A urinary tract infection (UTI) is an infection caused by bacteria in part of the urinary tract. In the lower urinary tract, it is known as a simple cystitis (a bladder infection). In the upper urinary tract, it is known as pyelonephritis (a kidney infection). Symptoms from a lower urinary tract infection include painful peeing and either frequent peeing or wanting to pee (or both). Symptoms of a kidney infection also include fever and side and back pain. In old people and young children, the symptoms are not always as clear. The main cause for both types is the bacteria *Escherichia coli*. Other bacteria, viruses, or fungus may be the cause in rare cases.

Women get urinary tract infections more often than men. Half of women have an infection at some point in their lives. It is common to have repeated infections. Risk factors include sexual intercourse as well as family history. Sometimes a person who had a bladder infection will get a kidney infection. Kidney infection also can be caused by bacteria in the blood. Diagnosis in young healthy women can be based on symptoms alone. Sometimes, the urine needs to be tested. A person with frequent infections can take low-dose antibiotics to prevent future infections.

Antibiotics are used to treat simple cases of urinary tract infections. Resistance to many of the antibiotics used to treat this condition, however, is increasing. People who have complicated urinary tract infections sometimes have to take antibiotics for a longer time, or might take antibiotics intravenously (through the veins). If symptoms have not improved in two or three days, a person will need further tests. In women, urinary tract infections are the most common form of bacterial infection. Ten percent of women develop urinary tract infections yearly.

In the previous issue we discussed UTI in Males, this issue delves deep into clinic-diagnostic aspects of UTI in Females under the segment “DISEASE DIAGNOSIS”.

INTERPRETATION is pictorially presenting all the Leukemias, while TROUBLESHOOTING outlines how to use various HIV testing formats and methodologies.

Of course, we never forget the most loved aspect of this communiqué.... THE BOUQUET
Background
Urinary tract infections (UTIs) are common in females, and cystitis (bladder infection) represents the majority of these infections. Related terms include pyelonephritis, which refers to upper urinary tract infection; bacteriuria, which describes bacteria in the urine; and candiduria, which describes yeast in the urine. Very ill patients may be referred to as having urosepsis. UTI is defined as significant bacteruria in the setting of symptoms of cystitis or pyelonephritis. These infections account for a significant number of emergency department (ED) visits, and 20% of women develop at least one UTI. Escherichia coli causes the majority of uncomplicated cystitis cases. Among the pathogens responsible for the remainder are Staphylococcus saprophyticus, Proteus mirabilis, Klebsiella pneumoniae, or Enterococcus faecalis. A presumptive diagnosis of uncomplicated cystitis can be made on the basis of findings on the history and physical examination, along with urinalysis. Proper specimen collection is necessary. In addition, clinicians need to appreciate the epidemiological and host factors that may identify patients with complicated cystitis or clinically apparent upper UTI, in whom more comprehensive assessment is indicated. Successful emergent management includes selection of appropriate antimicrobial therapy with recommendations for follow-up care. Oral therapy with an antibiotic effective against gram-negative aerobic coliform bacteria is the principal therapeutic intervention in patients with cystitis.

The following terms are defined for uniformity in this article:
- Asymptomatic bacteriuria (ASB) refers to 2 consecutive urine cultures growing more than 100,000 colony-forming units (CFU)/mL of a bacterial species in a patient lacking symptoms of a UTI
- Uropathogens are bacteria with specific virulence factors that facilitate their invasion of the urinary tract
- Complicated UTIs are defined as UTIs that are associated with metabolic disorders, that are secondary to anatomic or functional abnormalities that impair urinary tract drainage, or that involve unusual pathogens (eg, yeast), which increases the risk of therapeutic failure.

Pathophysiology
The urinary tract is normally sterile. Uncomplicated UTI involves the urinary bladder in a host without underlying renal, metabolic, or neurologic diseases. Cystitis represents bladder mucosal invasion, most often by enteric coliform bacteria (eg, Escherichia coli) that inhabit the periurethral vaginal introitus and ascend into the bladder via the urethra. In recurrent E. coli UTIs, peak colonization rates of the periurethral area 2-3 days prior to the development of the symptoms of acute cystitis range from 46-90%. During this same period, asymptomatic bacteriuria rates increase from 7% to 70%. Because sexual intercourse may promote this migration, cystitis is common in otherwise healthy young women. Generally, urine is a good culture medium. Factors unfavorable to bacterial growth include a low pH (5.5 or less), a high concentration of urea, and the presence of organic acids derived from a diet that includes fruits and protein. Organic acids enhance acidification of the urine. Frequent and complete voiding has been associated with a reduction in the incidence of UTI. Normally, a thin film of urine remains in the bladder after emptying, and any bacteria present are removed by the mucosal cell production of organic acids. If the defense mechanisms of the lower urinary tract fail, upper tract or kidney involvement occurs and is termed pyelonephritis. Host defenses at this level include local leukocyte phagocytosis and renal production of antibodies that kill bacteria in the presence of complement.

In general, there are 3 main mechanisms responsible for UTIs:
- Colonization with ascending spread
- Hematogenous spread
- Periuretrogenital spread

Bacterial virulence
Uropathogenic bacteria, derived from a subset of fecal flora, have traits that enable adherence, growth, and resistance of host defenses. These traits facilitate colonization and infection of the urinary tract. Adhesins are bacterial surface structures that enable attachment to host membranes. In E. coli infection, these include both pili (ie, fimbriae) and outer-membrane proteins (eg, Dr hemagglutinin). P simiae, which attach to globoseries-type glycolipids found in the colon and urinary epithelium, are associated with pyelonephritis and cystitis and are found in many E. coli strains that cause urosepsis. Type 1 fimbriae bind to mannose-containing structures found in many different cell types, including Tamm-Horsfall protein (the major protein found in human urine). Whether this facilitates or inhibits uroepithelial colonization is the subject of some debate. Other factors that may be important for E. coli virulence in the urinary tract include capsular polysaccharides, hemolysins, cytotoxic necrotizing factor (CNF) protein, and aerobactins. Several Kauffman serogroups of E. coli that contain these virulence factors may be more likely to cause UTIs, including O1, O2, O4, O6, O16, and O18. Another example of bacterial virulence is the swarming capability of Proteus mirabilis. Swarming involves the expression of specific genes when these bacteria are exposed to surfaces such as catheters. This results in the coordinated movement of large numbers of bacteria, enabling P mirabilis to move across solid surfaces. This likely explains the association of P. mirabilis UTIs with instrumentation of the urinary tract.

