Common Medical Problems of the College Student

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The college health physician cares for college students who present with a wide variety of medical disorders. College students can become ill, and it is important that they have health care services designed to deal with their health care issues. This article reviews the management of four common medical problems: infectious mononucleosis (IM), asthma, migraine headaches, and urinary tract infections (UTIs).

Infectious mononucleosis

IM is one of the most common serious infectious illnesses in the college-age population. IM is caused by Epstein-Barr virus (EBV); however, similar mono-like illnesses can be caused by other infectious agents, including cytomegalovirus, adenovirus, and \textit{Toxoplasma gondii}. The observed rate of heterophil-positive IM has been reported to be 12 per 1000 university students per
academic year [1]. In a prospective study of entering freshmen at the Chinese University of Hong Kong, 25% of EBV-seronegative students converted to seropositivity during their first academic year [2].

Most adults have acquired EBV infection by age 40. In developing countries, the infection usually is acquired in the first 3 years of life; when the infection is acquired in early childhood, there are usually no symptoms. In more affluent populations, however, approximately one third of EBV infections are first acquired during adolescence and young adulthood, and more than 50% of infected adolescents and young adults are symptomatic. Typical symptoms and signs include fever, sore throat, fatigue, generalized lymphadenopathy, and pharyngitis. The classic syndrome of IM resulting from EBV infection is estimated to occur in 1 of every 1000 young adults per year [3].

EBV is transmitted in oral secretions and can be spread by close oral contact, such as kissing. The virus can be shed for more than 6 months after the initial primary infection, then intermittently throughout life. Approximately 20% to 30% of healthy asymptomatic EBV-infected persons are shedding the virus at any time, and 60% to 90% of immunocompromised EBV-infected persons are shedding the virus at any time. It also is possible to spread the infection by sexual contact because EBV is found in the female genital tract. A study from Edinburgh University suggested that sexual activity and having numerous sexual partners was a highly significant risk factor for EBV seropositivity. Approximately 83% of sexually active students were seropositive compared with 67% of students who had never had intercourse [4].

The incubation period of IM in adolescents is 30 to 50 days. The initial symptoms are often vague and include malaise and fatigue. Other symptoms include fever, sore throat, headache, nausea, abdominal pain, and muscle aches. EBV initially infects the oral epithelial cells, then the entire lymphoreticular system, including the lymph nodes, liver, and spleen. Physical examination findings include generalized lymphadenopathy, pharyngitis, and splenomegaly; more than 90% of patients who have IM have lymphadenopathy. The most commonly affected lymph nodes are the anterior and posterior cervical nodes, but the inguinal, axillary, and epitrochlear nodes also may be enlarged.

Signs of pharyngitis typically include tonsillar enlargement with exudates. Approximately 50% of patients have splenomegaly, usually no more than 2 to 3 cm below the costal margin. The splenic enlargement may be rapid enough to cause right upper quadrant pain, whereas massive splenic enlargement is rare. Approximately 10% of patients also have hepatomegaly, but symptomatic hepatitis and jaundice are uncommon.

The differential diagnosis includes other infections that cause an IM-like illness and other causes of exudative pharyngitis, such as group A beta-hemolytic streptococcal infection. Because approximately 5% of the population may be chronic pharyngeal streptococcal infection carriers, a positive throat culture for group A beta-hemolytic streptococci in a patient who has mono-like symptoms does not exclude the diagnosis of EBV infection. If an adolescent who has symptoms and signs of pharyngitis associated with a positive streptococcal
throat culture fails to improve within 3 days of antibiotic therapy, further testing for IM should be considered.

In more than 90% of patients who have IM, the total leukocyte count is 10,000 to 20,000 cells/mm³ with at least 60% lymphocytes. Approximately 20% to 40% of the lymphocytes are atypical cells, which are larger and have a lower nuclear-to-cytoplasm ratio than normal lymphocytes. Although atypical lymphocytosis can be seen with other infections (including hepatitis A, cytomegalovirus, and rubella), the higher the percent of atypical lymphocytes, the more likely it is that the cause of the infection is EBV. Other abnormal laboratory findings that occur in 50% or more patients include mildly elevated liver transaminases and thrombocytopenia; elevated bilirubin levels and clinical jaundice are rare. Because the platelet count is usually greater than 50,000/mm³, purpura also is uncommon.

