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Evidence-Based Urgent Care

High-Yield Clinical Education • Practical Application

CLINICAL CHALLENGES:

- **What are the most current diagnostic methodologies used to evaluate patients who present with respiratory and genitourinary complaints?**
- **What are the advantages and disadvantages of various types of diagnostic tests available to the UC clinician?**
- **How are diagnostic tests for respiratory tract and genitourinary infections interpreted to aid diagnostic and treatment plans?**

Laboratory Testing in Urgent Care: Best Practices for Choosing and Interpreting Respiratory and Genitourinary Tests

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Prior to beginning this activity, see "CME Information" on page 2.

Abstract

Patients presenting to urgent care settings expect prompt diagnosis, treatment, and resolution of their symptoms. In order to provide high-quality, evidence-based care, urgent care clinicians must be familiar with currently available diagnostic tests and understand when to order or withhold those tests. This issue reviews diagnostic approaches used to evaluate respiratory and genitourinary complaints, including available testing modalities, their clinical utility and limitations, and practical recommendations for management. Key clinical pearls and common pitfalls are highlighted to support efficient, accurate diagnosis, and appropriate treatment decisions.

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Needs Assessment: The need for this educational activity was determined by a practice gap analysis; a survey of medical staff; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation responses from prior educational activities for urgent care and emergency medicine physicians.

Target Audience: This internet enduring material is designed for physicians, physician assistants, nurse practitioners, and residents in the urgent care and family practice settings.

Goals: Upon completion of this activity, you should be able to: (1) identify areas in practice that require modification to be consistent with current evidence in order to improve competence and performance; (2) develop strategies to accurately diagnose and treat both common and critical urgent care presentations; and (3) demonstrate informed medical decision-making based on the strongest clinical evidence.

CME Objectives: Upon completion of this activity, learners should be able to: (1) explain the advantages and disadvantages of various types of diagnostic tests available to the urgent care clinician; (2) develop a diagnostic and treatment plan for common upper respiratory tract infections and genitourinary complaints in the urgent care; and (3) distinguish between pathogens and flora when considering the patient presentation and diagnostic test results.

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QUICK READ

Points & Pearls

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Laboratory Testing in Urgent Care: Best Practices for Choosing and Interpreting Respiratory and Genitourinary Tests

Points

- Diagnostic testing is most beneficial when the clinical diagnosis is uncertain, or if the clinician needs to differentiate between pathologies that present with overlapping symptoms. **(See Figure 2.)**
- There is widespread use of antigen tests in the urgent care setting due to ease of use, portability, quick turnaround time, and relative cost savings.
- While molecular testing is more sensitive, antigen testing is more cost effective and likely to be available as a point-of-care test.
- Multiplex panels may reduce unnecessary antibiotic use.

Respiratory Tract Infections

- The most common diagnostic tests for respiratory tract infections (RTIs) in urgent care clinics are strep, influenza, COVID-19, and respiratory syncytial virus (RSV). **(See Table 10.)**
- Rheumatoid factor may cause persistent false-positive COVID-19 antigen tests.
- The prevention of acute rheumatic fever is the primary goal of treating strep pharyngitis.
- All patients aged 3 to 18 years with a negative rapid strep test should have confirmatory group A strep testing.
- If a patient who has clinical symptoms consistent with influenza tests positive on an antigen test, disease is likely. Antiviral medications are only recommended for high-risk patients.
- Some RSV tests are only validated for children and infants, as viral load is age dependent.
- Because detection of *Mycoplasma pneumoniae* cannot differentiate between a self-limited RTI and pneumonia, testing should be reserved for specific clinical situations. Patients with a positive test for *M pneumoniae* should be treated with antibiotics.

Pearls

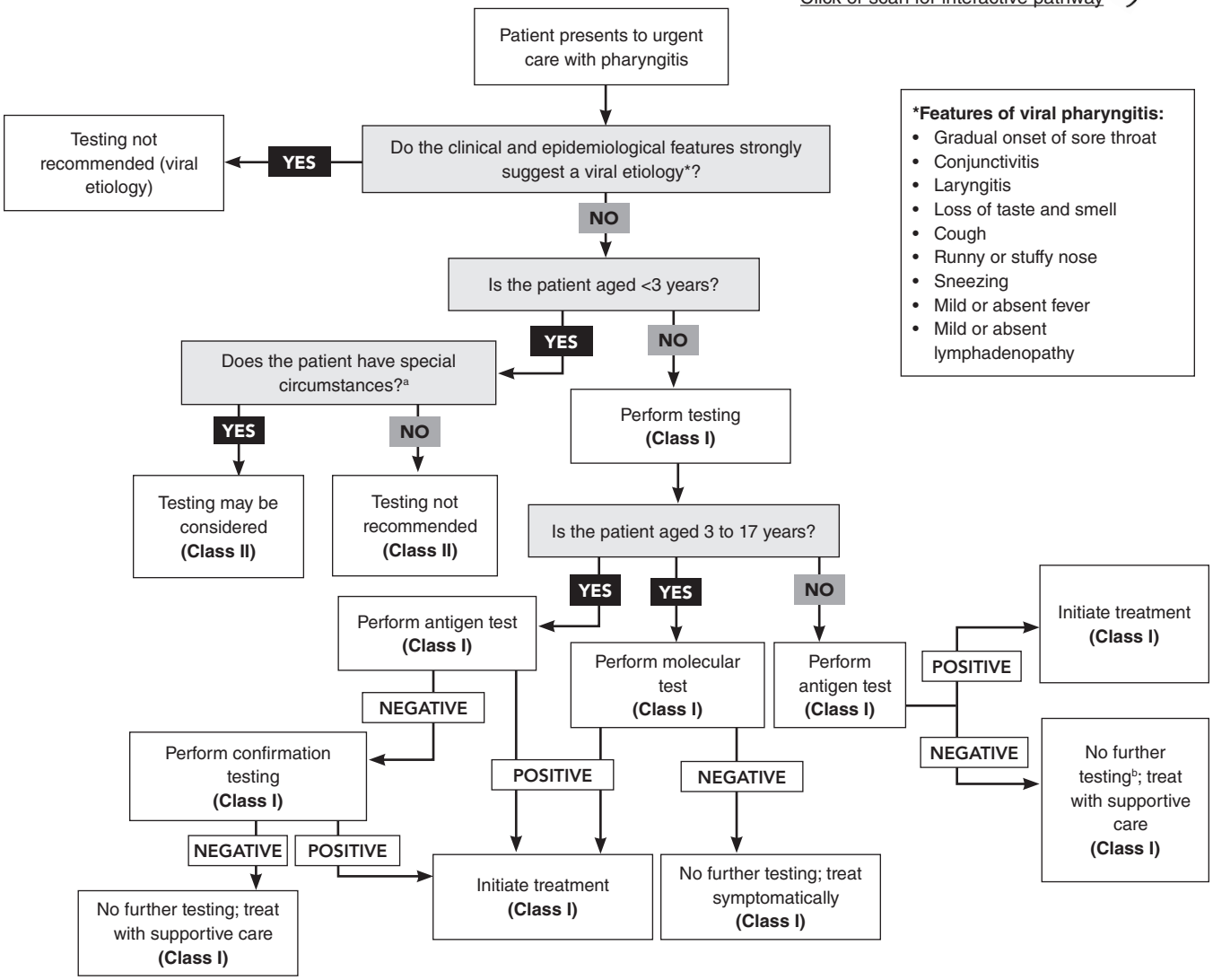
- Clinicians should carefully consider whether the test result will change clinical management and/or improve clinical outcomes.
- Clinicians should be aware of the testing platforms in their clinic, the limitations of the tests, and proper utilization practices.
- Be aware of clinical situations where normal bacterial flora is colonized and antibiotic treatment is not indicated.
- Antibiotics should only be prescribed for strep pharyngitis if there is a positive test.
- Test-of-cure is not recommended for most infections that are resolved or improving.
- Urgent care clinics consider costs and reimbursements when selecting in-house diagnostic tests.

Genitourinary Infections

- Though a positive urine culture and sensitivity test confirms the presence of bacteria in the urine, the patient's presenting symptoms determine whether the diagnosis is a urinary tract infection (UTI) or colonization.
- For bacterial vaginosis, vaginal candidiasis, trichomoniasis, gonorrhea, and chlamydia, a nucleic acid amplification test is preferred. A test of cure is recommended for oropharyngeal chlamydia or gonorrhea.
- Females with bacterial vaginosis should be assessed for HIV and other sexually transmitted infections based on their individual risk factors.
- Serological antibody testing for herpes simplex virus is not recommended due to the prevalence of positive antibodies in the general population.
- Molecular UTI panels are not recommended except under the guidance of a specialist. Nucleic acid amplification tests are recommended for select cases of *Mycoplasma* and *Ureaplasma*.

Clinical Pathway for the Laboratory Evaluation of Pharyngitis in Urgent Care

Click or scan for interactive pathway



[a]If a child has symptoms consistent with strep and known exposure (ie, sibling has strep), testing may be considered. Infectious Diseases Society of America guidelines do not recommend testing for strep in children aged <3 years due to the low risk of rheumatic fever.

[b]Patients at higher risk for severe infection or complications from group A strep pharyngitis (eg, patients with a history of acute rheumatic fever), as well as patients living in areas where acute rheumatic fever is endemic or where active epidemics are occurring, may require additional testing.

Class of Evidence Definitions

Each action in the clinical pathways section of *Evidence-Based Urgent Care* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

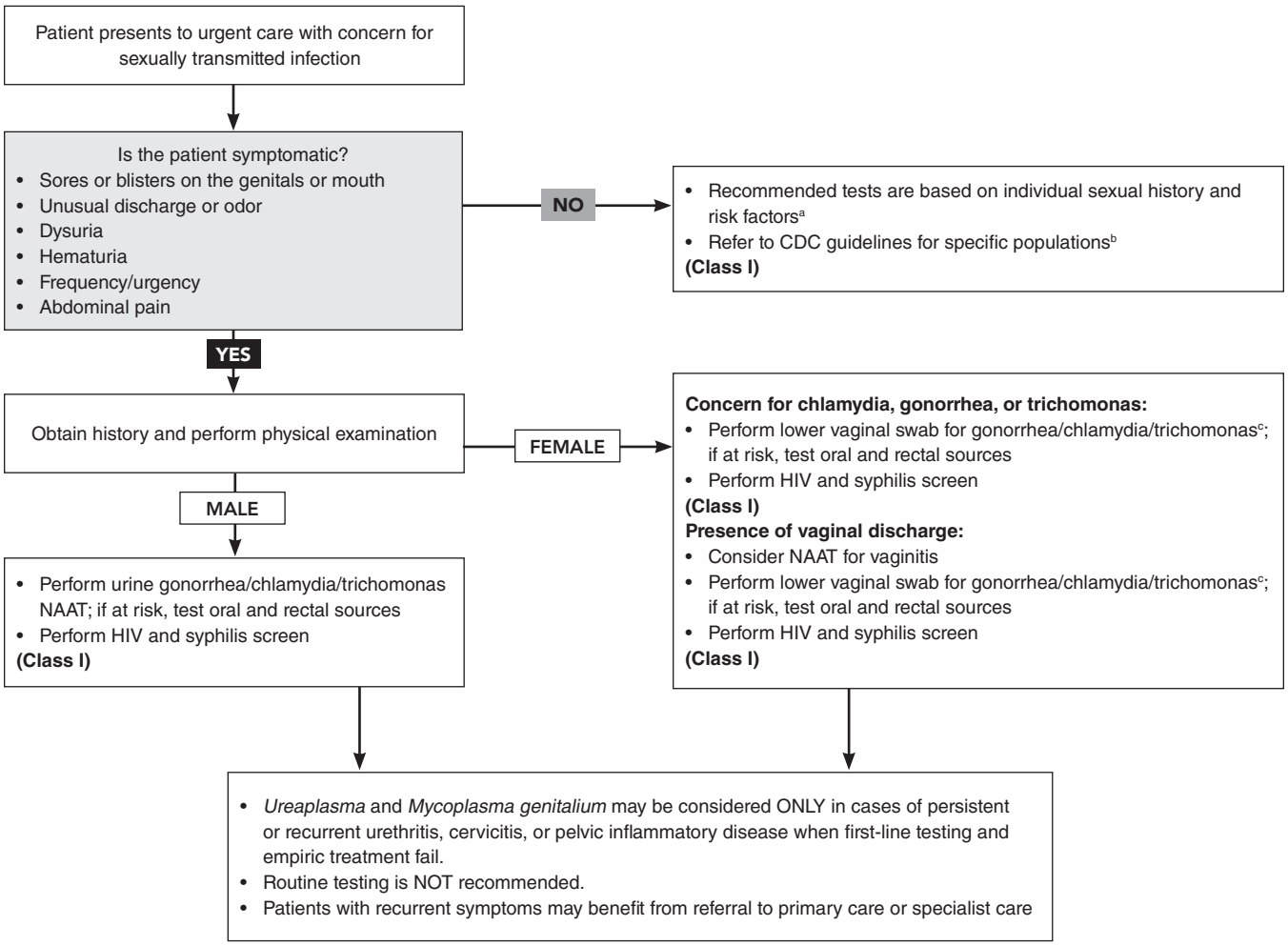
Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Clinical Pathway for Laboratory Evaluation for Sexually Transmitted Infections