Host resistance
Most uropathogens gain access to the urinary tract via an ascending route. The shorter length of the female urethra allows uropathogens easier access to the bladder. The continuous unidirectional flow of urine helps to minimize UTIs, and anything that interferes with this increases the host's susceptibility to UTI. Examples of interference include volume depletion, sexual intercourse, urinary tract obstruction, instrumentation, use of catheters not drained to gravity, and vesicoureteral reflux. Secretory defenses help promote bacterial clearance and prevent adherence. Secretory immunoglobulin A (IgA) reduces attachment and invasion of bacteria in the urinary tract. Women who are nonsecretors of the ABH blood antigens appear to be at higher risk for recurrent UTIs; this may occur because of a lack of specific glycosyltransferases that modify epithelial surface glycolipids, allowing E. coli to bind to them better. In premenopausal women, lactobacilli are the predominant vaginal flora and serve to suppress vaginal colonization by the uropathogens. Most antibiotics, except sulfamethoxazole and the quinolones, can eradicate these protective bacteria. Urine itself has several antibacterial features that suppress UTIs. Specifically, the pH, urea concentration, osmolarity, and various organic acids prevent most bacteria from surviving in the urinary tract.
**Etiology**

*E. coli* causes 70-95% of both upper and lower UTIs. Various organisms are responsible for the remainder of infections, including *S. saprophyticus*, *Proteus* species, *Klebsiella* species, *Enterococcus faecalis*, other Enterobacteriaceae, and yeast. Some species are more common in certain subgroups, such as *Staphylococcus saprophyticus* in young women. However, *S. saprophyticus* can produce acute cystitis in older women and in young men and should not be automatically regarded as a contaminant in the urine cultures of these individuals. Most complicated UTIs are nosocomial in origin. Increasingly, UTIs in patients in health care institutions and those with frequent antibiotic exposure are caused by multidrug-resistant gram-negative pathogens, such as extended-spectrum beta-lactamase (ESBL) and carbapenemase producers. However, the prevalence of multidrug-resistant pathogens varies by locale. The most important risk factor for bacteriuria is the presence of a catheter. Eighty percent of nosocomial UTIs are related to urethral catheterization, while 5-10% are related to genitourinary manipulation. Catheters inoculate organisms into the bladder and promote colonization by providing a surface for bacterial adhesion and causing mucosal irritation. Sexual intercourse contributes to increased risk, as does use of a diaphragm and/or spermicide. Routine pelvic examinations are also associated with an increased risk of a UTI for 7 weeks post procedure. Women who are elderly, are pregnant, or have preexisting urinary tract structural abnormalities or obstruction carry a higher risk of UTI. UTIs are the most common type of infection following renal transplantation. Susceptibility is especially high in the first 2 months following transplantation. Triggering factors include vesicoureteral reflux and immunosuppression. *Corynebacterium urealyticum* (ie, CDC group D2) has been reported to cause encrusted pyelitis and cystitis in these patients. Calculi related to UTIs most commonly occur in women who experience recurrent UTIs with *Proteus*, *Pseudomonas*, and *Providencia* species. Perinephric abscesses are associated most commonly with *E. coli*, *Proteus* species, and *S. aureus* but also may be secondary to *Enterobacter*, *Citrobacter*, *Serratia*, *Pseudomonas* and *Klebsiella* species. More unusual causes include enterococci, *Candida* species, anaerobes, *Actinomyces* species, and *Mycobacterium tuberculosis*. Twenty-five percent of infections are polymicrobial. Cандидура is defined as more than 1000 CFU/mL of yeast from 2 cultures. *Candida albicans*, which is germ tube positive, is the usual culprit. Germ tube–negative *Candida* species (*tropicalis, parapsilosis, glabrata, lusitaniae, krusei*) are less common. Risk factors for candiduria include diabetes mellitus, indwelling urinary catheters, and antibiotic use. Candiduria may clear spontaneously or may result in (or from) deep fungal infections.

**Epidemiology**

**International statistics**

UTIs have been well studied in Sweden and other parts of Europe. These studies have shown that 1 in 5 adult women experience a UTI at some point, confirming that it is an exceedingly common worldwide problem. The epidemiology of UTI in the tropics is less well documented. UTIs appear to be common and associated with structural abnormalities. Chronic infection from *Schistosoma haematobium* disrupts bladder mucosal integrity and causes urinary tract obstruction and stasis. *Salmonella* bacteruria, with or without bacteremia, is very common in patients with schistosomiasis. Treatment requires both antischistosomal and anti-*Salmonella* agents.

**Age- and sex-related demographics**

The largest group of patients with UTI is adult women. The incidence of UTI in women tends to increase with increasing age. Several peaks above baseline correspond with specific events, including an increase in women aged 18-30 years (associated with coitus-so-called honeymoon cystitis-and pregnancy). Rates of infection are high in postmenopausal women because of bladder or uterine prolapse causing incomplete bladder emptying; loss of estrogen with attendant changes in vaginal flora (notably, loss of lactobacilli), which allows periurethral colonization with gram-negative aerobes, such as *E. coli*; and higher likelihood of concomitant medical illness, such as diabetes.

**Prognosis**

Even with effective antibiotic treatment, the average duration of severe symptoms in women with cystitis is somewhat longer than 3 days. Features that have been associated with a more prolonged course than average include a history of somatization, previous cystitis, urinary frequency, and more severe symptoms at baseline. Although simple lower UTI (cystitis) may resolve spontaneously, effective treatment lessens the duration of symptoms and reduces the incidence of progression to upper UTI. Even with effective treatment, however, about 25% of women with cystitis will experience a recurrence. Younger patients have the lowest rates of morbidity and mortality. Factors associated with an unfavorable prognosis include the following:

- Old age
- General debility
- Renal calculi or obstruction
- Recent hospitalization
- Urinary tract instrumentation or antibiotic therapy
- Diabetes mellitus
- Chronic nephropathy
- Sickle cell anemia
- Underlying cancer
- Intercurrent chemotherapy

The mortality associated with acute uncomplicated cystitis in women aged 20-60 years appears to be negligible. A longitudinal cohort study of Swedish women showed a higher mortality in women with a history of UTI than in age-matched women without such a history (37% versus 28% in 10 y), but these cohorts were not matched for other mortality-related factors, making it difficult to attribute the increased mortality to UTIs. In contrast, the morbidity in terms of quality of life and economic measures is tremendous. Each episode of UTI in a young woman results in an average of 6.1 days of symptoms, 1.2 days of decreased class/work attendance, and 0.4 days in bed. Nosocomial infections develop in about 5% of patients admitted to hospitals, and UTIs account for 40% of these infections. From 2-4% of these patients become bacteremic, with a mortality of 12.5%.