IM is associated with elevated levels of heterophil antibodies. These antibodies agglutinate red blood cells from nonhuman species. The heterophil antibodies in serum from patients who have IM agglutinate sheep and horse red blood cells, but not guinea pig red blood cells. The most widely used heterophil antibody test is a slide test that uses horse red blood cells. Adolescents and young adults who have IM are more likely to have a positive heterophil antibody test than young children. The heterophil test may remain positive for 2 years after the acute infection. The false-positive and false-negative rate of heterophil testing is 5% to 10%. False-negative tests in patients who have clinical symptoms and signs consistent with IM may indicate an infection caused by another infectious agent associated with mono-like illness (eg, cytomegalovirus) instead of EBV.

Antibody testing

EBV-specific antibody testing can be useful in confirming the diagnosis of acute EBV infection (Box 1). During the early, acute phase of IM, the IgM–viral capsid antigen (IgM-VCA), IgG–viral capsid antigen (IgG-VCA), and early antigen (EA) titers usually are elevated. The IgM-VCA can be detected in the first 4 weeks of illness and usually disappears within 3 months. The IgG-VCA titer also can be detected in the first 4 weeks of illness, but persists for life. EA titers peak during convalescence and are detectable for several months after the illness, but may persist at low levels for many years. The IgM antibody to VCA is the most valuable and specific test for the diagnosis of IM resulting from EBV infection and is sufficient to confirm the diagnosis. High levels of antibody to EA

**Box 1. Useful antigen tests in infectious mononucleosis**

- Early antigen (EA)
- IgM-viral capsid antigen (IgM-VCA)
- IgG-viral capsid antigen (IgG-VCA)
- EBV-determined nuclear antigens (EBNA)
may occur in immunocompromised patients who have persistent infection and active EBV replication. High titers of antibodies to the diffuse-staining component of EA occur in patients who have nasopharyngeal carcinoma, and high titers of the cytoplasmic-restricted component of EA occur in patients who have EBV-associated Burkitt’s lymphoma. Because EBV-determined nuclear antigen (EBNA) antibodies are the last to develop, absence of these antibodies when other EBV antibodies are present suggests a recent infection, whereas positive EBNA antibody titers suggest that the acute EBV infection occurred more than 3 to 4 months ago.

Management

There is no specific treatment for IM. Decreased physical activity and symptomatic treatment are the mainstays of therapy. Participation in any strenuous athletic activities should be prohibited during the first 2 to 3 weeks of the illness. Activity can be increased gradually as symptoms resolve. Short courses of corticosteroids may be helpful in the treatment of IM complications (Box 2). There are no controlled studies, however, on the efficacy of corticosteroids; because EBV infection is associated with oncogenic complications (eg, nasopharyngeal carcinoma, Burkitt’s lymphoma), corticosteroids should not be used in patients who have uncomplicated IM [4].

IM complications are rare. One of the most common complications is airway obstruction secondary to swelling of the tonsils and oropharyngeal lymphoid tissue. Although less than 5% of patients develop this complication, it is the most common reason for hospitalization of patients with IM. Most patients with this complication can be treated successfully with intravenous fluids, humidified air, and corticosteroids. Splenic hemorrhage or rupture occurs in less than 0.5% of adolescent and young adult patients. This dreaded complication happens most commonly during the second week of illness and often is associated with mild abdominal trauma. To avoid this complication, patients who have splenomegaly should be advised to avoid all contact sports until the splenomegaly resolves.