Click or scan for interactive pathway

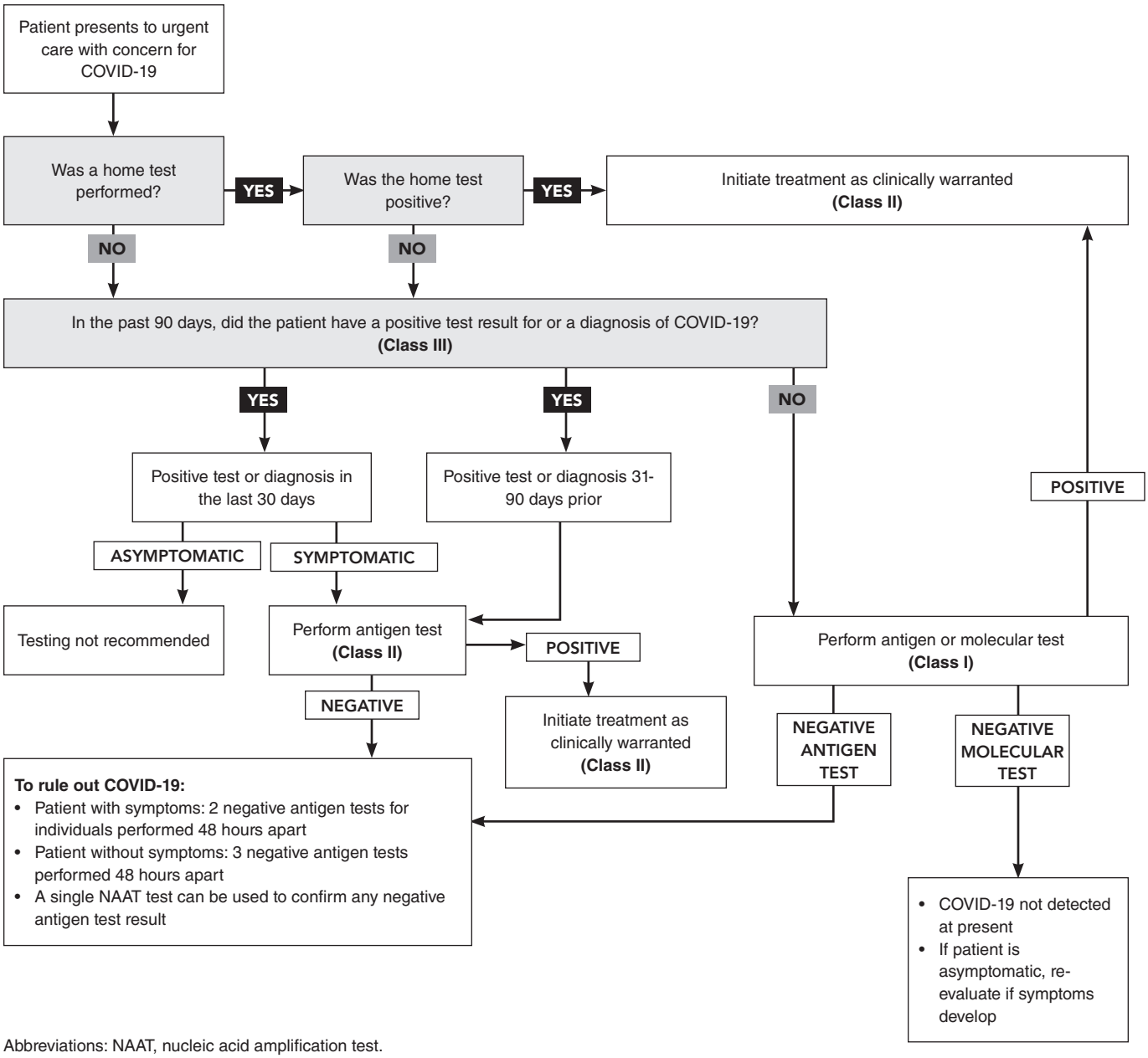


[a]Urgent care centers typically have access to testing for gonorrhea, chlamydia, trichomonas, HIV, and syphilis
[b]Sexually Transmitted Infections Guidelines, 2021
[c]May be self collection or clinician performed based on testing platform

Abbreviations: CDC, United States Centers for Disease Control and Prevention; NAAT, nucleic acid amplification test.
For Class of Evidence definitions, see page 4.

Clinical Pathway for the Laboratory Evaluation and Management of COVID-19

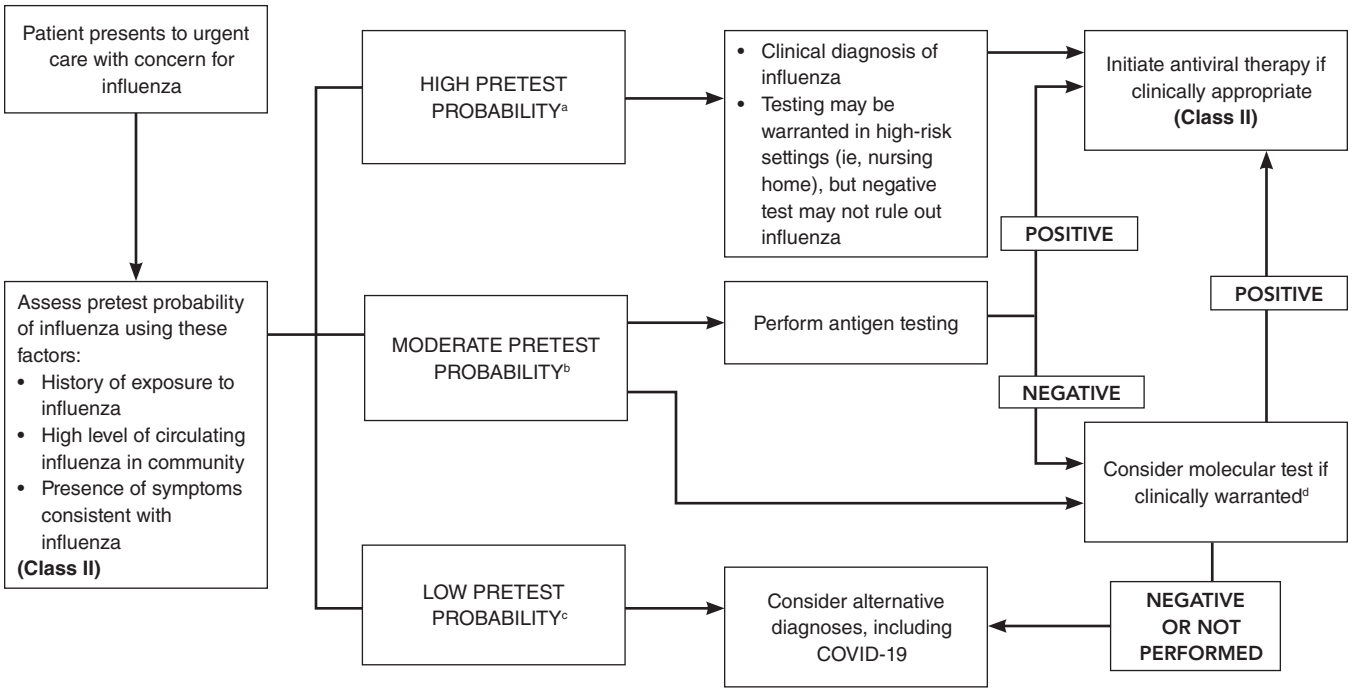
Click or scan for interactive pathway



Abbreviations: NAAT, nucleic acid amplification test.
For Class of Evidence definitions, see page 4.

Clinical Pathway for the Laboratory Evaluation and Management of Influenza

Click or scan for interactive pathway



[a]All 3 factors are present
[b]1-2 factors are present. Testing is most beneficial in this category
[c]0 factors present
[d]False negatives are higher with antigen versus molecular test

For Class of Evidence definitions, see page 4.

Case Presentations

CASE 1

A 15-year-old boy presents to the urgent care with a sore throat, fever, nasal congestion, cough, and fatigue for 2 days…

- The physical examination is significant for tonsillar exudates and bilateral tender anterior cervical lymph nodes.
- An in-office rapid strep antigen test is negative.
- The patient's mother asks you to prescribe an antibiotic for "strep throat."
- Are empiric antibiotics the appropriate management choice for this patient? Is additional testing needed and if so, which tests?

CASE 2

A 25-year-old woman presents to the urgent care complaining of urinary frequency and urgency…

- She states that she is certain this is "another UTI" and requests antibiotics.
- A review of her chart indicates that she has had 4 previous visits to urgent care in the past 6 months, with no growth indicated on urine culture at 2 of those visits.
- She reports that she is sexually active with her partner of 6 months. She says it is a monogamous relationship but notes that the urinary tract infections seemed to start around the same time she became sexually active with this partner.
- She has been taking over-the-counter phenazopyridine for symptom relief.
- A urine pregnancy test is negative. The patient declined a pelvic examination because she is convinced this is a urinary tract infection.
- Is a urinalysis helpful in the initial diagnostic workup for this patient? Is a urine culture needed? Is any additional testing indicated?

CASE 3

A 25-year-old woman calls your urgent care clinic asking to review her lab results…

- She presented to your clinic 2 days ago for vaginal discharge. The clinician who saw her had the patient self-swab for a molecular vaginitis and STI panels.
- Her results are negative for chlamydia, gonorrhea, *Trichomonas, Atopobium, Megasphaera*, bacterial vaginosis-associated bacteria, and *Candida glabrata* and *Candida krusei*. She has low positive results for *Gardnerella vaginalis, Candida albicans*, and *Ureaplasma hominis*.
- Should you treat for *Gardnerella, Candida*, and *Ureaplasma*? How do you distinguish normal flora from pathogen? Do the patient's history or physical examination alter your treatment plan?

CASE 4

A 30-year-old man presents to the urgent care with concern that he has pneumonia…

- He states that his 5-year-old son was seen by the pediatrician yesterday and diagnosed with "walking pneumonia." He requests a "pneumonia test" for himself.
- He reports a runny nose, low-grade fever, chest congestion, and cough for the past 2 days.
- He does not appear to be in any acute distress, and there are no adventitious lung sounds.
- What test(s) for atypical pneumonia, if any, should be performed? Are empiric antibiotics without testing appropriate?

Introduction

Diagnostic testing is an important tool for the urgent care (UC) clinician, as it can provide rapid diagnosis, guide treatment decisions, help to prevent unnecessary treatment, and offer reassurance to patients. Advances in technology have expanded the Clinical Laboratory Improvement Amendments (CLIA)-waived point-of-care (POC) testing options, making many test results available before patient discharge, which in turn can lead to improved clinical decision making and patient satisfaction.[1] At the same time, social media influence and access to medical information online have resulted in patient expectations for rapid testing and treatment, even when testing may not be clinically indicated.

Clinicians' knowledge gaps on best practices for diagnostic test selection and interpretation can result in inappropriate testing, ambiguous results, and poor care.[2] There are important but subtle nuances to the interpretation of test results. Test results are not necessarily binary: a positive result does not always indicate pathological disease, while a negative result does not always rule out disease. UC clinicians who

understand the strengths and limitations of various diagnostic tests can be more judicious in their test selection, which can result in improvements in clinical decision making, patient care, antibiotic stewardship, and cost management.[3]

This issue of *Evidence-Based Urgent Care* provides an overview of commonly available diagnostic tests for respiratory and genitourinary complaints—2 of the most frequent reasons patients visit UC clinics. Industry data show that COVID-19 and other respiratory complaints account for more than 30% of urgent care visits.[4] While data on genitourinary complaints in urgent care are limited, these conditions represented 13.3% of emergency department visits in 2022, up from 12.7% in 2017.[5] This issue offers a framework for approaching these presentations, including initial test selection guided by history and physical examination findings, follow-up testing when needed, and key insights for interpreting diagnostic results. This approach can help UC clinicians optimize their use of diagnostic testing and more effectively manage these common presenting conditions.

■ Select Abbreviations

CDC United States Centers for Disease Control and Prevention
CLIA Clinical Laboratory Improvement Amendments
FDA United States Food and Drug Administration
GAS Group A *Streptococcus*
HSV Herpes simplex virus
IDSA Infectious Diseases Society of America
NAAT Nucleic acid amplification test
PCR Polymerase chain reaction
PPM Provider-Performed Microscopy
POC Point of care
RADT Rapid antigen detection test
RIDT Rapid influenza diagnostic test
RST Rapid strep test
RSV Respiratory syncytial virus
RTI Respiratory tract infection
RT-PCR Reverse transcriptase polymerase chain reaction
STI Sexually transmitted infection
UC Urgent care
UTI Urinary tract infection

■ Etiology and Pathophysiology

Respiratory Tract Infections

Respiratory tract infections (RTIs) are most commonly caused by viruses such as adenovirus, rhinovirus, influenza, coronavirus (both COVID-19 and non–COVID-19 variants), and respiratory syncytial virus (RSV).[6] Bacterial etiologies include pathogens such as *Streptococcus pyogenes, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*, and *Mycoplasma pneumoniae*.[7] The vast majority of RTIs are spread through droplets, which are often transmitted by sneezing or coughing.[8] These infections can cause a wide range of symptoms, from mild viral upper respiratory infections (ie, common cold) to influenza-like illnesses to severe respiratory distress.