**Patient Education**

Proper adherence to the outpatient medical regimen should be stressed. Behavior modification, such as good oral fluid intake to enhance diuresis and frequent voiding (including postintercourse voiding) may be helpful in reducing recurrent infection. (See Prevention of Urinary Tract Infections.) For patient education information, see the Kidneys and Urinary System Center, as well as Urinary Tract Infections, Blood in the Urine, Birth Control Overview, Birth Control Spermicides, and Birth Control FAQs.
CLINICAL PRESENTATION

History
The classic symptoms of urinary tract infection (UTI) in the adult are primarily dysuria with accompanying urinary urgency and frequency. A sensation of bladder fullness or lower abdominal discomfort is often present. Because of the referred pain pathways, even simple lower UTI may be accompanied by flank pain and costovertebral angle tenderness. In the emergency department, however, assume that the presence of these symptoms represents upper UTI. Bloody urine is reported in as many as 10% of cases of UTI in otherwise healthy women; this condition is called hemorrhetic cystitis. Fevers, chills, and malaise may be noted in patients with cystitis, though these findings are associated more frequently with upper UTI (ie, pyelonephritis). A history of vaginal discharge suggests that vaginitis, cervicitis, or pelvic inflammatory disease is responsible for symptoms of dysuria; therefore, a pelvic examination must be performed. Important additional information includes a history of prior sexually transmitted disease (STD) and multiple current sexual partners.

Physical Examination
The patient appears uncomfortable but not toxic. The presence of toxic fever, chills, nausea, and vomiting suggests pyelonephritis rather than cystitis; however, immunosuppressed and even immunocompetent patients with pyelonephritis may exhibit few, if any, of these symptoms. In elderly women, 50% of cases of cystitis also involve the upper tracts. The clinician may appreciate signs of dehydration, such as dry mucous membranes and tachycardia. Clammy extremities and symptomatic orthostasis suggest poor vascular tone due to gram-negative bacteremia rather than simple cystitis. Most adult women with simple lower UTI have suprapubic tenderness. Pelvic examination should be performed to exclude vaginitis, cervicitis, or pelvic tenderness (eg, vaginal motion tenderness, which suggests pelvic inflammatory disease).

Acute Urethritis Versus Cystitis
The symptoms of acute urethritis overlap with those of cystitis, including acute dysuria and urinary hesitancy. Fever may be a component of urethritis-related syndromes (eg, Reiter syndrome, Behçet syndrome) but rarely is observed in acute cystitis. Urethral discharge is much more suggestive of urethritis, while bladder-related symptoms, such as urgency, polyuria, and incomplete voids, are more consistent with cystitis. The predominant complaints in acute cystitis relate to the inflamed bladder mucosa. Constitutional symptoms, such as fever, nausea, and anorexia, are rare or mild. The symptoms of dysuria, urgency, hesitancy, polyuria, and incomplete voids may be accompanied by urinary incontinence, gross hematuria, and suprapubic or low back pain. Patients may demonstrate some suprapubic tenderness to palpation. Abnormal physical examination findings are generally lacking in women with acute cystitis. The pelvic examination reveals no abnormalities unless another process, such as vaginitis, is mimicking or occurring simultaneously with cystitis.

Infection in Patients with Spinal Cord Injury
In patients with spinal cord injury, the following signs and symptoms are suggestive of a UTI:
- Malodororous and cloudy urine
- Muscular spasticity
- Fatigue
- FEVERS
- Chills
- Autonomic instability

Patients with lesions above T6 may exhibit autonomic dysreflexia to noxious stimuli, such as an overdistended bladder. The sympathetic response below the level of injury is uninhibited, producing severe vasoconstriction and reflexive bradycardia. If the patient is febrile, this may appear as a pulse-temperature dissociation. For more information on this topic, see the Medscape Reference article Urinary Tract Infections in Spinal Cord Injury.

Catheter-Related Infection
Symptoms of catheter-related UTI generally are nonspecific; most patients present with fever and leukocytosis. Significant pyuria generally is represented by more than 50 white blood cells per high-power field (WBC/hpf). Colony counts on a urine culture range from 100-10,000 CFU/mL. Infections may be polymicrobial. Pyuria and elevated bacterial colony counts are seen in all patients in whom a catheter has been in place for more than a few days. In this situation, their presence is not synonymous with a UTI.

Infection in Pregnant Patients
Asymptomatic bacteriuria (ASB) occurs in 5-10% of pregnant women. More than 100,000 CFU/mL of a single uropathogen is the classic definition of ASB, but more recent data support 10,000 CFU/mL from a clean-catch specimen as a threshold. ASB most commonly appears between the ninth and 17th weeks of pregnancy. ASB predisposes to preterm labor, intrauterine growth retardation, low-birth-weight infants, anemia, amnionitis, and hypertensive disorders of pregnancy. Risk factors include sexual activity, increasing age and parity, diabetes, lower socioeconomic class, a history of UTIs, sickle cell disease, and structural/functional abnormalities. Cystitis occurs in 0.3-1.3% of pregnancies but does not appear to be related to ASB. The recommendation is to screen pregnant women at their first prenatal visit and during the third trimester. Further screening is not indicated unless the initial test result is positive or the patient develops symptoms.

Infection in Patients with Diabetes Mellitus
Complicated UTIs in patients who have diabetes include renal and perirenal abscess, empysematous pyelonephritis, emphysematous cystitis, fungal infections, xanthogranulomatous pyelonephritis, and papillary necrosis. Susceptibility increases with longer duration and greater severity of diabetes.

Diagnostic Considerations
Occult pyelonephritis occurs in 15-50% (or more) of all urinary tract infections (UTIs), based on several studies on localization of organisms within the urinary tract. This usually occurs in older women. It appears that these patients are unable to mount a fever or develop an elevated white count or costovertebral angle (CVA) tenderness. These patients may present with an unexplained fall or a change in mental status. Postmenopausal women may also experience senile urethritis. In addition to urinary burning, frequency, and urgency, these patients may complain of vaginal and vulvar itching and discharge. Physical examination reveals a dry, pale vaginal epithelium and erosion of the urethral mucosa. Senile urethritis responds to topical estrogen therapy. The differential diagnosis for infectious causes of sterile pyuria includes perirenal abscess, urethral syndrome, renal tuberculosis, and fungal infections of the urinary tract system. Noninfectious causes of pyuria include the following:
- Uric acid and hypercalcermic nephropathy
- Lithium and heavy metal toxicity
- Sarcoidosis and other granulomatous diseases (eg, tuberculosis)
JAN/FEB

Interstitial cystitis
Poly cystic kidney disease
Genitourinary malignancy
Renal transplant rejection
Any periurethral process

Consider UTI in any condition involving pain the flank and back or pain in the abdomen and pelvis. Also consider cervicitis and Chlamydia infection. Do not assume that a sexually active female with dysuria has a UTI without first excluding the possibility of sexually transmitted disease–related cervicitis, vaginitis, or pelvic inflammatory disease. UTIs in pregnancy have potentially adverse outcomes for both the mother and the fetus. Obtain a urine culture in all pregnant patients with suspected UTI, as the results may provide the physician or the follow-up physician with valuable information if the patient does not respond as expected to treatment. Pyuria and bacteruria are always treated during pregnancy, regardless of whether symptoms are present.