Uncommon complications of IM include a variety of neurologic disorders, such as meningitis, seizures, ataxia, facial nerve palsy, transverse myelitis, and encephalitis. About 50% of patients who have IM complain of headache, but

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<th>Box 2. Infectious mononucleosis complications that may be improved with corticosteroids</th>
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<td>Marked tonsillar hypertrophy</td>
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<td>Thrombocytopenia associated with hemorrhage</td>
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serious neurologic complications occur in only 1% to 5% of patients. A perceptual disorder (metamorphopsia or “Alice in Wonderland” syndrome) is a peculiar neurologic manifestation in which spatial relationships and size and shape of objects are distorted. Guillain-Barré syndrome may follow the acute illness.

Approximately 3% of patients develop a Coombs-positive hemolytic anemia. Aplastic anemia, severe neutropenia (<1000 neutrophils/mm$^3$), and severe thrombocytopenia (platelet count <20,000/mm$^3$) are rare complications. Aplastic anemia usually presents 3 to 4 weeks after the onset of illness and lasts 4 to 8 days, whereas hemolytic anemia typically appears in the first 2 weeks and lasts 1 month. Other rare complications include myocarditis, pancreatitis, parotitis, and orchitis.

If there are no complications during the acute illness, the prognosis for complete recovery is excellent. Marked fatigue, headache, and pharyngeal symptoms usually resolve in 2 to 4 weeks. Mild fatigue and malaise may persist for a few months, however. Although there are some cases of prolonged fatigue after IM, there is no convincing evidence that EBV infection or recurrence of EBV infection is linked to a chronic fatigue syndrome.

**Asthma**

Although asthma is the most common chronic disease in children and is becoming increasingly prevalent in children and adults [5], little has been written about asthma in the college-age population. The National Heart, Lung and Blood Institute and World Health Organization, in their 1995 Workshop Report, defined asthma as follows [6]:

[A] chronic inflammatory disorder of the airways in which many cells play a role, in particular mast cells, eosinophils, and T lymphocytes. In susceptible individuals this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough particularly at night or in the early morning. These symptoms are usually associated with widespread but variable airflow limitation that is at least partly reversible either spontaneously or with treatment. The inflammation also causes an associated increase in airway responsiveness to a variety of stimuli.

**Epidemiology**

Asthma is prevalent worldwide in all age groups; its prevalence in children varies greatly in different countries. Some countries have reported prevalence rates among 6- to 7-year-olds of 1.4%, whereas other countries have prevalence rates of 27.1%. This same pattern is seen among 13- to 14-year-old adolescents [7,8]. In the United States, asthma prevalence increased 74% from 1988 to 1994 among children 5 to 14 years old [5]. Measures of morbidity, such as hospitalization rates and emergency department visits, and mortality also have
increased in the United States [9–11]. In addition, children and young adults from ethnic minority groups and lower socioeconomic groups are known to be at increased risk for poor outcomes secondary to asthma [12–14]. Asthma occurs in all races, although rarely in Eskimos [10]. The male and female lifetime prevalence of asthma diagnosis (in 2001) showed that females are more likely to be diagnosed with asthma—119 females/1000 population received the diagnosis of asthma versus 107 males/1000 population [15].

General features

The hallmarks of asthma are inflammation and airway responsiveness that lead to airflow limitations. A patient’s history, physical examination, laboratory evaluation, and response to a trial of therapy all are helpful in making the diagnosis of asthma. Typically a patient who has asthma complains of chronic cough, persistent wheezing, or chronic shortness of breath. There is frequently a history of asthma in other family members and allergies and eczema.

Common triggers that worsen asthma include tobacco smoke, cold air, exercise, and strong scents. Patients with asthma may be able to describe what happens when their disease worsens, listing not only the most salient consequences (eg, shortness of breath), but also the more subtle results (eg, increased nocturnal cough). It is important for clinicians to ask about the salient and subtle manifestations of asthma to improve asthma management.