Genitourinary Conditions

Common genitourinary conditions include urinary tract infections (UTIs), sexually transmitted infections (STIs), and vaginitis in females. Uncomplicated UTIs typically occur when bacteria in the gastrointestinal tract travel through the urethra and into the bladder, with *Escherichia coli* responsible for the majority of infections.[9] Occasionally, infections can travel from the bladder through the ureters into the kidney, causing pyelonephritis. STIs can be caused by viruses, bacteria, or parasites. The most common STIs tested for in the UC include *Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis*, and herpes simplex virus.[10] Atypical bacteria that can cause nongonococcal urethritis include *Ureaplasma urealyticum, Ureaplasma parvum*, and *Mycoplasma genitalium*.[11] Finally, nonsexually transmitted vaginitis is often caused by bacterial vaginosis or vaginal candidiasis. Both of these conditions result from an imbalance of the normal vaginal flora.[12] While bacterial vaginosis is not currently classified as an STI, research suggests that unprotected sexual intercourse may play a greater role in the pathophysiology of bacterial vaginosis than previously thought.[13]

■ Differential Diagnosis

Respiratory Tract Infections

RTIs may be more broadly categorized into upper respiratory infections (URIs) and lower respiratory infections. **(See Table 1, page 10.)** Many viruses and bacteria can cause some or all of these conditions **(Table 2, page 10)**, and concomitant infections with 2 or more pathogens are not uncommon. Respiratory viruses and bacteria detected on testing are not necessarily pathologic, as they may be colonized, nonpathologic, or residual from a recent infection.

A primary role of the UC clinician is to determine if the patient is clinically stable enough for discharge home or if care needs to be escalated. A thorough history and physical examination, appropriate diagnostic testing, and clinical gestalt are all vital in identifying the more concerning diagnoses with high rates of morbidity and mortality amidst the plethora of lower-acuity respiratory conditions.

Genitourinary Conditions

Genitourinary conditions can be broadly classified into cystitis, urethritis, and vaginitis. Associated

differential diagnoses and pathogens to consider when evaluating patients with genitourinary complaints are listed in **Tables 3 and 4,** respectively.

■ Urgent Care Evaluation

A focused but thorough history and review of systems provide important information during the initial evaluation of both respiratory and genitourinary complaints and are vital for judicious selection of diagnostic testing and treatment.

History

Respiratory Tract Infections

For respiratory complaints, onset and duration of symptoms and known recent exposures to other individuals with positive results will help to determine which tests should be ordered (if any) and whether prophylactic treatment is needed. Past medical history and an updated medications list are also important, as certain medications are risk stratified to patients with 1 or more comorbidities, and drug interactions or renal dysfunction will also affect the treatment course. The UC clinician should also inquire about red flag signs and symptoms, which will typically need a more extensive workup; for respiratory infections, these may include dyspnea, tachypnea, cyanosis, hypoxia, chest pain, and altered mental status. **Table 5 on page 11** lists examples of important questions that will help guide clinical decision-making.

Genitourinary Conditions

Understanding the etiology and transmission of various genitourinary pathogens is important to efficiently and effectively obtain the history of present illness. It is essential to ask the patient about previous similar symptoms, diagnoses, and treatments to help identify recurrent infections, possible resistance patterns, and the efficacy of previous treatments, which will further guide diagnostic and therapeutic decisions.

Table 1. Differential Diagnosis of Respiratory Tract Infections

Upper Respiratory Tract Infections
- Sinusitis
- Otitis media
- Pharyngitis

Complications of Upper Respiratory Tract Infection
- Periorbital and orbital cellulitis
- Tympanic membrane rupture
- Meningitis
- Peritonsillar abscess
- Retropharyngeal abscess
- Lemierre syndrome

Lower Respiratory Tract Infections
- Pneumonia
- Atypical pneumonia

Complications of Lower Respiratory Tract Infection
- Respiratory distress
- Pleural effusions (exudative)
- Lung abscess

Noninfectious Conditions With Overlapping Symptoms:
- Asthma
- Chronic obstructive pulmonary disease
- Transudative pleural effusions
- Pneumothorax
- Cardiac dysfunction
- Anxiety and panic disorders

Table 2. Common Pathogens Associated With Respiratory Tract Infections

Viruses
- Influenza virus
- Coronavirus (including COVID-19)
- Respiratory syncytial virus
- Adenovirus
- Rhinovirus
- Parainfluenza virus
- Human metapneumovirus
- Enterovirus
- Epstein-Barr virus
- Cytomegalovirus
- Coxsackievirus
- Parvovirus
- Avian flu
- Middle East Respiratory Syndrome

Bacteria
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Klebsiella pneumoniae*
- *Fusobacterium necrophorum*
- *Staphylococcus aureus*
- *Streptococcus pyogenes*
- *Legionella pneumophila*
- *Pseudomonas aeruginosa*
- *Moraxella catarrhalis*
- *Bordatella pertussis*

Table 3. Differential Diagnosis of Genitourinary Complaints

- Renal calculi (obstructive or nonobstructive)
- Hydronephrosis
- Pyelonephritis
- Pelvic inflammatory disease
- Urosepsis
- Pregnancy complications
- Interstitial cystitis
- Overactive bladder
- Atrophic vaginitis
- Benign prostatic hyperplasia
- Prostatitis
- Balanitis
- Testicular torsion
- Epididymitis
- Varicocele
- Hydrocele
- Inguinal hernia
- Gastrointestinal etiologies (appendicitis, diverticulitis, mesenteric ischemia)

Table 4. Pathogens Associated With Common Genitourinary Conditions

Cystitis
- *Escherichia coli*
- *Enterococcus faecalis/faecium*
- *Pseudomonas aeruginosa*
- *Klebsiella oxytoca*
- *Enterobacter cloacae/aerogenes*
- *Staphylococcus saprophyticus/aureus*
- *Serratia marcescens*
- *Proteus mirabilis/vulgaris*
- *Citrobacter freundii*
- *Morganella morganii*
- *Acinetobacter baumannii*

Vaginitis/Urethritis
- Bacterial vaginosis-associated bacteria (*Gardnerella vaginalis, Atopobium vaginae, Mobiluncus* spp, *Megasphaera*)
- *Chlamydia trachomatis*
- *Neisseria gonorrhoeae*
- *Trichomonas vaginalis*
- Herpes simplex virus 1 and 2
- *Candida* spp
- *Atopobium vaginae*
- *Ureaplasma* spp
- *Mycoplasma* spp
- *Haemophilus ducreyi*
- *Treponema pallidum*
- Monkeypox

Table 6 on page 12 provides a summary of important questions to consider when evaluating a patient with genitourinary complaints.

Physical Examination

Respiratory Tract Infections

Respiratory symptoms are a staple of UC visits, and clinicians must be well prepared to thoroughly and efficiently perform an appropriate physical examination. With practice, a routine examination will become second nature and can even be performed while obtaining part of the history.

The physical examination begins as soon as the clinician meets the patient, and a general evaluation can be performed quickly by assessing the overall appearance of the patient and taking immediate note of any acute distress. Examination of the head, eyes, ears, nose, and throat should follow, as otitis media, conjunctivitis, rhinorrhea, and pharyngitis are common findings with URIs. **(See Table 1, page 10.)** A check for lymphadenopathy should be performed, particularly focusing on the lymph nodes in the head and neck. A clavicular lymph node examination is quick and easy to perform and may elucidate a malignant process masquerading as a respiratory infection with fever, fatigue, night sweats, and chills. A cardiac and pulmonary examination is also crucial, particularly with lower respiratory symptoms, and findings can range from normal to murmurs, rhonchi, rales, and wheezing. Other body systems may also be examined and should be considered if the clinical presentation and history warrant it. **Table 7 on page 13** summarizes key components of the physical examination for respiratory complaints.

Genitourinary Conditions

The genitourinary examination should begin with a general assessment of the patient. For example, renal colic presents with a distinctive appearance that is often recognizable immediately upon entering the examination room: patients are typically hunched over on the examination table or constantly shifting positions in an unsuccessful attempt to find relief.[15] Testicular or ovarian torsion patients present with pain that is out of proportion to physical examination findings.[16] A patient with pelvic inflammatory disease or pyelonephritis may be visibly uncomfortable.

Following the general assessment, the abdominal examination should be performed, including evaluation for suprapubic and costovertebral angle tenderness to palpation. No further examination abdominal examination is necessary unless warranted by the clinical history and presentation. An external pelvic examination, speculum examination, or testicular examination must be performed in patients who may have a pathology such as testicular torsion, ovarian torsion, pelvic inflammatory disease, and endometritis.

Table 5. Suggested History of Present Illness Questions for Patients Presenting With Respiratory Complaints

Question	Considerations
Are your symptoms improving, worsening, or just not going away?	• If improving and symptom duration is consistent with a resolving URI, the patient may just need reassurance • Worsening symptoms after days 5-7 of symptom onset may indicate a secondary bacterial infection[14]
Have you had complete or near-complete resolution of symptoms just prior to a sudden worsening of symptoms?	• If yes, consider a new infection vs a secondary bacterial infection • The patient may need to be retested
Did you receive a vaccination in the past 3 days?	• Influenza-like symptoms may occur within the first 24 hours after vaccination due to the body's immune response and may last for a few days
Do you have a recurrent history of similar symptoms?	• Recurrent otitis media or streptococcal pharyngitis may warrant referral to an otolaryngologist • Consider seasonal allergic rhinitis if the occurrence pattern is similar each year • Ask about asthma or COPD exacerbations
Do you have any history of smoking, vaping, or inhaled recreational drug use?	• Patients with this history are more prone to pulmonary infections and complications • Consider EVALI in your differential diagnosis
Have you been out of the country recently?	• Broaden your differential and utilize CDC traveler resources to identify endemic pathogens when appropriate
Have you used any medications for your symptoms? If so, have they been helping?	• Prolonged use of oxymetazoline can cause rhinitis medicamentosa • If the patient has been using albuterol without any relief, consider causes other than bronchoconstriction • Recent antibiotic use may also cause a false negative with certain tests, such as group A strep antigen

Abbreviations: CDC, United States Centers for Disease Control and Prevention; COPD, chronic obstructive pulmonary disease; EVALI, E-cigarette or vaping-use associated lung injury; URI, upper respiratory infection.

For STIs, keep in mind that there are several important body systems to evaluate in addition to the genitourinary system. For example, suspected gonococcal conjunctivitis or pharyngitis would warrant an ocular and throat examination, followed by swabbing the affected site; testing only urine, urethral, or vaginal samples may miss isolated infections at other sites. Reactive arthritis caused by an STI can present with conjunctivitis and joint involvement. **Table 8 on page 13** summarizes key components of the physical examination for genitourinary complaints.

■ Diagnostic Studies

Diagnostic studies, which include point-of-care (POC) testing performed on-site as well as send-out testing, are crucial tools for the UC clinician to assist in making an accurate and timely diagnosis. Benefits of on-site testing include improved patient experience and compliance, more cost-effective care, and allowing the clinician to immediately incorporate test results into clinical decision making.[17] Advances in technology have expanded POC testing options and improved accuracy, efficiency, reliability, and cost. POC testing offers the advantage of delivering quick results, often in 30 minutes or less, allowing the clinician to view and discuss results with patients prior to discharge.[18] This is especially important for high-risk conditions such as STIs for which a patient can be treated prior to discharge, limiting the risk of loss to follow-up care.[19]

The ease and availability of diagnostic laboratory testing options cany lead to overordering and unnecessary testing. Clinicians may overorder tests for several reasons: fear of missing a diagnosis, concerns about malpractice liability, insufficient knowledge or confidence in clinical decision-making, stories about unexpected findings from previous tests, and pressure to meet patient expectations.[22] However, unnecessary testing is not benign. Overordering tests can lead to false negative and false positive results, increasing the likelihood that patients receive unnecessary treatments or additional workup. This increases the cost burden to the patient and healthcare costs, contributes to patient anxiety,

Table 6. Suggested History of Present Illness Questions for Patients Presenting With Genitourinary Complaints

Question	Considerations
When was your last menstrual period?	• Document consideration of urine pregnancy test if not performed • Consider postmenopausal diagnoses if warranted
Have you had any dysuria, hematuria, frequency, urgency, or urinary odor?	• Typical symptoms of a urinary tract infection
Have you had any vaginal discharge, itching, odor, or discomfort?	• Common symptoms of vaginitis
Have you had any difficulty stopping or starting urination, weak urinary stream, sensation of incomplete voiding, or incontinence?	• Common symptoms of benign prostatic hyperplasia
Have you had any painless or painful lesions or ulcers on the skin?	• If yes, evaluate for various infectious etiologies such as syphilis, herpes, and *Haemophilus ducreyi*
Do you have a recurrent history of similar symptoms?	• Referral may be warranted for consideration of differential diagnoses such as urinary retention, incontinence, atrophic vaginitis, incontinence, or other conditions related to anatomical abnormalities
Have you had any fever, dizziness, body aches, back pain, nausea, or vomiting?	• Systemic symptoms are typically associated with more serious conditions and complications
Have you had any recent exposures to STIs? Has there been any receptive oral or anal sex?	• Positive exposures can help guide initial diagnostic testing and treatment • Consider pharyngeal or rectal swabs as needed
Have you taken antibiotics or other medications recently?	• Recent antibiotic use can be associated with vaginal candidiasis • Consider nephrotoxicity for certain medications • Understand that some medications will likely affect the urinalysis • SGLT2 inhibitors will likely result in glycosuria and an increased risk of vaginal candidiasis[20]
Are you on a carbohydrate-restricted diet?	• A "keto diet" or other carbohydrate-restricted diet may result in increased ketonuria
Has there been any recent trauma or foreign bodies to or near the area of discomfort?	• If yes, expand the differential to include diagnoses such as testicular contusion, abdominal trauma, and foreign bodies • Consider nonaccidental trauma
Ask a family member if there has been any acute change in mental status.	• In elderly patients, an acute change in mentation should include a UTI workup[21]