Patients with diabetes mellitus are at increased risk for complicated UTIs. Diagnostic considerations include the following:

- Renal and perirenal abscess
- Emphysematous pyelonephritis
- Emphysematous cystitis
- Fungal infection
- Xanthogranulomatous pyelonephritis
- Papillary necrosis

Older patients who appear toxic are more likely to have obstruction complicating their UTI. Obtain a structural study to rule out this possibility.

Differential Diagnoses

- Acute Pyelonephritis
- Bladder Cancer
- Chlamydial Genitourinary Infections
- Cystitis, Nonbacterial
- Herpes Simplex
- Interstitial Cystitis
- Pelvic Inflammatory Disease
- Vaginitis

WORKUP

Approach Considerations

In the 1980s, many experts felt that urine cultures were unnecessary in young women with probable cystitis because almost all of these were caused by pan-susceptible isolates of *Escherichia coli*. Since then, however, antibiotic resistance in uropathogenic *E. coli* has become a significant concern. Resistance has also been emerging among other common cystitis pathogens, including *Enterococcus faecalis*, *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, and *Proteus mirabilis*. Trimethoprim-sulfamethoxazole (TMP-SMX) resistance has reached levels as high as 20% in some communities. Substitution of fluoroquinolones has resulted in an increase in resistance to these drugs, as well. Nevertheless, according to international guidelines, a urine culture is not required for the initial treatment of women with a symptomatic lower urinary tract infection (UTI) with pyuria or bacteriuria or both. In a United Kingdom study, dipstick diagnosis proved more cost-effective than positive midstream urine culture for targeting antibiotic therapy, Consider obtaining urine cultures in cases of cystitis in immunosuppressed patients and those with a recent history of instrumentation, exposure to antibiotics, or recurrent infection. Obtaining cultures is also advisable in elderly women, who have a high rate of upper tract involvement. Microscopic hematuria is found in about half of cystitis cases; when found without symptoms or pyuria, it should prompt a search for malignancy. Other possibilities to be considered in the differential diagnosis include calculi, vasculitis, renal tuberculosis, and glomerulonephritis. In some countries, hematuria is suggestive of schistosomiasis. Retention of *Schistosoma haematobium* eggs and formation of granulomas in the urinary tract can lead not only to hematuria but also to dysuria, bladder polyps and ulcers, and even obstructive uropathies. Schistosomiasis can also be associated with salmonellosis and squamous cell malignancies of the bladder. Bacteremia is associated with pyelonephritis, corticomedullary abscesses, and perinephric abscesses. Approximately 10-40% of patients with pyelonephritis or perinephric abscesses have positive results on blood culture. Bacteremia is not necessarily associated with a higher morbidity or mortality in women with uncomplicated UTI. Cervical swabs may be indicated in cases of possible pelvic inflammatory disease. Visual inspection of the urine is not helpful. Cloudiness of the urine is most often due to protein or crystal presence, and malodorous urine may be due to diet or medication use. No imaging studies are indicated in the routine evaluation of cystitis. Renal function testing is not indicated in most episodes of UTI, but it may be helpful in patients with known urinary tract structural abnormality or renal insufficiency. Renal function testing also may be helpful in older, particularly ill-appearing hosts or in hosts with other complications. A study of 196 women with painful or frequent urination found that most could be classified as having a low or high risk for UTI by asking the following questions:

- Does the patient think she has a UTI?
- Is there at least considerable pain on urination?
- Is there vaginal irritation?

History correctly classified 56% of patients as having a UTI risk of either less than 30% or more than 70%, and adding urine dipstick results increased this correct classification rate to 73%. Correct classification increased to 83% when patients with intermediate risk (30-70%) after history alone underwent an additional test. The strongest indicators of UTI were the patient’s suspicion of having a UTI and a positive nitrite test.

Urinalysis

The most accurate method to measure pyuria is counting leukocytes in unspun fresh urine using a hemocytometer chamber; greater than 10 white blood cells (WBCs)/mL is considered abnormal. Counts determined from a wet mount of centrifuged urine are not reliable measures of pyuria. A noncontaminated specimen is suggested by a lack of squamous epithelial cells. Pyuria is a sensitive (80-95%) but nonspecific (50-76%) sign of UTI. White cell casts may be observed in conditions other than infection, and they may not be observed in all cases of pyelonephritis. If the patient has evidence of acute infection and white cell casts are present, however, the infection likely represents pyelonephritis. A spun sample (5 mL at 2000 revolutions per min [rpm] for 5 min) is best used for evaluation of cellular casts. Proteinuria is commonly observed in infections of the urinary tract, but the proteinuria usually is low grade. More than 2 g of protein per 24 hours suggests glomerular disease. Approximately 70% of patients with corticomedullary abscesses have abnormal urinalysis findings, whereas those with renal cortical abscesses usually have normal findings. Two thirds of patients with perinephric abscesses have an
abnormal urinalysis.

Urine specimen collection

Urine specimens may be obtained by midstream clean catch, suprapubic aspiration, or catheterization. The midstream-voided technique is as accurate as catheterization if proper technique is followed. Instruct the woman to remove her underwear and sit facing the back of the toilet. This promotes proper positioning of the thighs. Instruct the patient to spread the labia with one hand and cleanse from front to back with povidone-iodine or soaped swabs with the other hand; then pass a small amount of urine into the toilet; and finally urinate into the specimen cup. The use of a tampon may allow a proper specimen if heavy vaginal bleeding or discharge is present. Midstream urine specimens may become contaminated, particularly if the woman has difficulty spreading and maintaining separation of the labia. The presence of squamous cells and lactobacilli on urinalysis suggests contamination or colonization (see image below). Catheterization may be needed in some women to obtain a clean specimen, although it poses the risk of introducing infection.