The physical examination of a patient with asthma may be completely normal if the patient is well controlled by medications and is not having an exacerbation. Conversely a patient who has experienced a profound exacerbation may appear in extremis. In between the two extremes, the pulmonary examination generally shows diffuse wheezing. The wheezing starts late in the expiratory phase, but as the disease progresses, it may last throughout expiration and involve the inspiratory phase as well. With continued progression, the airways may become so narrow (because of mucus production, airway edema, and smooth muscle bronchoconstriction) that no wheezing is heard at all. The patient with an asthma exacerbation often appears anxious and may be using accessory muscles to aid in breathing. A pulsus paradoxus is found during severe asthma exacerbations. Other associated findings include hives, eczema, allergic rhinitis, and nasal polyps (especially in patients with aspirin sensitivity).

The laboratory evaluation of asthma should be specific and straightforward. Pulmonary function tests are used to confirm the diagnosis of asthma, especially when used with a fast-acting inhaled β-agonist (eg, albuterol) or a part of a bronchoprovocation test. Rarely, flexible fiberoptic laryngoscopy is necessary to rule out vocal cord dysfunction, which may mimic asthma [16,17]. For a patient in whom the diagnosis has been established, regular, at-home measurements of the peak expiratory flow rate (PEFR) are helpful for spotting trends that reveal whether control is adequate; many patients appropriately self-manage their medications on the basis of their PEFR readings (with prior clinician input). Spirometry also may be employed to assess asthma severity and help guide the
medication regimen. Other laboratory tests (eg, chest radiographs, allergy testing, blood tests for IgE) should be ordered as indicated.

Management

The approach to asthma management comprises four elements (Box 3), according to the 1997 National Asthma Education and Prevention Program (NAEPP) Expert Panel II [18,19]. Monitoring generally refers to PEFR, especially in a patient with moderate-to-severe disease who is seeking a trend as opposed to a determination of airflow limitation [20,21]. Some clinicians use sputum eosinophilia to monitor asthma control and guide therapy, although it is unclear whether sputum eosinophilia independently predicts a patient’s response to inhaled or oral corticosteroids [22–25].

Asthma triggers are numerous and include allergens, respiratory infections (especially viruses), irritants, chemicals, physical activity, and emotional stress. It is important to identify and avoid or at least limit exposure to the trigger. In cases in which the trigger cannot be avoided and limited exposure is impossible, an additional dose of bronchodilator may be advisable. Influenza vaccination should be administered annually to patients with asthma.

Pharmacologic treatment is an extensive topic, and only a brief outline is offered here. For more extensive information, review the 1997 NAEPP Guidelines (updated in 2002) [18]. A patient’s asthma typically is categorized into one of four “steps,” based on the severity of symptoms (eg, nocturnal awakenings, necessity of bronchodilator use for wheezing or shortness of breath during the day, PEFR [as a percentage of predicted or best] and PEFR variability). Step 1 disease, known as mild intermittent asthma, is the mildest form and requires no long-term treatment. It has the fewest and least severe symptoms. Therapy for step 1 asthma is a fast-acting inhaled β-agonist as necessary.

Step 2 disease is known as mild persistent asthma and is more severe than step 1 disease. Mild persistent asthma requires long-term medication—generally an inhaled corticosteroid—in addition to a fast-acting inhaled β-agonist if control is not maintained. Other types of long-term medications used in step 2 disease (and beyond) include leukotriene-modifying agents, mast cell–stabilizing agents, and long-acting inhaled β-agonists. The last-mentioned are recommended for use only in conjunction with inhaled corticosteroids [26,27].

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<th>Box 3. Approach to asthma management</th>
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<td>1. Monitoring</td>
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<td>2. Controlling trigger factors</td>
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<td>3. Pharmacologic treatment</td>
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Step 3 disease, moderate persistent asthma, is more severe than Step 2 disease and may require high-dose inhaled steroids. The other long-term medications mentioned and theophylline may be a part of the patient’s medication regimen. A patient with step 4 disease, severe persistent asthma, has symptoms almost continuously and may require regular bursts or daily dosing of oral corticosteroids, in addition to other long-term medications and fast-acting inhaled β-agonists. In principle, clinicians should get newly diagnosed or poorly controlled asthma under control quickly. As the asthma is brought under control, medications, especially corticosteroids, should be weaned to the lowest dose at which there is good control.