Abbreviations: SGLT2, sodium-glucose cotransporter 2; STI, sexually transmitted infection; UTI, urinary tract infection.

and can create malpractice risk. Diagnostic testing is most beneficial when the clinical diagnosis is uncertain or if the clinician needs to differentiate between pathologies that present with overlapping symptoms.[23]

Characteristics of Diagnostic Tests

Sensitivity and specificity measure a particular test's ability to rule in or rule out disease.[24] *Sensitivity* is the percentage of patients who have disease that will have a positive test (positive in disease), whereas *specificity* is the percentage of patients who test negative and do not have disease (negative in health). While sensitivity and specificity are important test characteristics to consider when choosing testing, the predictive value is more clinically relevant. Positive predictive value (PPV) is the likelihood that a positive test predicts the presence of disease, and negative predictive value (NPV) is the likelihood that a negative test rules out disease.[25]

CLIA Certificates and Provider Performed Microscopy

The most common types of CLIA certificates used in UC are CLIA-waived tests, CLIA-moderate complexity tests, and Provider-Performed Microscopy (PPM) procedures. See **Table 9 on page 14** for examples of tests performed under each of these certificate types. CLIA-waived tests are simple and low-risk tests that do not require special training to perform and require minimal interpretation;[26] examples include urine pregnancy tests, strep antigen tests, and glucometers. Most UC centers utilize CLIA-waived tests.[27] Some UC centers may utilize moderate complexity tests, which require the facility to complete the proper instrument validation process, develop quality assurance protocols, and undergo periodic on-site inspections. A PPM certificate allows clinicians to perform 9 different moderate complexity microscopic tests in an office setting.[28] The most common PPM-allowed test, wet prep/potassium hydroxide preparation, has historically been used to evaluate for vaginitis. Because the Amsel criteria (which include presence of clue cells on wet mount microscopy) for the diagnosis of bacterial vaginitis and wet prep for the diagnosis of trichomoniasis have largely been replaced by molecular testing, most UC centers no longer use microscopes.[29]

The classification of tests as CLIA waived or moderate complexity is determined by the complexity and the risk of error associated with each test and is specific to each test system, not just the test type in general (eg, molecular testing for *Neisseria gonorrhoeae* and chlamydia may be CLIA moderate complexity or CLIA waived, depending on the manufacturer). **Table 9 on page 14** also highlights common tests in each of the CLIA-certificate categories most often utilized in UC.

Direct Detection Versus Serology Testing

Diagnostic tests for infectious diseases can be categorized as either direct detection (ie, methods that look for evidence of the pathogen in the sample) or serology testing. Direct detection methods include visualization (eg, wet prep for *Trichomonas*), culture, antigen tests, and molecular tests. Antigen tests detect protein associated with an infectious agent, whereas molecular tests detect pathogen

Table 7. Key Components of a Physical Examination for Respiratory Illnesses

Area	Components
Vitals	Blood pressure, heart rate, respiratory rate, temperature, oxygen saturation
General	Hygiene, dress, posture, demeanor, alertness, orientation, cognition, discomfort
Head	Sinus tenderness to palpation (low sensitivity/specificity)
Eyes	Visual acuity, pupil size, pupillary response to direct and consensual light reaction, extraocular movements, conjunctival injection, discharge
Ears	Auricle, ear canal, tympanic membrane
Nose	Nasal mucosa/turbinates, rhinorrhea, epistaxis
Throat	Lips, oral mucosa, tongue, hard and soft palate, posterior pharynx, tonsils
Neck	Lymphadenopathy (cervical, occipital, submandibular, submental, clavicular nodes)
Heart	Rate, rhythm, murmurs, rubs, gallop
Lungs	Respiratory distress, dyspnea, rhonchi, wheezing, crackles, decreased/absent breath sounds

Table 8. Key Components of a Physical Examination for Genitourinary Complaints

Area	Components
General	Hygiene, dress, posture, demeanor, alertness, orientation, cognition, discomfort
Eyes	Pupil size, pupillary direct and consensual reaction to light, conjunctival injection, discharge
Throat	Lips, oral mucosa, tongue, hard and soft palate, posterior pharynx, tonsils
Neck	Lymphadenopathy (cervical, occipital, submandibular, submental, clavicular nodes)
Heart	Rate, rhythm, murmurs, rubs, gallops
Lungs	Respiratory distress, rhonchi, wheezing, crackles, decreased/absent breath sounds
Abdomen	Abdominal tenderness to palpation, costovertebral tenderness to palpation, suprapubic tenderness to palpation
Genitourinary (female)	External examination, speculum examination, bimanual examination
Genitourinary (male)	External examination, prostate examination

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nucleic acid (DNA or RNA). **(See Figure 1.)** Serology testing involves analyzing host serum to look for an immunological response to infection, including antibodies or biomarkers.

Historically, culture has been the gold standard for pathogen detection, but culture-based methods for pathogen detection are costly, time-consuming, labor-intensive, and require skilled personnel to perform each step of the test.[30] In addition, some pathogens are difficult to grow in traditional culture media; fastidious pathogens such as *Mycoplasma* require special cultures and may take weeks to grow. Advances in molecular testing technology have allowed molecular testing to replace cultures as the preferred test for several disease states.

Antigen tests are CLIA waived and deliver fast results at a low cost; as a result, they are commonly used in UC centers. Molecular tests use a variety of techniques to amplify nucleic acid, including polymerase chain reaction (PCR) and isothermal nucleic acid amplification. These tests are highly sensitive and have higher analytic sensitivity as compared to antigen tests.[31] The higher analytic sensitivity of molecular tests allows for earlier detection of disease compared to antigen tests, which have lower analytic sensitivity. However, this higher analytic sensitivity may result in positive test results during the postinfectious period when the patient is clinically improved and no longer contagious.[32] While molecular tests are more sensitive and more specific than antigen tests, the costs and availability of antigen tests sustain their essential role in UC diagnostic testing.[33]

Table 9. Clinical Laboratory Tests Commonly Performed in Urgent Care

Certificate Type	Examples
CLIA-waived (low risk of error) tests	• Blood glucose (glucometer) • Urine pregnancy test • Urinalysis • Antigen testing for strep, influenza, COVID-19, RSV • Tests waived by the FDA from January 2000 to present
Non–CLIA-waived[a] (moderate complexity) tests	• Complete blood count[b] • Blood chemistries[b] • Thyroid function tests • Antibody serology testing
PPM tests	• Wet prep • KOH prep • Pinworm examination • Fern test • Urine microscopy • Semen analysis • Fecal leukocyte examination

Abbreviations: CLIA, Clinical Laboratory Improvement Amendments; FDA, United States Food and Drug Administration; KOH, potassium hydroxide; PPM, provider-performed microscopy; RSV, respiratory syncytial virus.

[a]Any test that is not CLIA waived, specifically test systems that require more steps, training, reagents or materials, calibration, and/or have higher risk of errors

[b]There are CLIA-waived platforms for complete blood count and blood chemistries.

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Diagnostic Test Utilization

Despite technological advances, no diagnostic test is "perfect" (ie, 100% sensitive, 100% specific, able to deliver instant results, noninvasive, easy to use, low cost, and widely available). Every testing platform has strengths and weaknesses. Clinicians should familiarize themselves with the tests that are available in their clinic,[34] which will help them to determine when to order tests and how to interpret results (ie, predictive value).[26] Before ordering any test, clinicians should ask themselves if the test result will change clinical management or improve the patient outcome.[35,36] **Figure 2 on page 15** illustrates a systematic approach to diagnostic test utilization.

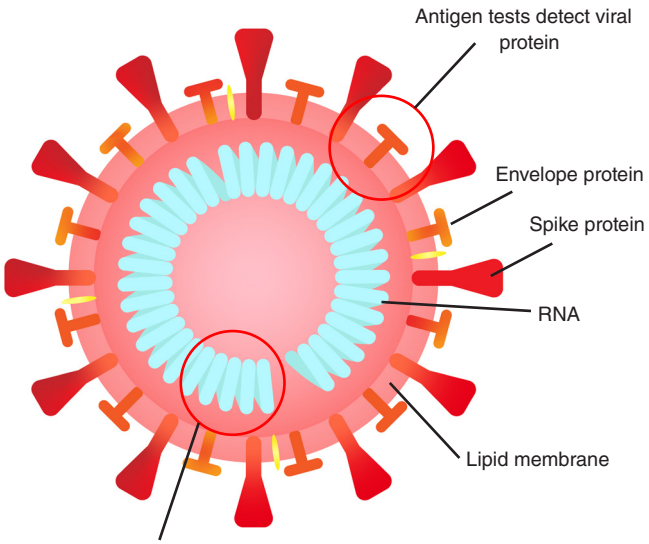
Diagnostic Tests for Respiratory Tract Infections

Common RTIs for which diagnostic testing may indicated in the UC setting include streptococcal pharyngitis, influenza, COVID-19, respiratory syncytial virus (RSV), and *M pneumoniae*. **(See Table 10, page 16.)**

Streptococcal Pharyngitis

Streptococcal (or "strep") pharyngitis accounts for 5% to 15% of pharyngitis cases in adults and 15% to 30% of cases in children. There is considerable variability worldwide in expert recommendation in regard to

Figure 1. Viral Structures Showing Target Sites for Antigen and Molecular Testing



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testing and treatment.[37,38] The 2012 guidelines from the Infectious Diseases Society of America (IDSA) no longer recommend empiric treatment; instead, testing is recommended only for patients at higher risk for strep pharyngitis, with antibiotic administration deferred until confirmation by testing.[39] This recommendation is reflected in both the Health Effectiveness and Data Information Set - National Committee Quality Assurance (HEDIS-NCQA) and Merit Incentive Pay System (MIPS) quality metrics, which track the percentage of cases among patients aged ≥3 years in which the patient received a group A *Streptococcus* (GAS) test, was diagnosed with pharyngitis, and was prescribed an antibiotic.[40,41] Because it is impossible to differentiate between strep pharyngitis and non-strep pharyngitis on clinical examination alone, the IDSA recommends testing to support the diagnosis unless overt viral features are present.[36,39]

The historic gold standard for the diagnosis of streptococcal pharyngitis is microbial culture.[30] However, cultures require up to 48 hours for results, so are rarely used as an initial POC test in the urgent care setting. Most UC clinics use an antigen or molecular test for initial strep testing.

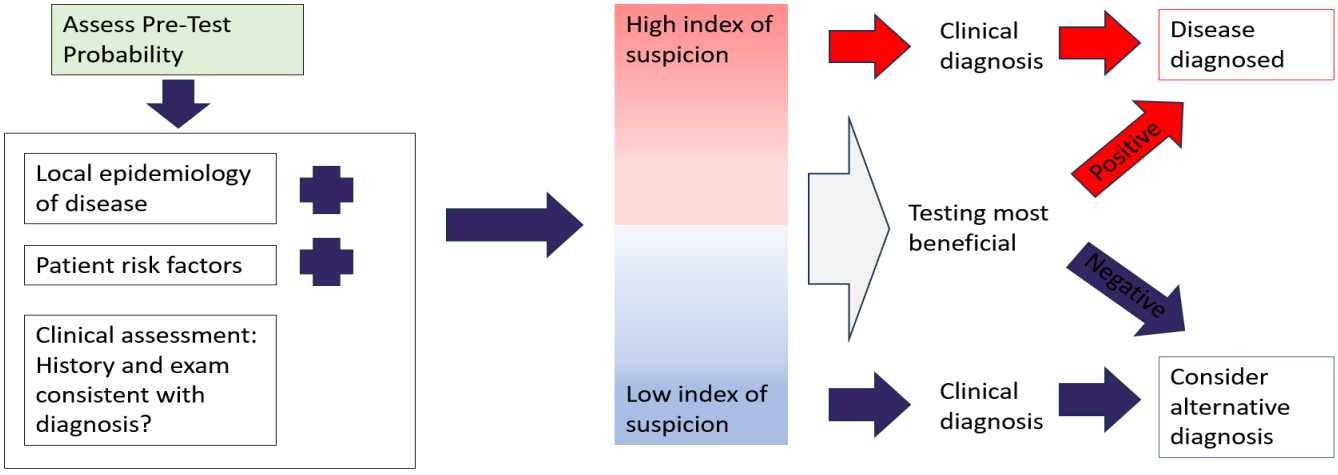
Antigen testing, also known as RST (rapid strep testing) or strep RADT (rapid antigen diagnostic testing), is widely used in clinics for the diagnosis of group A streptococcal pharyngitis. While antigen RST has the lowest costs, fast results, and a specificity >95%, it has a lower sensitivity as compared to a molecular test or culture. A positive test identifies the presence of GAS and confirmation testing is not needed. However, a negative test may not exclude strep. For most adults, a negative RST is sufficient and confirmation testing is not necessary. For children aged 3 to 18 years and special populations (ie, adults who have a history of rheumatic fever and patients who are from an area where rheumatic fever is endemic), confirmation testing after a negative antigen test is recommended by the American Academy of Pediatrics, the United States Centers for Disease Control and Prevention (CDC), and most procedure manuals.[30,42,43] The IDSA states that routine testing for GAS in patients aged <3 years is not indicated.[39] Molecular testing offers high sensitivity; therefore, confirmation testing is not necessary.[44]

Clinicians should be aware that up to 20% of school-aged children may be asymptomatic carriers of GAS. Neither antigen nor molecular testing can differentiate between invasive streptococcal disease or carrier state. Therefore, IDSA does not recommend strep testing if there are overt signs of a viral infection, as a positive strep test is more likely to detect noninvasive strep than invasive disease. Additionally, GAS is very rare among patients aged <3 years. Therefore, the negative predictive value of a negative strep antigen test is high, and confirmation testing is not generally advised.[30] Home strep tests are not commercially available at this time.