Dipstick testing

Dipstick testing should include glucose, protein, blood, nitrite, and leukocyte esterase. Leukocyte esterase is a dipstick test that can rapidly screen for pyuria; it is 57-96% sensitive and 94-98% specific for identifying pyuria. Given this broad range of sensitivity, it is important to consider the possibility of false-positive results, particularly with asymptomatic patients undergoing evaluation for recurrent UTI. Pyuria, as indicated by a positive result of the leukocyte esterase dipstick test, is found in the vast majority of patients with UTI. This is an exceedingly useful screening examination that can be performed promptly in any ED setting. If pyuria is absent, the diagnosis of UTI should be questioned until urine culture results become available.

Urine microscopy

A microscopic evaluation of the urine sample for WBC counts, RBC counts, and cellular or hyaline casts should be performed. In the office, a combination of clinical symptoms with dipstick and microscopic analysis showing pyuria and/or positive nitrite and leukocyte esterase tests can be used as presumptive evidence of UTI. Low-level pyuria (6-20 WBCs per high-power field [hpf]) microscopy on a centrifuged specimen) may be associated with an unacceptable level of false-negative results with the leukocyte esterase dipstick test. In females with appropriate symptoms and examination findings suggestive of UTI, urine microscopy may be indicated despite a negative result of the leukocyte esterase dipstick test. Current emphasis in the diagnosis of UTI rests with the detection of pyuria. As noted, a positive leukocyte esterase dipstick test suffices in most instances. According to some researchers, levels of pyuria as low as 2-5 WBCs/hpf in a centrifuged specimen are important in females with appropriate symptoms. The presence of bacteriuria is significant. However, the presence of numerous squamous epithelial cells raises the possibility of contamination. Low-level or, occasionally, frank hematuria may be noted in otherwise typical UTI; however, its positive predictive value is poor.

Nitrate test

Nitrate tests detect the products of nitrate reductase, an enzyme produced by many bacterial species. These products are not present normally unless a UTI exists. This test has a sensitivity and specificity of 22% and 94-100%, respectively. The low sensitivity has been attributed to enzyme-deficient bacteria causing infection or low-grade bacteriuria. A positive result on the nitrate test is highly specific for UTI, typically because of urease-splitting organisms, such as Proteus species and, occasionally, E. coli; however, it is very insensitive as a screening tool, as only 25% of patients with UTI have a positive nitrate test result.

Urine Culture

Urine culture remains the criterion standard for the diagnosis of UTI. Collected urine should be sent for culture immediately; if not, it should be refrigerated at 4°C. Two culture techniques (dip slide, agar) are widely used and accurate. The limits for cystitis and pyelonephritis in women are more than 1000 colony-forming units (CFU)/mL and more than 10,000 CFU/mL, respectively, for clean-catch midstream urine specimens. Historically, the definition of UTI was based on the finding at culture of 100,000 CFU/mL of a single organism. However, this misses up to 50% of symptomatic infections, so the lower colony rate of greater than 100 CFU/mL is now accepted. The definition of asymptomatic bacteriuria still uses the historical threshold. Asymptomatic bacteriuria in a female is defined as a urine culture (clean-catch or catheterized specimen) growing greater than 100,000 CFU/mL in an asymptomatic individual. Note that any amount of uropathogen grown in culture from a suprapubic aspirate should be considered evidence of a UTI. Approximately 40% of patients with perinephric abscesses have sterile urine cultures. An uncomplicated UTI (cystitis) does not require a urine culture unless the woman has experienced a failure of empiric therapy. Obtain a urine culture in patients suspected of having an upper UTI or a complicated UTI, as well in those in whom initial treatment fails. If the patient has had a UTI within the last month, relapse is probably caused by the same organism. Relapse represents treatment failure. Reinfection occurs in 1-6 months and usually is due to a different organism (or serotype of the

Lactobacilli and a squamous epithelial cell are evident on this vaginal smear. The presence of squamous cells and lactobacilli on urinalysis suggests contamination or colonization.

Although the use of midstream urine specimens is widely advocated, one randomized trial in young women showed that the rate of contamination was nearly identical among those who used midstream clean-catch technique and those who urinated into a container without cleansing the perineum or discarding the first urine output. Use of a vaginal tampon in addition to clean-catch technique had no significant effect on the contamination rate.

Midstream-voided urine specimens are more than 1000 colony-forming units (CFU)/mL and more than 10,000 CFU/mL, respectively, for clean-catch midstream urine specimens. Historically, the definition of UTI was based on the finding at culture of 100,000 CFU/mL of a single organism. However, this misses up to 50% of symptomatic infections, so the lower colony rate of greater than 100 CFU/mL is now accepted. The definition of asymptomatic bacteriuria still uses the historical threshold. Asymptomatic bacteriuria in a female is defined as a urine culture (clean-catch or catheterized specimen) growing greater than 100,000 CFU/mL in an asymptomatic individual. Note that any amount of uropathogen grown in culture from a suprapubic aspirate should be considered evidence of a UTI. Approximately 40% of patients with perinephric abscesses have sterile urine cultures. An uncomplicated UTI (cystitis) does not require a urine culture unless the woman has experienced a failure of empiric therapy. Obtain a urine culture in patients suspected of having an upper UTI or a complicated UTI, as well in those in whom initial treatment fails. If the patient has had a UTI within the last month, relapse is probably caused by the same organism. Relapse represents treatment failure. Reinfection occurs in 1-6 months and usually is due to a different organism (or serotype of the
same organism). Obtain a urine culture for patients who are reinfected. If a Gram stain of an uncentrifuged, clean-catch, midstream urine specimen reveals the presence of 1 bacterium per oil-immersion field, it represents 10,000 bacteria/mL of urine. A specimen (5 mL) that has been centrifuged for 5 minutes at 2000 rpm and examined under high power after Gram staining will identify lower numbers. In general, a Gram stain has a sensitivity of 90% and a specificity of 88%.

Complete Blood Cell Count
A CBC is not helpful in differentiating upper from lower UTI or in making decisions regarding admission. However, significant leukopenia in hosts who are older or immunocompromised may be an ominous finding. The WBC count may or may not be elevated in patients with uncomplicated UTI, but it is usually elevated in patients with complicated UTIs. Patients with complicated UTIs may have anemia; for example, anemia is observed in 40% of patients with perinephric abscesses.

Diagnostic Catheterization
Catheterization is indicated if the patient cannot void spontaneously, if the patient is too debilitated or immobilized, or if obesity prevents the patient from obtaining a suitable specimen. Measurement of postvoiding residual urine volume by catheterization may reveal urinary retention in a host with a defective bladder-emptying mechanism. Measurement of the postvoid residual volume should be strongly considered in all patients who require hospital-level care. Handheld portable bladder scans may also be used as a noninvasive alternative. Proper guidelines must be followed under acute care hospital settings, aseptic technique and sterile equipment for catheter insertion must be used to minimize the risk of catheter-associated UTI. Only properly trained individuals who are skilled in the correct technique of aseptic catheter insertion and maintenance should take on this task.