Patient education is an essential component of keeping patients with asthma healthy. Patient education consists of teaching patients how to monitor their symptoms, how to identify and avoid their triggers, why and how to use their medications and their devices, and what to do in the event of an emergency or deteriorating control. The last-mentioned is often assisted through the use of an asthma management plan (or asthma action plan). Education is the key to clinician-directed self-management of patients. Motivated, educated patients have reduced hospitalizations because of asthma, improved daily function, and improved patient satisfaction [28].

Challenges of asthma in the college population: potential areas of research

There are a few challenges to the clinician in working with college-age patients with asthma. First, asthma is not well characterized in this population; specifically, data collected on asthma morbidity and mortality do not focus on the college population (eg, the Centers for Disease Control and Prevention and National Center for Health Statistics report 15- to 34-year-old or 18 and older age groups rather than the traditional college age group). Second, college is a time of development from late adolescence to early adulthood. Students may function semi-independently and be educationally “primed,” but they also are highly influenced by their peers. In addition, college students may be challenged by sleep deprivation, living in older college buildings with mold and dust mite infestation, and the likelihood of increased respiratory infections owing to the close proximity to other students. No studies on the successes or failures of patient education and self-management of the college-age population with asthma exist. These and other areas of interest should provide directions for future research.

Migraine

Migraine is a common neurovascular disorder in the college-age population. It is characterized by severe headache and autonomic nervous system dysfunction and, in some patients, an aura. Although attacks may start at any age, the incidence peaks in early to mid adolescence. The 1-year overall prevalence of
migraine in the United States is 11%; the prevalence is higher in women (15–18%) than in men (6%) [29].

The International Headache Society has developed diagnostic criteria for migraine (Boxes 4 and 5) [30]. The headache begins gradually, often in the morning, and the most common locations are the frontal and temporal regions. The headache episode may last hours to days and is associated with symptoms such as nausea, vomiting, photophobia, and phonophobia. The pain is often uni-

**Box 4. Criteria for migraine without aura**

- Headaches last 4–72 hours
- With ≥ 2 of the following:
  - Unilateral location
  - Throbbing quality
  - Severe enough to inhibit or prohibit daily activities
  - Aggravated by routine physical activity (eg. walking stairs)
- And during the headache, at least 1 of the following:
  - Nausea or vomiting or both
  - Photophobia or phonophobia


**Box 5. Criteria for migraine with aura**

- At least 2 headaches
- With at least 3 of the following:
  - One or more fully reversible aura symptoms indicating focal cerebral cortical dysfunction or brainstem dysfunction or both
  - At least 1 aura symptom develops gradually over > 4 minutes or ≥ 2 symptoms occur in succession
  - No single aura symptom lasts > 60 minutes
  - Headache follows aura within 60 minutes or before or during aura

lateral, throbbing, aggravated on movement, and severe [30]. The severity of the pain causes the patient to interrupt activities. The frequency of migraine headaches in affected patients averages 1.5 per month, but 10% have weekly attacks [29].

Migraine without aura is the most common type, but in 15% to 18% of patients, the headache always is preceded or accompanied by an aura; in 13% of patients, the headache is accompanied by an aura sometimes [31]. Prodromal symptoms in patients who have migraine without aura may include mood changes, irritability, increased thirst, fluid retention, or food cravings. Behavioral changes that may result in curtailing activities are the most common prodromal symptoms. Migraine with aura may be associated with visual, sensory, motor, or psychic aura. However, Visual auras are the most common and include transient visual deficits and visual distortions. Sensory auras may consist of numbness or tingling of the extremities, perioral numbness, and dysesthesias. Motor auras include monoparesis and hemiparesis. Psychic auras may be characterized by confusion, dysequilibrium, and amnesia [32].

