cystoscopic study with urethral dilatation has fallen out of fashion, largely because of the careful work of Stamey. In addition, several studies have demonstrated the lack of cost-effectiveness of radiologic and urologic studies in the evaluation of women with recurrent UTIs.

Therefore, it would appear that the routine anatomic evaluation of women with recurrent UTI cannot be recommended. This is not to say that a few patients might not benefit from such studies. Characteristics that select a population of women who might benefit from such anatomic studies include patients who fail to respond to appropriate antimicrobial therapy or who rapidly relapse after such therapy; patients with continuing hematuria; patients with infection with urea-splitting bacteria; patients with symptoms of continuing inflammation, such as night sweats; and patients with symptoms of possible obstruction, such as persistent back or pelvic pain despite adequate antimicrobial therapy. In our experience, a disappointing response to antimicrobial therapy has been the most useful indicator for the need for radiologic and urologic evaluation.

Treatment

General Principles of Antimicrobial Therapy

The rational deployment of antimicrobial agents in the management of UTI is based on certain important clinical pharmacologic principles. Superficial mucosal infection, such as bladder infection, can be easily cured by the delivery of effective concentrations of antibiotic into the urine, with serum levels being of less importance. Thus, penicillin, which would not be used to treat *E. coli* or *Proteus* infection outside the urinary tract, is effective in treating bladder infections due to these organisms. Similarly, tetracycline in the concentrations achieved in the urine, but not in serum or tissue, can be effective in treating UTIs due to "resistant" gram-negative bacilli including *P. aeruginosa*.

Therapy of deep tissue infection, such as that involving the kidney or the prostate, likewise requires delivery of effective concentrations of drug to the site of

involvement. In addition, effective serum concentrations would seem to be advantageous. Whether bactericidal as opposed to bacteriostatic therapy, or synergistic two-drug therapy as opposed to single-drug therapy, is better suited for this purpose remains to be determined. These considerations are given particular emphasis by studies demonstrating in an experimental pyelonephritis model that the prompt reduction of intrarenal suppuration, as is achieved with effective antimicrobial therapy, was important in the prevention of chronic pyelonephritic scars.

The goals in treating UTI are to prevent or treat systemic sepsis, to relieve symptoms, to eradicate sequestered infection, to eliminate uropathogenic bacterial strains from fecal and vaginal reservoirs, and to prevent long-term sequelae all at minimal cost, with the lowest rate of side effects, and with the least selection of an antibiotic-resistant bacterial flora. These goals can be best achieved by prescribing different forms of therapy for different types of UTI.