Patients with Spinal Cord Injury
Diagnosing a UTI in a patient with a spinal cord injury is difficult. In patients with SCI, signs and symptoms suggestive of a UTI are malodorous and cloudy urine, muscular spasticity, fatigue, fevers, chills, and autonomic instability. In these patients, suprapubic aspiration of the bladder is the criterion standard for diagnosing a UTI, although it is not performed often in clinical practice.

Patients with Diabetes Mellitus
Patients with diabetes are at risk for complicated UTIs, which may include renal and perirenal abscess, emphysematous pyelonephritis, emphysematous cystitis, fungal infections, xanthogranulomatous pyelonephritis, and papillary necrosis.

Cystitis Caused by Candida
Cystitis caused by Candida is clinically similar to cystitis from other pathogens. The presence of fungus in the urine should be verified by repeating the urinalysis and urine culture. Other features of diagnosis are as follows:

- Pyuria is a nonspecific finding
- C. glabrata may be differentiated from other species by morphology
- Candida casts in the urine indicate renal candidiasis but are rarely seen
- Colony counts have not proved diagnostically useful

Ultrasonography of the kidneys and collecting systems is the preferred initial study in symptomatic or critically ill patients with candiduria, but computed tomography is better for detecting pyelonephritis or perinephric abscess.

TREATMENT AND MANAGEMENT

Approach Considerations
Appropriate antibiotic treatment leads to significantly higher symptomatic and bacteriologic cure rates and better prevention of infection in women with uncomplicated cystitis. Unfortunately, treatment also selects for antibiotic resistance in uropathogens and commensal bacteria and has adverse effects on the gut and vaginal flora. Consequently, evolving practice seeks to achieve good symptom control for uncomplicated acute cystitis while reducing antibiotic use. For example, European practice increasingly includes the option of offering a 48-hour delayed antibiotic prescription to be used at the patient’s discretion. The first-choice agents for treatment of uncomplicated acute cystitis in women include nitrofurantoin monohydrate/macrocrystals, trimethoprim-sulfamethoxazole (TMP-SMX), or fosfomycin. Beta-lactam antibiotics may be used when other recommended agents cannot be used. Fosfomycin and nitrofurantoin monohydrate/macrocrystals should be avoided in patients with possible early pyelonephritis. Fluoroquinolones are typically reserved for complicated cystitis. Empirc antibiotic selection is determined in part by local resistance patterns. In addition, clinicians may wish to limit use of TMP-SMX in order to reduce the emergence of resistant organisms. Resistance to TMP-SMX has been associated with concomitant resistance to other antibiotics. Because of the importance of maintaining the effectiveness of TMP-SMX for treatment of serious infections, German national guidelines no longer recommend this agent as first-line empirical treatment for uncomplicated cystitis. Patients who have been hospitalized in urology units tend to have uropathogenic E coli infections with higher antimicrobial resistance, especially ESBL isolates. On average, women with cystitis who receive effective antibiotic treatment experience severe symptoms for somewhat longer than 3 days. Complete resolution of symptoms may require approximately 6 days. Features that have been associated with a more prolonged course include a history of somatization, previous cystitis, urinary frequency, and more severe symptoms at baseline. Patients who respond to antibiotics do not require follow-up urine cultures. Without treatment, 25-42% of uncomplicated acute cystitis cases in women will resolve spontaneously. Even without effective treatment, the likelihood that uncomplicated acute cystitis will progress to pyelonephritis is only around 2%.

Patient disposition
With few exceptions, the vast majority of women with urinary tract infection (UTI) present on an ambulatory basis and can be treated as outpatients. Exceptions include immunocompromised or elderly patients who have a UTI manifesting as a sepsis syndrome with circulatory insufficiency. In this situation, mental status changes (eg, confusion) or profound weakness may prompt paramedical transport to the hospital. Patients with hypotension, tachycardia, and delayed capillary refill require intravenous (IV) fluid resuscitation in the field. Hospital admission may be indicated for some patients with complicated UTI. Complicating factors include the following:

- Structural abnormalities (eg, calculi, tract anomalies, indwelling catheter, obstruction)
- Metabolic disease (eg, diabetes, renal insufficiency)
- Impaired host defenses (eg, HIV, current chemotherapy, underlying active cancer)

Adequate fluid resuscitation restores effective circulating volume and generous urinary volumes. Antipyretic pain medications may be
administered, as appropriate.

**Uncomplicated Cystitis in Nonpregnant Patients**

Uncomplicated cystitis occurs in patients who have a normal, unobstructed genitourinary tract; who have no history of recent instrumentation; and whose symptoms are confined to the lower urinary tract. Uncomplicated cystitis is most common in young, sexually active women. Patients usually present with dysuria, urinary frequency, urinary urgency, and/or suprapubic pain. Treatment regimens for uncomplicated cystitis in nonpregnant women are to be followed as per country specific protocols. If culture and sensitivity reports are available, it is ideal.

**Complicated Cystitis in Nonpregnant Women**

Complicated cystitis is associated with an underlying condition that increases the risk of therapeutic failure. Some underlying conditions include diabetes, symptoms for 7 days or longer before seeking care, renal failure, functional or anatomic abnormality of the urinary tract, renal transplantation, an indwelling catheter, or immunosuppression. Treatment regimens for complicated cystitis in nonpregnant women are available as country specific protocols, follow them. Availability of culture and sensitivity report is the ideal circumstance.

**Antimicrobial Therapy**

Oral therapy with an antibiotic effective against gram-negative aerobic coliform bacteria, such as E. coli, is the principal treatment intervention in patients with lower urinary tract infections. For women with acute bacterial cystitis who are otherwise healthy and not pregnant, 3 days of therapy with most antimicrobial agents is generally more effective than single-dose therapy and as effective as the same drug administered for a longer duration.

**Adjunctive Therapy**

Patients with intense dysuria may obtain symptomatic relief from a bladder analgesic, such as phenazopyridine, to be used for 1-2 days. Do not prescribe phenazopyridine if the patient has a sulfa allergy. Avoid long-term use, as this agent may mask symptoms of therapeutic failure or recurrence. Many authors advise stressing the intake of plenty of fluids to promote a dilute urine flow.