Influenza and COVID-19

Historically, influenza was primarily a clinical diagnosis due to the limited sensitivity of antigen-based tests, and patients were often treated empirically even if there was not a positive test result. However, since the emergence of COVID-19, diagnostic testing has become increasingly important. It is critical to distinguish between influenza and COVID-19 because each illness has distinct treatment protocols and management recommendations. It is not possible to differentiate between COVID-19 and influenza infections clinically. **(See Table 11, page 17.)** There are individual tests for influenza A+B and COVID-19, as well as multiplex testing (ie, testing for 2 or more pathogens) that includes both influenza A+B and COVID-19. Both antigen and molecular platforms are

Figure 2. Clinical Decision-Making Framework for Diagnostic Testing



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available as POC testing and home testing.

Because nucleic acid fragments may remain present for days to weeks, molecular testing may be positive for COVID-19 for weeks to months,[45] and for influenza for up to 7 to 10 days. Molecular tests are not recommended to clear a patient to return to work or to demonstrate noncontagium. A test of cure is unnecessary, and clearance should follow validated clinical recommendations.[46]

Influenza Antigen Test

In 2017, the United States Food and Drug Administration (FDA) required influenza antigen tests to meet minimum criteria for sensitivity and specificity. Compared to reverse transcriptase polymerase chain reaction (RT-PCR), FDA-cleared rapid influenza diagnostic tests (RIDTs) must achieve 80% sensitivity and 95% specificity for detection of influenza A and B viruses. Even so, the predictive values vary considerably depending on the level of influenza activity. False positives may occur when the influenza prevalence is low, generally at the beginning and end of flu season. More importantly, false negatives are more likely to occur when the prevalence of influenza is high. Therefore, both the clinical presentation and local influenza activity are important factors when considering whether to order a test and how to interpret its result.

Influenza antigen tests require higher viral loads for detection and false negative tests may occur early in disease onset. If a patient who has clinical symptoms consistent with influenza tests positive on an antigen test, disease is likely, and no further testing is needed. It is important to remember that the sensitivity of antigen tests is lower in the first few days of illness. A high-risk patient with a high pretest probability who tests negative should receive empiric treatment rather than waiting for additional confirmation testing.[47] Reflex testing to a molecular platform may still be considered in a high-risk patient to differentiate between COVID-19 and influenza.[31,48,49]

COVID-19 Antigen Test

COVID-19 antigen tests also require higher viral loads for detection and false negative results may occur. Because a single antigen test does not always rule out disease, the FDA and CDC recommend serial antigen tests when there is clinical suspicion of COVID-19. For symptomatic individuals, a single negative antigen test should be confirmed with a molecular test or repeat antigen test after 48 hours. For asymptomatic individuals, the FDA recommends 3 antigen tests, each 48 hours apart.

Respiratory Syncytial Virus

The viral load in RSV infections is age dependent. Children aged <4 years and infants will have high viral loads compared to older children and adults, so some RSV antigen tests are only validated for children and infants. RSV is a self-limited disease with mild symptoms for healthy adults and older children. There is no specific outpatient antiviral treatment for RSV and test results do not change management, so

Table 10. Diagnostic Laboratory Tests for Common Respiratory Tract Infections

Suspected Diagnosis	Testing Method	Advantages	Disadvantages
Streptococcal pharyngitis	Antigen (RST or strep RADT)	• Lowest cost • Fast results	• Negative tests in children require confirmation testing
	Molecular testing	• No confirmation testing needed	• Higher costs relative to antigen test • May require reader
Influenza	Antigen (RIDT)	• Fast results	• Low sensitivity
	Molecular testing	• High sensitivity/specificity	• Higher cost relative to antigen test • May require reader
COVID-19	Antigen	• Lowest cost • Fast results	• False negatives early on in disease course
	Molecular	• High sensitivity/specificity	• Higher cost relative to antigen test • May require reader
RSV	Antigen	• May only be validated for patients aged <6 years and >60 years	• Viral load may be insufficient for detection especially in older children and adults
	Molecular	• Preferred testing for all ages	• Results do not change clinical outcomes or management for most patients
Mycoplasma pneumoniae infection	Molecular (nasopharyngeal swab)	• Much easier to perform than sputum culture	• Cannot differentiate between self-limited tracheobronchitis versus pneumonia

Abbreviations: RADT, rapid antigen detection test; RIDT, rapid influenza diagnostic test; RST, rapid strep test; RSV, respiratory syncytial virus.

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routine testing does not change outcomes in most patients. Routine RSV testing is not recommended.[50] The American Academy of Pediatrics recommends RSV testing for neonates aged <6 weeks with severe disease.[51] Testing may be considered in high-risk patients, including infants, elderly individuals, or immunocompromised individuals. In these circumstances, a positive test result may influence treatment decisions such as initiating ribavirin, activating isolation precautions in hospitals or long-term care facilities, and offering monoclonal antibody prophylaxis for asymptomatic high-risk close contacts.

CLIA-waived POC RSV antigen tests should not be used for testing in adults aged <60 years and older children. Viral loads and shedding are lower in these populations, so RSV antigen tests will have poor sensitivity and performance. If there is a specific situation in which RSV testing is warranted in adults, molecular testing is the preferred test.[52]

Mycoplasma pneumoniae

Historically, laboratory diagnosis of *M pneumoniae* has been challenging. Many molecular platforms include *M pneumoniae* as a target on their respiratory panels, and some platforms allow clinicians to specifically test for *M pneumoniae* alone. Detection of *M pneumoniae* cannot differentiate between a self-limited RTI versus pneumonia. Clinical correlation is necessary.[53] Cultures are time-consuming because the bacteria grow slowly, making them impractical for guiding immediate treatment decisions. Serological tests are problematic. Antibodies may take several days or longer to develop, and testing too early in the disease course may result in false negatives. Cross-reactivity with antibodies from other infections may lead to false-positive serology results. With advances in molecular technology, nucleic acid amplification tests (NAATs) are now the test of choice.

The most common manifestation of *M pneumoniae* infection is tracheobronchitis. These infections are mild, self-limited, and do not require antibiotics. Less commonly, *M pneumoniae* may cause pneumonia, which can be serious and require hospitalization. Clinical literature shows that *M pneumoniae* accounts for 10% to 30% of community-acquired pneumonia.[54]

Testing for *M pneumoniae* should be reserved for specific clinical situations (eg, patients with signs and symptoms of severe pneumonia, during outbreaks in schools or nursing homes, or in immunocompromised patients). Testing may also be beneficial for patients who are being treated with antibiotics for community-acquired pneumonia.[55] Testing is not recommended for patients with mild upper respiratory disease.

Diagnostic Tests for Urinary Tract Infections

Cystitis, commonly referred to as a UTI, may be either uncomplicated or complicated. The IDSA released new UTI classifications in July 2025, defining an uncomplicated UTI as an "infection confined to the bladder in afebrile women or men" and a complicated UTI as an "infection beyond the bladder in women and men" (including patients with pyelonephritis, febrile or bacteremic UTI, and catheter-associated UTI).[56] Guidelines published by the American College of Obstetricians and Gynecologists in 2025 recommend against routine urine cultures for healthy nonpregnant women with typical symptoms of uncomplicated UTI. The diagnosis can be made clinically, and testing via urinalysis or dipstick may be used to support the diagnosis but is optional. Urine cultures should be reserved for pregnant women, patients with complicated or recurrent UTIs, immunocompromised patients, patients who fail initial therapy, patients with symptoms that are atypical, or situations in which antibiotic resistance is a concern.[57,58]

A urine culture, also known as a culture and sensitivity test, has traditionally been the confirmatory test for UTIs, providing the name of the pathogen(s) as well as a minimum inhibitory concentration for common antibiotics. The sensitivity report allows for the detection of antibiotic-resistant bacteria and the selection of the most appropriate antibiotic. Urine cultures provide a preliminary report at 24 hours, with either "no growth" or a gram stain result. Final reports can take 48 hours or more. Commercial laboratories have developed molecular UTI panels that promote quicker turnaround times, identification of fastidious bacteria, and genetic resistance

Table 11. Symptom Comparison Among COVID-19, Influenza, and Streptococcal Pharyngitis*

Symptom	COVID-19	Influenza	Streptococcal Pharyngitis
Fever/chills	Common	Common (may be afebrile)	Common
Cough	Common	Common	Uncommon
Shortness of breath/dyspnea	Common	Common	Uncommon
Fatigue	Common	Common	Common
Sore throat	Common	Common	Common
Runny nose/congestion	Common	Common	Uncommon
Myalgias/body aches	Common	Common	Common
Headache	Common	Common	Common
Diarrhea	Common	More common in children than adults	Uncommon
Loss of taste and smell	Common	Uncommon	Uncommon

*Due to symptom overlap, testing may be needed to differentiate between diagnoses.

markers. The primary advantage of these tests is that the turnaround can be <24 hours. However, molecular UTI panels have several disadvantages. There is currently no standardized resistance gene marker for nitrofurantoin, a first-line treatment for cystitis. Additionally, when multiple organisms are detected, molecular tests cannot determine which resistance gene belongs to which pathogen. Molecular assays are extremely sensitive and can detect trace amounts of DNA or RNA, including residual genetic material from noninfectious organisms, prior infections, or environmental contamination, which may lead to false-positive results. They can also identify pathogens that are known colonizers rather than true causes of UTI symptoms (eg, group B *Streptococcus*, *Lactobacillus, Ureaplasma*, or *Mycoplasma*), potentially resulting in overtreatment if clinicians are not trained to interpret the results. For these reasons, molecular UTI panels are not recommended except under the guidance of a specialist.

Diagnostic Tests for Vaginitis and Sexually Transmitted Infections

Historically, wet preparation (or "wet prep") was used to identify bacterial vaginosis, vaginal candidiasis, and trichomoniasis. Wet prep is inexpensive and provides immediate results but also requires a PPM waiver and clinician training for proper interpretation. At best, utilization of the Amsel criteria for bacterial vaginosis achieves only 80% sensitivity with skilled clinicians, and many UC clinicians have lower sensitivities due to low volumes of tests. With improved technology, NAATs are now preferred for diagnosis of bacterial vaginosis, vaginal candidiasis, and trichomoniasis.[29] The downsides of NAATs are overdiagnosis, cost, and lack of outcomes data, especially in patients with asymptomatic bacterial vaginosis.[59] Patients who have recurrent or persistent bacterial vaginosis symptoms need re-evaluation. Unfortunately, there are limited data regarding optimal management strategies for women with persistent or recurrent bacterial vaginosis, and specialty consultation is recommended.

A NAAT is preferred for diagnosis of gonorrhea and chlamydia. For male patients, first-void urine (often referred to as "dirty urine") is preferred over urethral swabs.[60] Ideally, for a first-void urine, patients should not have urinated for 1 to 2 hours prior to specimen collection.[61] Studies have shown that in female patients, a patient-collected lower vaginal swab is superior to a clinician-performed endocervical swab for the detection of gonorrhea and chlamydia.[62-64] A urine sample may be considered in female patients, but the sensitivity is lower than for a vaginal sample, and a vaginal swab is preferred.[65] NAAT for oropharyngeal and rectal sites are advised in individuals that engage in receptive oral or anal intercourse.[66]

Testing for HIV and syphilis should be considered for any patient who is at risk for STIs. Women with bacterial vaginosis should be assessed for HIV and other STIs based on their individual risk factors, as bacterial vaginosis can increase susceptibility to these infections.[67] Risk factors that warrant screening include new or multiple sexual partners, history of prior STIs, age <25 years, and high-risk sexual behaviors. The fourth-generation HIV test includes immunoglobulin G/immunoglobulin M testing for HIV-1 and HIV-2, as well as the p24 antigen.[68,69] This allows for detection of HIV disease in as few as 18 days after exposure. Current guidance recommends that syphilis testing utilize a 3-step testing algorithm (rapid plasma reagin, titer, then confirmatory test).[70] Repeat testing is recommended if initial tests are negative and there is continued clinical suspicion.[71]

Patients may present to UC clinics to request herpes simplex virus (HSV) testing. Serological antibody testing for HSV is not recommended due to the prevalence of positive antibodies in the general population. In the United States, up to 16% of adults will test positive for antibodies for HSV-2 and 66% of adults will test positive for antibodies for HSV-1.[72,73] A positive test for HSV antibodies does not mean that a patient will develop herpetic lesions. An NAAT for HSV-1 and HSV-2 may be performed, but only if the patient has a skin lesion with vesicular fluid that may be swabbed.