The differential diagnosis of migraine includes complex partial seizures, intracranial hemorrhage, brain tumor, acute intoxication, and central nervous system infection. Occasionally, migraine presents with dramatic neurologic signs and symptoms, such as hemiparesis, ataxia, blindness, ophthalmoparesis, vertigo, and acute confusional states in addition to severe headache. In these cases, neuroimaging studies often are needed to exclude more ominous neurologic conditions.

Management

The appropriate treatment of a patient who has migraine depends on the frequency, duration, and intensity of the headache and the patient’s pain tolerance and disability. A headache calendar in which the patient tracks the frequency and severity of the headaches may be helpful in determining the optimal treatment approach and monitoring its efficacy. In a patient who has migraine, the brain does not seem to tolerate irregular lifestyles well. College students, who often have irregular sleep and eating patterns and increased stress, may benefit particularly from a discussion of the importance of regular sleep, regular meals, adequate exercise, and avoidance of stress as the first step in decreasing the frequency of headaches. Insufficient sleep is associated with increased headache frequency, so counseling the student on the importance of going to bed and getting up at the same time each day may be helpful. The influence of diet on migraine is unclear. About 10% to 30% of migraineurs can identify foods that trigger their migraine episodes. If so, avoiding these foods may be helpful. It is especially important to ask about intake of caffeine because there is a link between caffeine intake and migraine episodes [33]. Alcohol also may precipitate migraine in susceptible individuals.

Drugs used in the treatment of migraine can be divided into two categories: (1) drugs taken at the time of a migraine episode and (2) drugs taken daily to prevent migraine episodes. For an acute migraine episode, drug therapies can be
divided further into nonspecific pain relievers and drugs that are used specifically for treatment of migraine. For patients who have infrequent migraine episodes of short duration, an oral analgesic (eg, aspirin, acetaminophen, naproxen, or ibuprofen) may be sufficient. It is important to avoid narcotics because they leave the patient cognitively impaired and can be addictive. The analgesic should be taken at the first sign of a headache and at an appropriate dose (eg, 400–800 mg of ibuprofen; 500–1000 mg of naproxen). Because migraine episodes are associated with decreased gastric motility, which may interfere with absorption of oral analgesics, metaclopramide taken promptly at the onset of the headache along with the analgesic may help increase absorption and control the nausea that often is associated with migraine episodes. If oral analgesics are ineffective or must be taken more often than 2 to 3 days per week, alternative medications should be considered because overuse of analgesics can lead to an increase in headache frequency (analgesic rebound).

If analgesics are ineffective in treating acute episodes, triptans should be considered [34]. Triptans are serotonin 5-HT1 receptor agonists. Their potential mechanism of action includes cranial vasoconstriction, peripheral neuronal inhibition, and inhibition of transmission through second-order neurons of the trigeminocervical complex. The five triptans most commonly used are sumatriptan, naratriptan, rizatriptan, zolmitriptan, and almotriptan. Because absorption of these drugs may be delayed when administered orally during a migraine episode, the use of nonoral formulations, such as nasal sprays, inhalers, injectables, or suppositories, should be considered.

Sumatriptan is available in a formulation for subcutaneous self-injection, an oral formulation, and a nasal spray. The injectable formulation and the nasal spray begin to produce relief in 10 to 15 minutes, whereas the tablet may take 1 to 2 hours to produce relief. Injectable sumatriptan is effective in 70% to 80% of patients who have moderate-to-severe migraine episodes, the nasal spray is effective in 60% of patients within 2 hours, and the oral tablets are effective in 50% to 60% of patients within 2 hours and 70% within 4 hours [34]. A meta-analysis of the triptans revealed that 100 mg of sumatriptan, 2.5 mg of zolmitriptan, 5 mg of rizatriptan, 40 mg of eletriptan, and 12.5 mg of almotriptan were equally effective in providing pain relief within 2 hours of ingestion, whereas higher doses of rizatriptan (10 mg) and eletriptan (80 mg) were more effective than 100 mg of sumatriptan [35].