**Fungal Infection**

In catheterized patients, the catheter is essential for clearance of funguria. If the catheter is still needed, replace it (preferably a day later). Treatment options vary from topical treatment to systemic therapy. A regimen of amphotericin-B bladder washes for 7 days provides a prompt but nonsustained response. It does not treat systemic mycoses and is inconvenient to administer. Amphotericin B, 0.3 mg/kg IV for 1 dose, is an option that provides a more sustained and systemic response. Fluconazole 200 mg orally, followed on subsequent days by 100 mg orally once a day for 4-7 days, is a simpler option. This drug is effective against azole-responsive Candida organisms. Generally, azole resistance is observed only in C. krusei and C. glabrata. Fluconazole provides a good long-term effect but takes a few days to clear the urine.

**Treatment in Patients with Spinal Cord Injury**

Once a urethral catheter is in place, the daily incidence of bacteriuria is 3-10%. Antibiotics should be reserved for patients with clear signs and symptoms of UTI. In these patients, suprapubic aspiration of the bladder is the criterion standard for diagnosing a UTI, although it is not performed often in clinical practice. Oral fluoroquinolones are the drugs of choice for empiric treatment of acute UTIs. However, these drugs have a propensity for collateral damage and should be reserved for important uses other than acute cystitis.

**Pregnant Patients**

The physiologic changes associated with pregnancy increase the risk of serious infectious complications from symptomatic and asymptomatic urinary tract infections even in healthy pregnant women. Consequently, treatment is indicated for pregnant women with asymptomatic bacteriuria, as well as for those with symptomatic UTIs; antibiotic selection may differ, and regimens are typically more prolonged.

**Renal Transplantation Patients**

Treatment of UTIs in renal transplant patients is preferably with a fluoroquinolone. TMP-SMX poses the risk of inducing renal failure in the transplanted kidney and consequently should be avoided unless the patient's creatinine clearance is normal. Asymptomatic bacteriuria should be treated for 10 days. Parenteral antibiotics should be used for severe infections. The duration of antibiotics for severe infections is 4-6 weeks.

**Asymptomatic Bacteriuria**

In most patient populations, asymptomatic bacteriuria has not been shown to be harmful. Furthermore, although persons with bacteriuria at increased risk of symptomatic urinary tractions, treatment of asymptomatic bacteriuria does not decrease the frequency of symptomatic infections or improve other outcomes. Consequently, screening for or treatment of asymptomatic bacteriuria is not appropriate and should be discouraged. Asymptomatic bacteriuria in women should be treated only in pregnant patients, in patients undergoing a urologic procedure that may produce mucosal bleeding, and in the significantly immunosuppressed (e.g., renal transplantation patients). It should not be treated in diabetic persons, elderly individuals, and patients with indwelling catheters. Diabetic women have a high rate of asymptomatic bacteriuria with nonpathogenic strains, which can persist for long periods without progressing to infection.

**Diet**

Hydration to accentuate unidirectional clearance of bacteriuria is recommended, especially if an obstruction was relieved recently. Drinking cranberry juice (10 oz/day) or taking cranberry tablets may offer some benefit in reducing recurrent UTI and does not appear to be harmful. Cranberries contain type A proanthocyanidins. This compound and its urinary metabolites interfere with the adhesiveness of uropathogenic bacteria to the bladder epithelium. Their effect is not as significant as antibiotics, but they do not induce bacterial resistance. Because of their variable intestinal absorption, it is difficult to design a valid study comparing them head-to-head with antimicrobials.

**PREVENTION**

**Prevention and Long-Term Monitoring**

Prophylactic measures are indicated for patients with any of the following:

- Recurrent UTIs
- Spinal cord injury
- Urinary catheters
- Renal transplants

Sexually active women may attempt voiding immediately after intercourse to lessen the risk of coitus-related introduction of bacteria into the bladder. Some authors recommend large urinary flow volumes as a measure that will reduce the risk of UTI. Prophylactic regimens for women with frequent recurrent UTIs include postcoital or continuous antibiotics. Women with fewer than 3 UTIs per year may benefit from
### INTERPRETATION

**LEUKEMIAS**

<table>
<thead>
<tr>
<th>AML M6</th>
<th>ALL L1 (B CELL)</th>
<th>ALL L2 (B cell)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ALL L3 (B CELL)</th>
<th>ALL (T CELL)</th>
<th>AML MO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AML M1</th>
<th>AML M2</th>
<th>AML M2 (AUER RODS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AML M3</th>
<th>AML M4</th>
<th>AML M5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AML M5b</th>
<th>AML M6</th>
<th>AML M7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML M3</td>
<td>ALL T CELL (ATL)</td>
<td>AML M5a</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------</td>
<td>--------</td>
</tr>
<tr>
<td>CLL (B CELL)</td>
<td>CML</td>
<td>CMLL (CHRONIC MYELOMONOCYTIC LEUKEMIA)</td>
</tr>
<tr>
<td>HAIRY CELL LEUKEMIA (LYMPHOBLASTIC)</td>
<td>CHRONIC PROLYMPHOCYTIC LEUKEMIA (B CELL)</td>
<td>CHRONIC PROLYMPHOCYTIC LEUKEMIA (T CELL)</td>
</tr>
<tr>
<td>CHRONIC T CELL LEUKEMIA (SEZARY CELL TYPE)</td>
<td>CLL</td>
<td>SEZARY CELL</td>
</tr>
<tr>
<td>AML M2e</td>
<td>CML</td>
<td>MYELOMA (FLAME CELL)</td>
</tr>
<tr>
<td>BURKITT'S LYMPHOMA</td>
<td>ACUTE ERYTHROID LEUKEMIA</td>
<td>MANTLE CELL LEUKEMIA</td>
</tr>
</tbody>
</table>
In Lighter Vein

They say we learn from our mistakes...
That’s why I’m making as many as possible.
I’ll soon be a genius!

I’m not short, I’m just more down to earth than other people.

My boss told me to have a good day...
I’m so good at sleeping, I can do it with my eyes closed.

So I went home.

Brain Teasers

1. SHBG (Sex Hormone Binding Globulin) interferes in immunoassay of
   A. Testosterone
   B. Estradiol
   C. Both of the above
   D. None of the above.

2. TBG, (Thyroxine Binding Globulin) and NEFA (Non-Esterified Fatty Acid) interfere with the estimation of
   A. Free T4
   B. Free T3
   C. TSH
   D. All of the above.

3. Assays that are affected by heterophilic antibodies include:
   A. CEA
   B. CA 125

   C. hCG
   D. All of the above.

4. The hook effect can be reduced/eliminated by
   A. Doubling the volume of sample to be used
   B. Tripling the volume of sample to be used
   C. Appropriately diluting the sample to be used
   D. None of the above.