Mycoplasma and *Ureaplasma* are considered secondary pathogens, and testing should be reserved for select cases rather than routine screening. Common species include *M genitalium, M hominis, U urealyticum*, and *U parvum*. These bacteria are difficult to grow and require special procedures and media; thus, NAATs are preferred.[11] In the urgent care setting, testing for these organisms is generally not appropriate as part of the first-line evaluation for dysuria, urethritis, or cervicitis. Instead, testing should be considered only in patients with persistent or recurrent symptoms after standard testing and treatment for more common causes such as *Chlamydia trachomatis, Neisseria gonorrhoeae*, and *Trichomonas vaginalis*. Up to 80% of sexually active, asymptomatic females have *Ureaplasma* spp and 50% have *M hominis* as part of their normal vaginal flora.[74] Current guidelines do not recommend routine testing for asymptomatic individuals.[75]

Antimicrobial resistance is a growing concern with *M genitalium*. Macrolide resistance, particularly to azithromycin, is now common and associated with treatment failures. Prevalence of genetic markers indicating resistance to macrolides ranges from 44% to 90%. Fluoroquinolone resistance is also emerging, further limiting options. As a result, the CDC recommends resistance-guided therapy when available.[76] In settings without access to resistance testing, a 2-stage approach is often used: initial treatment with doxycycline to reduce bacterial load,

followed by moxifloxacin for definitive therapy if symptoms persist.

Molecular testing panels or cultures may report the presence of *Lactobacillus* and group B *Streptococcus agalactiae*. Positive results do not necessarily correlate with infection: *Lactobacillus* is a common colonizer in the vaginal microbiome, and group B strep is a colonizer of the intestine, vagina, and rectum of healthy women.[77]

Multiplex Testing

Multiplex testing is becoming more common. The multiplex test most commonly used in UC is an influenza A/influenza B/COVID-19 combination. One major advantage of multiplex testing is that multiple targets can be tested using a single swab. Multiplex tests can detect common respiratory pathogens including adenovirus, rhinovirus, human metapneumovirus, and parainfluenza virus.[78] Confirming viral etiology via testing may reduce inappropriate antibiotic use, as patients may be more agreeable to avoiding antibiotics if a clinician can definitively tell a patient they have a viral illness. Standard multiplex panels can detect >20 pathogens and gene resistance markers.[79] The downsides of multiplex testing include high cost and the possibility of detecting a colonized organism or nonpathological nucleic acid fragments. The patient responsibility for a standard URI or UTI panel can easily exceed $500 in the United States. In 2023, the median cost of multiplex testing for outpatient UTIs was >70 times higher than the median cost of a urine culture ($585 vs $8).[80] Patients with high deductible insurance plans or an insurance policy that does not cover multiplex testing may receive an unexpectedly large bill. In addition, it is not feasible to test for every possible viral etiology, so a negative multiplex test may not deliver a conclusive answer.

Treatment

Respiratory Tract Infections

The majority of respiratory tract infections are caused by viral pathogens and are self-limited illnesses requiring only supportive care.[81,82] Studies have shown that despite public education campaigns, clinician education, and patient counseling, inappropriate antibiotic use remains problematic.[83-85] Even when viral pathology is identified through testing, patients may still ask for and receive antibiotics. Due to increased patient awareness, patients often present to UC centers requesting antiviral therapy for influenza and COVID-19. There are currently 4 FDA-approved treatment regimens for influenza and 1 FDA-approved oral treatment for COVID-19.

Influenza

For healthy individuals and low-risk patients, influenza is generally a self-limited disease. In this patient population, antiviral therapy for influenza may reduce duration of illness by up to 1 day if started within 48 hours of onset of symptoms. Available antivirals used to treat influenza in the United States include oseltamivir, baloxavir, zanamivir, and peramivir.[86] A systematic review and meta-analysis of 15 randomized trials found that oseltamivir, the most commonly prescribed influenza antiviral, did not significantly reduce hospitalization risk in older patients or in patients considered high risk for hospitalization and was associated with increased gastrointestinal side effects.[87] However, antivirals are recommended as soon as possible for patients who are at increased risk for complications, including young children, patients aged ≥65 years, patients with comorbid conditions (ie, asthma, diabetes, heart disease), and immunocompromised, chemotherapy, and transplant patients, even if 48 hours have elapsed.[88-90]

COVID-19

Nirmatrelvir/ritonavir is an oral antiviral agent that has activity against SARS-COV-2. The benefit of nirmatrelvir/ritonavir is risk reduction for progression to severe disease requiring hospitalization. Adults and children aged ≥12 years who are at high risk for progression to severe disease, including patients aged >65 years, with immunodeficiencies, or with a transplant history, are advised to start nirmatrelvir/ritonavir within 5 days of symptoms onset.[91] It is important to check medication interactions when prescribing nirmatrelvir/ritonavir,[92] as there are numerous drug interactions, including but not limited to statins, anti-arrhythmics, anticoagulants, benzodiazepines, and antipsychotics. Patients with a creatinine clearance <60 mL/min will require dose adjustments, and nirmatrelvir/ritonavir is contraindicated if creatinine clearance is <30 mL/min.

Streptococcal Pharyngitis

GAS pharyngitis is generally a self-limited disease with a resolution of 7 to 10 days without antibiotic treatment. The potential benefits of antibiotic treatment for GAS pharyngitis are a shortened duration of symptoms, prevention of suppurative and nonsuppurative complications, and decreased risk of transmission to family members and close contacts. A 2021 Cochrane study showed that treatment with antibiotics reduces symptoms at day 3 as compared to management without antibiotics, but both treated and untreated patients were symptom free by day 7. Treatment with antibiotics modestly decreases the risk of suppurative complications such as peritonsillar abscess, cervical lymphadenitis, and mastoiditis.[93] The prevention of rheumatic fever is the primary goal of treatment. Treatment with antibiotics reduces contagium. A patient is considered noncontagious after 24 hours of taking an antibiotic, whereas without treatment, they may be contagious for up to 2 to 3 weeks.

Preferred treatment is oral penicillin or amoxicillin for 10 days. In patients with non–immunoglobulin E (IgE)-mediated allergic reactions, cephalosporins are recommended. For patients with a history of significant IgE-mediated allergic reactions including anaphylaxis, macrolide antibiotics (azithromycin, clarithromycin, or erythromycin) or lincosamides (clindamycin) are recommended.[42] With the exception of very rare infections, antibiotics have no proven benefit for treatment of acute pharyngitis due to organisms other than GAS.[39] Notably, infections with group C and group G streptococci are self-limited and do not require antibiotic treatment.

If a throat culture is ordered, it should only be reported as positive if GAS (*Streptococcus pyogenes*) is identified. Other organisms such as *S pneumoniae, Haemophilus influenzae*, and *Moraxella catarrhalis* are considered part of the normal oropharyngeal flora and are not clinically significant.

If a multiplex molecular panel is ordered, only clinically relevant pathogens (ie, GAS) should be interpreted as potential pathogens. Detection of other respiratory organisms should be interpreted with caution and correlated with clinical findings, as these may represent colonization rather than true infection.

Mycoplasma pneumoniae

Most infections caused by *M pneumoniae* are mild and self-limited, resolving without antibiotic treatment. *M pneumoniae* may cause a mild tracheobronchial infection or, less commonly, progress to pneumonia. Detection of *M pneumoniae* in nasopharyngeal tissue alone cannot differentiate between RTI and pneumonia. If a patient has clinical signs of pneumonia, further evaluation with a chest x-ray and complete blood count can be helpful to determine the appropriate course of management. Patients with a positive test for *M pneumoniae* should only be treated with antibiotics (eg, macrolides, tetracycline, or fluoroquinolones) if there are clinical signs and diagnostic tests consistent with pneumonia.[94]

Genitourinary Infections

Vaginitis

Treatment for vaginitis is directed towards the cause. Symptomatic vaginal yeast infection secondary to *C albicans* is treated with vaginal antifungal creams such as 1-, 3- or 7-day courses of miconazole or oral antifungal agents such as fluconazole. *C glabrata* and *C krusei* have a high rate of resistance to fluconazole,[95,96] so alternative treatments such as boric acid suppositories may be necessary. Symptomatic bacterial vaginosis is treated with vaginal or oral antibiotics. Initial treatment is with oral metronidazole 500 mg orally twice a day for 7 days, or with metronidazole 0.75% gel or clindamycin 2% cream applied intravaginally.

Gonorrhea and Chlamydia

The preferred treatment for chlamydia is doxycycline 100 mg orally twice a day for 7 days. The preferred treatment for gonorrhea is ceftriaxone 500 mg administered intramuscularly for patients <150 kg, and 1 g administered intramuscularly for patients ≥150 kg.[97] Due to higher rates of treatment failure, a test of cure performed 7 to 14 days after treatment is recommended by the CDC for pharyngeal infections, with a preference closer to the 14-day mark, as testing at 7 days has a higher risk for false-positive results due to the detection of residual DNA fragments.

Mycoplasma genitalium

Treatment for symptomatic *M genitalium* infection is dependent on the availability of resistance testing. If resistance testing is not available, patients should be treated with doxycycline 100 mg orally twice a day for 7 days, followed by moxifloxacin 400 mg orally once a day for days 8 to 14. If resistance testing is available, it can help guide treatment. For the bacteria are sensitive to macrolides, the dosage is doxycycline 100 mg orally twice a day for 7 days, followed by azithromycin 1 g orally on day 8, followed by 500 mg orally once daily on days 9 through 11. For macrolide-resistant bacteria, doxycycline is prescribed 100 mg orally twice a day for 7 days followed by moxifloxacin 400 mg orally once a day for 7 days.[75] The evidence is unclear whether or not treatment of asymptomatic sexual partners who test positive reduces partner reinfection risk. Nevertheless, sexual partners of patients with symptomatic *M genitalium* infection can be tested, and those with a positive test can be treated.[76]

■ Disposition

If testing is diagnostic and appropriate treatment is initiated, no further follow-up is required. Complications of viral RTIs include secondary bacterial infections such as pneumonia. Patients with viral RTIs who present with worsening symptoms or persistent symptoms after 10 days should be instructed to return to the clinic for re-evaluation for secondary bacterial infections. Routine test of cure is not recommended for the patient if symptoms are resolved or improving. Molecular platforms may detect nucleic fragments days, weeks, or months after the infection has cleared and the patient is noncontagious. However, test of cure may be necessary for conditions that have a high rate of treatment failure. For STIs, test of cure is recommended for oropharyngeal chlamydia or gonorrhea but is not necessary for rectal or cervical/

urethral disease unless therapeutic adherence is in question, symptoms do not resolve, or reinfection is suspected. Test of cure for chlamydia should not be performed until 4 weeks after completion of therapy due to the risk of false-positive results.[10]

■ Special Populations

High-Risk Patients

High-risk individuals with comorbidities that increase the risk for complications of severe disease or who have direct patient contact may benefit from molecular testing if available. If antigen testing is initially used, confirmation testing may be beneficial for epidemiological purposes and to guide isolation protocols in nursing homes, rehabilitation facilities, prisons, or hospitals.

Cross-reactivity With Rheumatological Conditions

Patients with rheumatoid or autoimmune disease may produce markers that react with antibodies used in rapid antigen tests. Specifically, there is evidence that rheumatoid factor may cause persistent false positive COVID-19 antigen tests.[45] Since testing is usually performed in patients who are symptomatic, false positive results may not be recognized clinically.

Age-Dependent Testing

Because prevalence and incidence of certain RTIs are age dependent, testing recommendations and indications may be different for the pediatric population.

■ Controversies and Cutting Edge

Molecular Testing Versus Antigen Testing

While the sensitivity of molecular tests is higher than that of antigen tests, there is widespread utilization of antigen tests in the UC setting. This is due to the ease of use, portability, and relative cost savings that an antigen test offers. Antigen tests also have a better turnaround time compared with molecular tests, which can have an effect on throughput and workflow. Most of the antigen tests currently available have a turnaround time of ≤15 minutes compared to molecular tests, which have a turnaround time between 20 to 36 minutes. UC clinicians should be cognizant of clinical situations in which the antigen test is never appropriate (ie, RSV antigen testing in age groups for which testing is not validated), when a negative antigen test needs confirmation (ie, strep testing in children), and when an antigen test does not need confirmation (ie, strep testing in patients aged ≥19 years). Clinicians should also be aware that a negative antigen test in a patient with a high pretest probability may be a false negative. Molecular testing platforms are relatively more costly compared to antigen tests, and these platforms may not be universally available in all ambulatory clinics.

Because molecular assays are highly sensitive to nucleic acid contamination, cross-contamination in POC molecular testing can occur from specimen handling errors, poor operator technique, or environmental contamination. Even trace amounts of nucleic acid (eg, DNA) from surfaces or prior runs can cause false-positive results. Collected swabs placed on a counter in the bathroom or examination room can contaminate surfaces and cause false positive downstream readings. To minimize this risk, clinical staff must adhere to manufacturer-recommended cleaning protocols, change gloves, disinfect surfaces between samples, and implement a unidirectional workflow from clean to contaminated areas.

Clinics performing POC molecular testing should also conduct regular quality control and environmental monitoring. Although waived devices generally carry a lower risk of contamination as compared with moderate-complexity systems, the risk is not zero, making ongoing staff training and competency assessment essential.