For patients who have frequent or debilitating headaches, preventive medications should be discussed collaboratively with the patient. Patients who have five or more headaches per month or have acute attacks that are unresponsive to therapy are good candidates for preventive therapy. It is not clear how preventive therapies work, but it is generally thought that they modify the sensitivity of the brain that underlies migraine [35]. A variety of drugs have been used (Box 6), although there are few controlled studies on their efficacy in adolescents. The choice of drug to use for preventive therapy should be made after discussing with the patient the common side effects of each medication. Propranolol is contraindicated in patients who have asthma because it may cause
bronchospasm. Other side effects include drowsiness, bradycardia, lightheadedness, and decreased energy. Valproate has teratogenic effects, so it should not be used by women who are at risk for pregnancy owing to unprotected sexual activity. Serious side effects of valproate also include liver and hematologic abnormalities. Amitriptyline side effects include drowsiness, dizziness, postural hypotension, and nausea. The use of methysergide for prophylaxis should be avoided because of the risk of retroperitoneal fibrosis.

**Urinary tract infections**

UTIs usually are described by their location as urethritis, cystitis, or pyelonephritis. The diagnosis is based on the isolation of a single pathogenic organism in sufficient number from either a clean-catch or catheterized urine specimen. Although UTIs traditionally have been defined by the isolation of greater than $10^5$ colony-forming units (CFUs), it has been suggested that for women who have symptoms consistent with a lower UTI (urethritis or cystitis), isolation of at least $10^2$ CFUs is sufficient for diagnosis.

Symptoms of an acute UTI include pain or burning on urination (dysuria), frequent voiding of urine (frequency), urge to void urine (urgency), blood in the urine (hematuria), and lower abdominal discomfort. If fever, suprapubic tenderness, or costovertebral tenderness are present, the infection is more likely to involve the upper urinary tract; if these symptoms and signs are absent, the infection is more likely to be limited to the bladder (cystitis) or urethra (urethritis).

Four symptoms significantly increase the probability of UTI: dysuria, frequency, hematuria, and pain [36]. In primary care settings, the probability of cystitis is approximately 90% in women who present with dysuria and frequency

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**Box 6. Medications used for migraine prevention**

- **β-Adrenergic receptor antagonists**
  - Propranolol
  - Metoprolol

- **Antidepressants**
  - Amitriptyline
  - Nortriptyline
  - Fluoxetine

- **Anticonvulsants**
  - Carbamazepine
  - Valproate
  - Topiramate
  - Lamotrigine
  - Gabapentin
without vaginal discharge [36,37]. Physical examination findings are of little value in the diagnosis of UTI; however, the examination may be helpful in the diagnosis of other conditions that are in the differential diagnosis of UTI, including vaginitis, cervicitis, pelvic inflammatory disease, and sexually transmitted infections. Symptoms or signs of vaginal discharge and vaginal irritation significantly decrease the likelihood that a UTI is present [36], but because UTIs are most likely to occur in sexually active women, these diseases frequently overlap. The only physical examination finding that increases the likelihood of UTI is costovertebral angle tenderness, but this finding is characteristic only of upper UTIs.

Although older studies recommended that a urine culture be done in all women with suspected UTI, more recent guidelines suggest that women who have typical symptoms can be diagnosed accurately by urine dipstick and that a urine culture is not necessary [38]. A urine dipstick that is positive for leukocyte esterase or nitrite has a sensitivity of 75% and a specificity of 82% in the diagnosis of UTI [39]. The presence of pyuria on urinalysis has high (95%) sensitivity but relatively low (40–70%) specificity for UTI. The presence of bacteria on microscopic examination of the urine is a more specific (85–95%) but less sensitive test [37].

Cystitis is common in college-age women because the most important risk factor for this infection is sexual activity. Celibate women rarely have cystitis. The risk of acute cystitis during the 48 hours after sexual intercourse increases by a factor of 60. The incidence of cystitis among sexually active young women is approximately 0.5% per year [36]. The risk of UTI and UTI complications is increased in women who have diabetes, immunosuppression, or structural abnormalities of the urinary tract or who are pregnant.