5. CORRELATE THE FOLLOWING
   A. Multiple inherited tumors,
   B. Carcinoma, muscle weakness
   C. Ovarian fibroma, Ascites,
   D. Pulmonary tumour
   E. Papilloedema, scotoma, anosmia
   F. CSF

   1. Froin’s Syndrome ?
   2. Foster Kennedy’s Syndrome ?
   3. Pancoast Syndrome ?
   4. Meigs syndrome
   5. Lambert-eaton Syndrome ?
   6. Gardner’s Syndrome ?

Overview of HIV Testing Technologies

Learning Objectives
At the end of this module, you will be able to:
• Discuss settings where HIV testing will be part of service delivery during an era of expanded services
• Discuss the spectrum of testing technologies for HIV
• Explain the advantages and disadvantages of HIV rapid tests
• Accurately recognize individual test result as reactive, non-reactive, or invalid

HIV Testing Occurs in a Variety of Settings

Expansion of Testing Services
• Integrate HIV laboratory services and diagnostics fully into national health laboratory structures
• Facilitate testing in non-traditional settings
• Consider all our testing options

Use of HIV Testing Technologies in the Continuum of Care
Use HIV rapid diagnostic test to identify an HIV infection
Initiate treatment with ARVs minimal diagnostics required
Monitor effectiveness of ARVs with diagnostics (viral load, CD4) and safety with basic laboratory tests

Spectrum of HIV Tests
• HIV diagnosis (Antibody/Antigen testing)
  • Enzyme Immunoassays (EIAs)
  • Rapid tests
  • Western blot (WB)
• Early diagnosis in infants
  • p24
• Initiation and monitoring of ART
  • CD4
  • Viral Load

Challenges of HIV Testing
• Early detection of seroconversion
• Early detection in infants born to HIV positive mothers
• Effect of HIV subtypes on test performance
• Impact of other health conditions on test performance
• Product specific equipment
• Technical skill
9. **Enzyme Immunoassays (EIAs)**
   - Quantitative assay to measure HIV antibodies
   - Most detect antibodies to HIV-1 and HIV-2
   - Antigens coated in microwells
   - HIV Antigen/ Antibody reaction is detected by color change
   - Intensity of color reflects amount of antibody present serum
   - Some assays can detect both HIV antibody and HIV antigen (close window period)
   - Issues:
     - Skilled lab technician
     - Large volume testing
     - Properly maintained equipment required

10. **Enzyme Immunoassays (EIAs) Cont’d**
    After several incubation and wash steps, a colour reaction occurs if HIV antibody is present
    An Automated reader gives a measurement of optical density. (Presence of colour) for each well

11. **HIV Rapid Tests**
    - Qualitative assay to detect HIV antibodies
    - Most detect HIV 1 and HIV 2
    - As reliable as EIAs
    - Issues:
      1. Small volumes
      2. Validation of use
      3. Appropriate training

12. **Western Blot / Line Immunoassays**
    - Used as supplemental test for confirmation (only difficult cases)
    - Detects antibodies to specific HIV antigens on cellulose strip
    - Issues:
      - Multiple standards for performance and interpretation
      - Expensive
      - Limited commercial availability

13. **HIV p24 Antigen**
    - Core protein of the virus
    - ELISA detects p24 antigen before antibody can be detected
    - Detected 2 to 3 weeks after HIV infection
    - Detected about 6 days before antibody tests become reactive
    - Used for:
      - Diagnosis of paediatric HIV-1 infections
      - Blood bank safety (high incidence countries)
    - Issues:
      - Level 4 complexity
      - Properly maintained equipment required

14. **CD4 T - Lymphocyte**
    - CD4 T-lymphocyte counts used for:
      - Determining clinical prognosis
      - Assessing criteria for antiretroviral therapy
      - Monitoring therapy
    - Manual and automated methods
    - Issues:
      - Requires high level of technical skill for test performance and interpretation
      - Properly maintained equipment

15. **Viral Load**
    - Quantitative molecular assay measures amount of HIV in blood products
    - Used to:
      - Predict disease progression
      - Assist with deciding when to initiate antiretroviral therapy
      - Monitors response to antiretrovirals
    - Issues:
      - Expensive
      - Labour-intensive
      - Special facilities

16. **Complexity of HIV Tests Varies**
    Level 1: No additional equipment and little or no laboratory experience needed
    Level 2: Reagent preparation or a multi-step process is required; Centrifugation or optimal equipment
    Level 3: Specific skills such as diluting are required
    Level 4: Equipment and trained laboratory technician are required

*WHO Reports
HIV Rapid Tests provides excellent tool for expansion of services

**HIV Rapid Tests: Advantages**
- Increases access to prevention (VCT) and interventions (PMTCT)
- Supports increased number of testing sites
- Same-day diagnosis and counseling
- Robust and easy to use
- Test time under 30 minutes
- Most require no refrigeration
- None or one reagent
- Minimal or no equipment required
- Minimum technical skill

**HIV Rapid Tests: Disadvantages**
- Small numbers for each test run
- Quality Assurance/Quality Control at multiple sites
- Test performance varies by product
- Refrigeration required by some products
- Reader variability in interpretation of results
- Limited end-point stability of test results

**Body Fluids Used for HIV Rapid Testing**
- Serum
- Plasma
- Whole blood
- Oral fluids

**Three Formats of HIV Rapid Tests**
- Immunoconcentration (flow-through device)
- Immunochromatography (lateral flow)
- Particle agglutination

**How Immunochromatography Works**
- Add Sample
- Conjugate
- Test Line
- Control line
- IgG Antibodies
- Colloidal gold conjugated to HIV antigen
- HIV antigen
- Anti-IgG antibodies
Tests Based on Immunochromatography

Lateral Flow Devices: RETROCHECK WB

Specimen Flow

Control
HIV Antigen
Sample pad

Reading Results: RETROCHECK

Non-reactive
Reactive

How Particle Agglutination Works

Anti-HIV antibodies bind to the antigen-coated latex particles

Key Messages

• HIV rapid tests can be as reliable as EIA
• All tests require attention to training, supervision, and monitoring at points of service.
• As testing is expanding and decentralized, training, supervision, and monitoring must follow accordingly and become all the more important.

Tests Based On Agglutination

Agglutination devices:
• Capillus
• Serodia

Reading Results: Capillus

Non-reactive
Weak Reactive
Strong Reactive

There Are Only Three Possible Outcomes for Single HIV Antibody Tests

Reactive or "Positive"
- Test band
- Control band
Non-reactive or "Negative"
- Control band only
Invalid
- No control band present
- Test has failed. Repeat with new device.

Prevention is BETTER than DIAGNOSIS & MANAGEMENT
One-touch operation, quick & convenient.
Non-contact measurement, no need to disturb patient.
Large LCD backlight.