In-House Molecular Testing

The first CLIA-waived PCR test became available in 2015.[27] Since then, molecular testing capabilities have greatly expanded and have become more accessible to UC clinics. Additionally, the public became more aware of PCR testing during the COVID-19 pandemic. While the costs of PCR tests have become more affordable, they remain more expensive than antigen tests. From a business standpoint, UC clinics must consider costs and reimbursements when selecting in-house diagnostic tests. Each clinic must negotiate their own contracts with insurance companies, as the payor mix of fee-for-service contracts, global contracts, case rate contracts, and percentage of self-pay patients greatly affect the bottom line. If a UC clinic has a high percentage of global and case rate contracts, it may lose money if the cost of molecular tests exceeds the fixed payment amount negotiated in the contract. UC clinics that see a higher percentage of fee-for-service patients tend to be reimbursed better for molecular tests. Even though the cost per test is higher for molecular tests compared to antigen tests, the reimbursement rate tends to be higher. It is essential to closely monitor the cost per test and reimbursement rates per contract, as the reimbursement for some insurances may be lower than the actual cost of the test. Furthermore, with fee-for-service contracts, UC clinics must be careful to identify which tests the insurance companies deem "investigational," which would leave the billed cost as patient responsibility.

Moderate- and high-complexity tests require a CLIA certificate of compliance, which comes with higher fees, more stringent lab director requirements, and periodic laboratory inspections. While this would

expand the in-house testing capabilities of the clinic and potentially increase the quality of patient care, the financial component prohibits many clinics from offering these tests. A clinic must have the right payor mix, sufficient reimbursement from insurance companies, and a high enough volume to financially justify a more robust diagnostic selection of tests. If a certain test is not profitable or not available, clinicians who want to order that test will send it out to a reference laboratory. The reference laboratory negotiates their own contracts with insurance companies, and the test itself is cost neutral to the UC clinic. However, if patient expectations are not met regarding cost, this could result in negative repercussions when the patient contacts the clinic upset about their bill, as they could blame the clinician for ordering an expensive test. The decision to bring molecular testing in-house should be subject to ongoing discussion and evaluation among clinicians and key decision makers, as the cost per test and reimbursement rates change frequently.

Management of Bacterial Vaginosis

An open-label, randomized controlled trial conducted between 2019 and 2023 demonstrated that the treatment of male partners significantly decreased the rate of recurrence in patients diagnosed with bacterial vaginosis. The trial was stopped early after 150 couples completed the 12-week follow-up because nontreatment of partners (previously standard care) was found to be inferior.[98] Research regarding screening, testing, and treatment of bacterial vaginosis is ongoing.

Molecular Testing Detection of Resistance Patterns

Newer molecular platforms are being developed to look for gene sequences that are associated with antibiotic resistance. For example, next-generation gonorrhea testing will identify the gyrA mutation that indicates gonorrhea that is susceptible to fluoroquinolones. Not all antibiotic resistance mechanisms are directly linked to identifiable resistance genes, which limits the scope of molecular testing in identification of resistance.

Host-Based Diagnostic Testing

Host-based diagnostics utilize biomarkers to identify immune responses. Algorithms can predict whether an infection is more likely to be bacterial or viral. The potential applications for host-based diagnostic testing are huge. Currently, there are several regulatory-cleared platforms that use machine-learned algorithms to differentiate between bacterial and viral infections.

Syndromic Multiplex Testing for Antibiotic Stewardship

Literature supports the theory that multiplex panels may improve timely treatment and reduce unnecessary antibiotics. Respiratory multiplex PCR testing increases timely antiviral prescriptions for influenza, particularly because of the short window for efficacy of antiviral treatment. Patient educational interventions and clinician training when implementing multiplex PCR panels may be useful in improving antibiotic stewardship, as clinicians and patients may be less likely to prescribe and take an antibiotic if a virus is identified and multiplex PCR panels are interpreted appropriately.[99] Conversely, inappropriate testing and interpretation can also increase unnecessary antibiotic prescriptions, particularly if identified normal flora are treated as pathogens. This is important, as inappropriate antibiotic use contributes to increased antimicrobial resistance, drug interactions, and medication side effects (eg, nausea, vomiting, diarrhea, *Clostridioides difficile* infections, rash, tendon injury, hepatotoxicity, renal injury, and anaphylaxis). Currently, there is insufficient evidence to determine whether multiplex PCR testing by itself decreases antibiotic utilization, and further studies are needed.

Nonlaboratory Diagnostics Utilizing Artificial Intelligence

Research is ongoing to determine whether artificial intelligence (AI) platforms are able to screen or diagnose respiratory infections without the use of laboratory testing. Specific applications include the use of AI to analyze photos of the pharynx to diagnose strep pharyngitis, or breath sounds to differentiate between lower respiratory infections. While initial results show promise, further research and validation are needed.

■ Summary

Diagnostic testing is vital for ambulatory UC centers and their day-to-day operations. Diagnostic testing, especially POC tests, allows for quick diagnosis, which is crucial for timely treatment and patient care. Due to the time and expense of validating testing platforms, UC clinicians are beholden to the platforms the clinic uses. Therefore, it is important to know when to use the tests that are available, as well as recognize the pitfalls that may lead to misdiagnosis.

The concept of "right test, right patient, right time" emphasizes the importance of diagnostic stewardship. Because no test is perfect, it is the clinician's responsibility to be aware of the testing platforms in their clinic, the limitations of the tests, and proper utilization. Unnecessary testing may lead to misinformation either in the form of overdiagnosis or missed diagnosis.

Patients may demand testing because they want

reassurance, and clinicians may acquiesce to these demands because they fear a missed diagnosis or medicolegal implications. The clinician must determine whether ordering a test compromises the quality of care or even increase risk of harm to the patient.

While sensitivity and specificity define the accuracy of diagnostic testing, highly accurate tests may still lead to false negative and positive results. A common pitfall is testing too early in disease. Patients who are not properly counseled may have false reassurance, which may lead to disease spread, delayed diagnosis, and delayed treatment. Another common pitfall is failure to recognize that testing may not be able to differentiate between colonization and an invasive organism that is causing disease.

Diagnostic testing is a process that requires the clinician to obtain a careful history and perform a diagnostic examination. Once the pretest probability is assessed, testing is chosen to rule in or rule out disease process. This framework helps modify the probabilities of the working diagnosis and ultimately will help the clinician make the most appropriate diagnosis.

■ Time- and Cost-Effective Strategies

- Avoid diagnostic tests that do not have any bearing on clinical management.
- Develop patient-friendly algorithms and instructions for interpreting initial test results.
- Recognize the diagnostic test window for your tests. Molecular testing may offer an earlier diagnostic window but may also remain positive during the postinfectious period.

■ References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the author, are noted by an asterisk (*) next to the number of the reference.

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5 Things That Will Change Your Practice

1. All patients aged 3 to 18 years with a negative rapid strep test should have confirmatory GAS testing.
2. Females with bacterial vaginosis should be evaluated for HIV and other STIs based on their risk factors.
3. A test of cure for pharyngeal gonorrhea should be performed 14 days after treatment.
4. Avoid treating *S pneumoniae, M catarrhalis*, and *H influenzae* identified on a URI or pharyngitis PCR panel when there is a clear viral etiology and no symptoms of bacterial infection.
5. Avoid routine testing for *Ureaplasma* and *Mycoplasma* in patients with genitourinary symptoms. Testing for these pathogens should only be performed in cases with persistent genitourinary symptoms after more common etiologies have been evaluated such as UTI, bacterial vaginosis, vaginal candidiasis, gonorrhea, chlamydia, or *Trichomonas*.

Risk Management Pitfalls for Laboratory Testing in Urgent Care

1. **"URI panels are great and should always be used! I can check for more than 20 viruses and bacteria at the same time!"** Avoid the "spray and pray" approach. Does the testing change clinical outcomes? If a test result does not change your clinical decision making, the test may not be necessary.

2. **"I am going to choose PCR testing over antigen testing every chance I get."** While molecular testing is more sensitive, antigen tests are still useful. Antigen tests are generally more cost-effective and more likely to be available as a POC test. Additionally, antigen testing is more useful than molecular testing in the convalescent phase, as molecular testing can be persistently positive for several weeks.

3. **"If it looks like strep and the rapid antigen test is negative, I typically go ahead and treat with antibiotics while waiting for the throat culture results."** The IDSA and CDC recommend against empiric treatment, stating that antibiotics should be prescribed for strep pharyngitis only if there is a positive test. It is not possible to clinically differentiate GAS pharyngitis from viral pharyngitis based solely on the history and physical examination.

4. **"I don't typically order GAS confirmatory testing when the rapid antigen test is negative, unless the patient or parent requests it."** Per the CDC, confirmatory testing is recommended if the antigen strep test is negative in patients aged 3 and 18 years.

5. **"A patient with a negative antigen test for COVID-19 and flu after the first 48 hours of symptoms does not need further molecular testing."** Confirmation molecular testing should not be used routinely but may be appropriate in special circumstances or high-risk individuals.

6. **"If a bacteria shows up on a diagnostic test, it should be treated with an antibiotic."** Be aware of clinical situations where bacteria are colonized and antibiotic treatment is not indicated. For throat cultures, *S pneumoniae, M catarrhalis*, and *H influenzae* are usually considered normal respiratory flora and do not need treatment, especially if there is a viral pathogen that is detected. *Ureaplasma* is a common colonizer in healthy, sexually active females. Do not test for or treat bacterial vaginosis-associated bacteria if there are no associated symptoms.

7. **"A urinalysis and urine culture should be ordered on every patient with UTI symptoms."** If a patient has recently taken phenazopyridine and their urine is a reddish-orange color, a urinalysis should not be performed, as the results will be unreliable. Phenazopyridine will not affect urine culture results. Female patients who are not pregnant and present with a classic, uncomplicated cystitis may be treated empirically with or without a confirmatory urine culture. A urine culture should be ordered for patients with complicated cystitis.

8. **"Knowing which *Candida* species is unnecessary, because all *Candida* species can be treated with fluconazole."** *C glabrata* and *C krusei* may be a cause of persistent *Candida* vaginitis and may not respond to fluconazole.

9. **"If a patient has a UTI panel that shows a common UTI pathogen (eg, *E coli, Klebsiella, Proteus*) and *Ureaplasma* spp, both should be treated."** Recognize *Ureaplasma* as normal flora and avoid treating asymptomatic patients and symptomatic patients when there is another clear pathogen present.

Case Conclusions

CASE 1

For the 15-year-old boy with sore throat, fever, nasal congestion, cough, and fatigue for 2 days…

You recalled that there are numerous viral pathogens that can cause the exact same symptoms as strep. The patient and his mother were not aware of any recent strep exposures. Since the rapid strep test was negative and the patient's age was between 3 and 18 years, you explained that the correct course of action would be to obtain a confirmatory test for group A strep; if the POC test had been a negative molecular strep test, then no further testing would have been necessary. You notified mom that results of a molecular test for group A strep would most likely be back in the morning, while a group A strep culture would take at least 2 days for a result. The mom and patient were fine with holding off on antibiotics pending the test results, and using ibuprofen and acetaminophen in the meantime.

The next morning, the molecular group A strep test returned negative, and the patient was told to manage his symptoms as a viral infection. However, his mother called back 2 days later, stating that she took her son to another testing center for a multiplex panel to determine the pathogen causing his symptoms. The multiplex panel was positive for high levels of rhinovirus, moderate levels of *Moraxella catarrhalis*, and low levels of *Streptococcus pneumoniae* and *Haemophilus influenzae*. You explained to her that rhinovirus was the most likely cause of the patient's symptoms, as *M catarrhalis, S pneumoniae*, and *H influenzae* are common nasopharyngeal colonizers that do not need to be treated when there is clear evidence of a viral pathogen, particularly when there are no signs or symptoms consistent with bacterial sinusitis, otitis media, or pneumonia.[100-103] When she asked why those bacteria showed up on the lab report, you explained that multiplex PCR panels provide a positive or negative result for every virus or bacteria on the panel; the results must be interpreted by a clinician to determine what is most likely a pathogen and what is most likely a colonizer. You further explained that with a traditional throat culture, these bacteria would be designated on the lab report as "normal respiratory flora." The patient treated his viral pharyngitis conservatively and made a full recovery within 1 week.

CASE 2

For the 25-year-old female with urinary frequency and urgency…

Your clinical staff performed a urinalysis, and the results were as follows:

- Glucose: 3+
- Bilirubin: 2+
- Ketones: 3+
- Blood: 3+
- pH: 6.0
- Protein: 2+
- Urobilinogen: 3+
- Nitrites: 2+
- Leukocyte esterase: 3+
- SG: 1.030
- Color: Orange

You recalled that this patient had presented to UC multiple times for a urinary tract infection, yet previous culture results did not identify pathological bacteria. The timeline of infections raised suspicion that her symptoms could be related to sexual activity with her new partner. You considered performing confirmation urine testing, but recognized that the clinical presentation was not consistent with an UTI. Given the history, your differential diagnosis included vaginitis and STI. You discussed this with the patient and also informed her that phenazopyridine can interfere with the urinalysis results, rendering the result uninterpretable. She consented to a pelvic examination for further evaluation. On examination, you noticed a malodorous greenish discharge with friable vaginal tissue. A vaginitis molecular test was positive for *Trichomonas*, negative for gonorrhea, and negative for chlamydia.

You prescribed metronidazole 500 mg orally twice a day for 7 days, resulting in resolution of symptoms. A urine culture obtained at the visit returned negative for pathological bacteria.