*Escherichia coli* causes 75% to 90% of acute episodes of cystitis. *Staphylococcus saprophyticus* is the second most common cause and accounts for 5% to 15% of infections. Other organisms include enterococci, *Klebsiella* species, and *Proteus mirabilis*. In the past, a 3-day course of trimethoprim-sulfamethoxazole (TMP-SMX) was effective in eliminating pathogens from the urine in 94% of women who had cystitis [40]. Because of increasing resistance of urinary pathogens to TMP-SMX, however, some authorities now recommend that TMP-SMX be used only if prevalence of resistance in a community is less than 15% to 20% and the patient has not received antibiotics recently.

Ofloxacin is equally or more effective than TMP-SMX, and other fluoroquinolones are likely to be equally efficacious. When TMP-SMX is contraindicated, a 3-day course of ciprofloxacin, levofloxacin, or norfloxacin is a reasonable alternative. These drugs should not be considered first-line therapy, however, because of their higher cost and the concern that using these medications increases the risk of bacterial resistance in the community. Fluoroquinolones are active against *S. saprophyticus* and most typical gram-negative uropathogens, but are effective against only 60% to 70% of enterococci.

Approximately 95% of urinary pathogens are sensitive to nitrofurantoin, but this antibiotic is less active than TMP-SMX against aerobic gram-negative uropathogens other than *E. coli* and is not effective against *Pseudomonas* or
Proteus species. Nitrofurantoin also usually must be taken for 7 days and may cause gastrointestinal upset. The macrocrystalline form must be taken every 6 hours, but the monohydrate macrocrystal is taken just twice daily and causes fewer gastrointestinal symptoms. β-lactams (eg, amoxicillin) should be avoided because bacterial resistance is common.

Women who have acute pyelonephritis should be treated for 14 days with a fluoroquinolone if the organism is susceptible to it. Hospitalization may be necessary for women who are unable to take oral medications, have signs of systemic toxicity, or have underlying structural urinary tract abnormalities or are pregnant. Gram-positive organisms may require treatment with amoxicillin or amoxicillin-clavulanate [40].

Approximately 90% of women have symptomatic relief within 72 hours after initiation of antibiotic therapy. If dysuria is severe, more rapid symptomatic relief can be achieved with the use of phenazopyridine, which is now available without prescription. Routine follow-up is unnecessary after treatment of cystitis unless symptoms persist. Imaging studies and cystoscopy are not indicated.

After an initial UTI, most women have sporadic recurrences, and at least 25% of women have a recurrence within 1 year. Alternative contraceptive methods should be considered by women who have frequent recurrences and use spermicidal-coated condoms or diaphragms because vaginal spermicides increase the risk for UTIs. Continuous or postcoital prophylaxis with low-dose antimicrobial agents may be effective in preventing recurrences. Nitrofurantoin, TMP, TMP-SMX, ciprofloxacin, and norfloxacin all are effective when taken once daily in preventing recurrences. Prophylaxis usually is initiated for 6 months. Postcoital treatment with nitrofurantoin, TMP-SMX, or a fluoroquinolone also is effective in preventing recurrences. Cranberry juice contains proanthocyanidins, which seem to inhibit attachment of uropathogens to the urinary tract epithelium. Studies have shown that 200 to 750 mL of cranberry juice daily can reduce recurrences by 15% to 20%. Although tablets containing cranberry products are sold commercially, the actual cranberry content of these products is highly variable; the cranberry content of juices marketed as cranberry juice may vary from 5% to 100%.

Although women commonly are advised to void after coitus to prevent UTIs, there is no evidence that this prevents cystitis. There also is no evidence that poor urinary hygiene leads to infection. There is no rationale for advising women who have had a UTI to increase their frequency of urination; change wiping patterns; or avoid pantyhose, douching, or use of hot tubs [37].

References