Case Conclusions

CASE 3

For the 25-year-old female who called the UC to review lab results…

You recalled that *Ureaplasma* is likely nonpathologic; while bacterial vaginosis and *Candida* may present as coinfection, it is possible that the presence of these pathogens is nonpathologic. You reviewed her chart and noted that no examination was documented. You advised the patient to return to the clinic for re-evaluation and to review her history. You explained to her that without a complete history and physical examination, the results were uninterpretable. Upon further evaluation and discussion, the patient stated that she recently completed a course of antibiotics and noticed thick, white, nonodorous vaginal discharge and itching. You explained that, while *Gardnerella vaginalis* can cause bacterial vaginosis, it is also part of the normal vaginal flora, and bacterial vaginosis occurs when the microbiome of the vagina is altered or unbalanced, resulting in overgrowth of normal flora such as *Gardnerella, Megasphaera, Atopobium*, and other bacterial vaginosis-associated bacteria. You counseled her that treatment is not warranted unless there are signs of bacterial vaginosis, as positive test results only indicate that there are normal vaginal flora present at the time of testing; taken alone, these results are insufficient to determine pathogenicity. You also explained that *Ureaplasma* is often found as normal vaginal flora in healthy, sexually active females and does not need treatment unless there are genitourinary symptoms present that are not better explained by another pathogen.[74] You prescribed intravaginal miconazole for 7 days, and the patient reported symptom improvement in a few days.

CASE 4

For the 30-year-old man who presented to the UC concerned about pneumonia…

You engaged in shared decision making by informing the patient that there are several different options regarding testing and treatment. You explained that *M pneumoniae* is the most common cause of "walking pneumonia," also known as atypical pneumonia, and that most cases of pneumonia caused by *M pneumoniae* are associated with mild symptoms that resolve without antibiotics, though a 5-day course of azithromycin can hasten recovery.[94] You informed him that pneumonia symptoms include fever, body aches, night sweats, chills, and productive cough but could be more mild. You discussed that a standard workup for pneumonia includes vital signs, physical examination, and chest x-ray. Because the patient presents with mild symptoms, you told him that a full workup was not necessary. Furthermore, you discussed that antibiotic therapy is not needed for upper respiratory symptoms even if caused by *M pneumoniae*.[104,105]

Regarding testing, you told the patient that testing directly for *M pneumoniae* using a molecular test was an option, but the test would be unable to differentiate between a self-limited tracheobronchitis and pneumonia, and again emphasized that his symptoms could also be viral. You discouraged empiric treatment with azithromycin at that point, summarizing the risk of side effects and briefly touching on antibiotic resistance and stewardship. After discussion, the patient agreed that his symptoms were mild and stated that he did not want to take antibiotics if they were not needed. He declined testing. The patient continued to treat his symptoms with over-the-counter medications and was fully recovered 1 week later.

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Coding & Charting: What You Need to Know

Documenting a respiratory tract infection (RTI) or genitourinary illness that requires laboratory testing for proper diagnosis and management ensures that patients receive high-quality care while maintaining defensible documentation for both clinical and reimbursement purposes. In addition to the patient's history and physical examination findings, documentation of any laboratory testing should include patient identifiers, test orders with clinical indications, specimen details including date and time of collection, interpreted results, and actions taken.

Determining the Level of Service

The level of service is determined from 3 factors based on medical decision making: (1) the nature of the problems addressed; (2) the complexity of data reviewed; and (3) the risk of patient management. At least 2 of these must meet or exceed the requirements of the 4 levels of medical decision making: straightforward, low, moderate, and high. **(See Box 1 on page 32.)**

Number and Complexity of Problems Addressed

A typical *acute, uncomplicated illness* is expected to resolve with conservative treatment. These illnesses carry a low risk of morbidity. However, even an uncomplicated presentation can require laboratory evaluation if the result of the testing affects treatment. Laboratory evaluation of an acute presentation can be classified as a more complex condition depending on patient presentation, symptom severity, and red flag features.

Complexity of Data

The *complexity of data* element refers to the information the provider reviews and analyzes, such as medical records, tests, and reports from other providers or sources. Each distinct lab test ordered or reviewed, including those within a panel, contributes to the data complexity if it has a separate CPT code or provides unique information. However, clinicians should consider whether a specific test and/or its result will change clinical management or improve the patient's outcome, rather than focusing on the billing and reimbursement aspect. Urgent care clinicians should be familiar with the tests that are available in their clinic, as molecular testing platforms are more costly than antigen tests and the results typically take more time.

Risk of Patient Management

Risk of patient management assesses the potential for complications, morbidity, and mortality associated with the patient's condition, diagnostic procedures, and management. The complexity of the patient's presenting problem, their existing health issues, and their prognosis impact risk. If diagnostic procedures are needed, the potential risks of ordering, administering, and reviewing the results are considered.

Documentation Tips

Laboratory documentation and coding must adhere to the Health Insurance Portability and Accountability Act (HIPAA) for privacy, Clinical Laboratory Improvement Amendments (CLIA) for lab quality, and payor policies for reimbursement. Errors or omissions can result in denied claims or compliance audits.

Coding for a test of cure involves choosing CPT codes to describe the laboratory procedure and ICD-10 codes to detail the clinical reason for repeating the test. For certain sexually transmitted infections (eg, gonorrhea with resistance concerns), guidelines recommend a test of cure at specified intervals. Best practice is to base coding on the specific infection, the timing after treatment, and clinical guidelines, ensuring medical necessity is documented to support the repeat test.

Coding Challenge

By Bradley Laymon, PA-C, CPC, CEMC
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Presentation
A 13-year-old female, established patient, presents with cold and flu symptoms for the past 2 days. Mom is in the room. Mom states her daughter developed fever yesterday, with a maximum temperature of 99.7°F measured at home. Associated symptoms include cough, nasal congestion, body aches, and reduced appetite. No vomiting or diarrhea reported. Patient also denies chest pain, dyspnea, rash, or abdominal pain. No known sick contacts, recent travel, or exposure to COVID-19. No history of underlying asthma, allergies, or prior hospitalizations for respiratory illness.

PATIENT HISTORY
Past medical history: Unremarkable
Current medications: Ibuprofen, as needed for fever; last dose given this morning
Allergies: None

OBJECTIVE FINDINGS
BP: 102/68 mm Hg
HR: 87 beats/min
RR: 16 breaths/min
Temp: 98.1°F
SpO2: 97% on room air
Height: 5'2"
Weight: 110 lbs
General: Alert, nontoxic appearing. Speaking in complete sentences. No accessory muscle use.

PHYSICAL EXAMINATION
Head: Normocephalic
Eyes: PERRLA
Ears: Clear without erythema
Nose: Clear rhinorrhea with drainage
Throat: Mild erythema, no tonsillar hypertrophy or exudates, moist mucous membranes
Neck: Supple with no adenopathy
Lungs: No rhonchi, rales, or wheezing to auscultation bilaterally
Heart: Regular rate and rhythm, S1/S2 normal. No murmur, click, rub, or gallop
Skin: No rash, warm and dry

LABORATORY STUDIES
POCT COVID-19 NAAT: Negative
POCT Influenza NAAT: Positive for influenza A

IMPRESSION/PLAN
Diagnosis: Influenza A
Treatment Plan: Discussed the diagnosis with the patient and her mother. Prescribed treatment with oseltamivir phosphate 75 mg BID for 5 days. OTC medication for symptomatic relief to include ibuprofen PRN for fever >100.5°F. Encouraged the patient to increase fluids and rest. She should follow up with her pediatrician or return to our clinic if there is no improvement in 2 to 3 days. Consider emergency department evaluation for fever >102°F, rash, chest pain, dyspnea, or symptoms of dehydration.

Abbreviations: BID, twice a day; BP, blood pressure; CBC, complete blood count; HR, heart rate; NAAT, nucleic acid amplification test; OTC, over the counter; PERRLA, pupils are equal, round, and reactive to light and accommodation; POCT, point-of-care testing; PRN, as needed; RR, respiratory rate; RSV, respiratory syncytial virus; SpO2, oxygen saturation of peripheral capillaries; temp, temperature.

Consider this patient encounter using the Simplified Elements of Medical Decision Making table provided in **Box 1**, then select the appropriate E/M code for this visit.

Number and Complexity of Problems Addressed

The patient has cough, body aches, loss of appetite, and sinus congestion. She does not look ill or toxic. Her vital signs are within normal limits. This would meet the criteria for an *acute uncomplicated illness*, which is **Low, Level 3** of problems addressed.

Amount and/or Complexity of Data to be Reviewed and Analyzed

Two POCT were ordered (COVID-19 and influenza), and the results were discussed with the patient and her mother, who also acted as an independent historian by sharing details about the present illness. This meets the criteria for **Moderate, Level 4** in the Complexity of Data.

Risk of Complications and/or Morbidity or Mortality of Patient Management

The patient is positive for influenza A and is prescribed oseltamivir phosphate. This would meet the criteria for **Moderate, Level 4** risk.

ANSWER: Two of the 3 Elements of medical decision making need to be met when choosing your level of service. We successfully met **Level 4** criteria in the Complexity of Data and in the Risk category, so this is a **99214**.

Box 1. Simplified Elements of Medical Decision Making

MDM Level*	Problems Addressed	Complexity of Data	Risk of Patient Management	E/M Service Codes
Level 2: Straightforward	• Minor/self-limited	• Minimal/none	• Minimal risk of morbidity	• 99202 (new) • 99212 (established)
Level 3: Low	• ≥1 minor/self-limited problem • 1 stable chronic illness • 1 acute, uncomplicated illness • 1 acute, uncomplicated injury	At least 1 of these: • 2 data sources (eg, ordering or reviewing tests) • Independent historian	• Low risk of morbidity • Example: Over-the-counter medication management	• 99203 (new) • 99213 (established)
Level 4: Moderate	• ≥1 chronic illnesses with exacerbation/progression/treatment side effects • 1 acute, complicated injury • ≥2 stable chronic illnesses • 1 undiagnosed new problem • 1 acute illness with systemic symptoms	At least 1 of these: • 3 data sources (eg, ordering or reviewing tests); can include independent historian • Independent interpretation of test results • Discussion of management or test interpretation	• Moderate risk of morbidity • Examples: Prescription drug management; significant social determinants of health	• 99204 (new) • 99214 (established)
Level 5: High	• ≥1 chronic illnesses with **severe** exacerbation/progression/treatment side effects • Illness or injury that threatens life or bodily function	At least 2 of these: • 3 data sources (eg, ordering or reviewing tests); can include independent historian • Independent interpretation of test results • Discussion of management or test interpretation	• High risk/severe without emergent treatment	• 99205 (new) • 99215 (established)

*Level is determined by meeting or exceeding 2 out of 3 elements of medical decision making.
Abbreviations: E/M, evaluation and management; MDM, medical decision making.
Based on data from: American Medical Association. *Evaluation and Management (E/M) Services Guidelines,* 2023.

■ CME Questions

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1. **Which of the following diagnostic tests is an example of a molecular test?**
   a. Polymerase chain reaction
   b. Wet prep
   c. Urinalysis
   d. Strep antigen

2. **Which of the following statements regarding testing in the clinical setting is CORRECT?**
   a. Molecular tests are less expensive than antigen tests.
   b. Molecular tests offer earlier detection of a pathogen as compared to antigen tests.
   c. Molecular tests have a much faster turnaround time than antigen tests.
   d. Molecular tests have a lower risk of false positives than antigen tests.

3. **Which of the following is the best description of the positive predictive value of a diagnostic test?**
   a. The likelihood that a negative test rules out disease
   b. The likelihood that a positive test predicts disease
   c. The percentage of patients who test positive that have disease
   d. The percentage of patients who test positive that do not have disease

4. **What is the diagnostic test of choice for gonorrhea and chlamydia?**
   a. Wet prep
   b. Urine culture
   c. Nucleic acid amplification test (NAAT)
   d. Serology

5. **What is the recommended window of treatment for healthy, low-risk patients who test positive for influenza and are considering antiviral therapy?**
   a. Within 48 hours of symptom onset
   b. Within 72 hours of symptom onset
   c. Within 5 days of symptom onset
   d. Within 10 days of symptom onset

6. **Which of the following patients would require group A strep confirmatory testing?**
   a. A 13-year-old girl with pharyngitis and a negative group A strep antigen test
   b. A 7-year-old boy with a history of cystic fibrosis who has a positive group A strep antigen test
   c. A 47-year-old man with no significant past medical history, recent group A strep exposure, and a negative group A strep antigen test
   d. A 51-year-old woman with systemic lupus erythematosus and a negative group A strep antigen test

7. **Which of the following possible complications of group A strep is most reduced with antibiotic treatment?**
   a. Peritonsillar abscess
   b. Splenomegaly
   c. Rheumatic fever
   d. Scarlet fever

8. **Which of the following diagnostic tests should always be considered for patients at risk for sexually transmitted infections?**
   a. Fourth-generation HIV test and rapid plasma reagin
   b. HSV-1 and HSV-2 IgG
   c. NAAT for *Ureaplasma* and *Mycoplasma*
   d. NAAT for bacterial vaginosis-associated bacteria

9. **Which of the following is most often considered to be normal respiratory flora in a patient presenting with pharyngitis?**
   a. Rhinovirus
   b. Human metapneumovirus
   c. *Streptococcus pyogenes*
   d. *Streptococcus pneumoniae*

10. **A 32-year-old female patient presents with 3 days of thin, gray-white, vaginal discharge that has a fishy odor. A vaginitis panel comes back positive for *Atopobium vaginae, Gardnerella vaginalis, Streptococcus agalactiae* (group B strep), and *Ureaplasma* species. Which of the following would be considered normal flora that does not warrant immediate treatment?**
    a. *Atopobium* and *Gardnerella vaginalis*
    b. *Streptococcus agalactiae* only
    c. *Ureaplasma* species only
    d. *Streptococcus agalactiae* and *Ureaplasma* species

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