Clinical Diagnostic Tests
How to Avoid Errors in Ordering Tests and Interpreting Results

Michael Laposata, MD, PhD

Clinical Diagnostic Tests is a convenient, quick-reference guide to common errors and pitfalls in test selection and result interpretation for practitioners and trainees in all areas of clinical medicine. Authored by recognized experts and educators in laboratory medicine, it provides timely, practical guidance about what to do—and what not to do—for practitioners ordering or interpreting clinical tests. Each topic features a concise overview and summary followed by a list of bulleted "standards of care" that will enable practitioners to quickly recognize and avert a potential problem. Organized for easy access to critical information, this guide addresses all major issues practitioners are likely to encounter during their day-to-day clinical work. It is intended for practitioners in pathology, laboratory medicine, primary care as well as nurse practitioners and physician assistants. It is also a valuable resource for clinical trainees and students who need to learn effective, efficient use of the clinical lab in practice.

Key Features:
- Provides practical guidance for avoiding common errors and pitfalls in lab test selection and interpretation
- Includes overviews and recommendations for quick reference
- Written by expert educators in laboratory medicine
- Presents bulleted "standards of care"
- Serves as a concise, to-the-point teaching guide

Recommended shelving category: Laboratory Medicine

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Preface

The Institute of Medicine in the United States has recently organized a committee, of which I am a member, on diagnostic error in health care. It has become clear that major contributors to diagnostic mistakes include the incorrect selection of laboratory tests and the misinterpretation of laboratory test results. As the clinical laboratory test menu has greatly expanded in the past decade in size, complexity, and cost, the challenge of ordering the right tests, and only the right tests, and correctly interpreting complex test results, has become a significant challenge for most health care providers for a larger and larger percentage of their patients.

The idea to produce books describing medical errors related to inappropriate selection of laboratory tests and misinterpretation of laboratory test results first emerged in a discussion in a restaurant in Chicago. The first challenge was to determine whose medical errors would be reported. Would this be a compilation of medical errors reported in the literature, personally observed medical errors in the experience of an author, or admissions of unpublished mistakes by medical colleagues? Ultimately, it was decided to invite established experts in the different areas of laboratory medicine to become authors who could bring forward errors that they had read about, personally encountered, or learned from discussions with clinical and laboratory colleagues. The goal for each author was to identify and describe the most common mistakes in his or her specialty area of laboratory medicine, and then use those mistakes to create a set of “standards of care.”
that would lead to a reduction in the frequency of those errors. Six separate books were produced in the series, and they describe errors in laboratory testing for coagulation, transfusion medicine, clinical chemistry, clinical microbiology, hematology and immunology, and the often overlooked area of laboratory management. The organization of each book is similar. A major group of diagnostic errors associated with the clinical laboratory (such as those in which an abscess is mistakenly concluded to be a malignancy because of findings in the microbiology laboratory) is introduced with a brief background on that group of medical errors, followed by an actual case to illustrate this error, then a short statement that describes the clinical pitfall, and finally a list of standards of care related to, in this example, appropriate testing to minimize the number of cases mistakenly identified as abscesses that are, in fact, malignancies. After production of the last of the six books, it was recognized that removal of the case examples would allow all six books to be combined into the one clinically valuable book which follows this preface.

It is with great hope that this book, which identifies medical errors associated with laboratory testing, will be useful in the education of medical students, interns and residents in all medical fields, clinical laboratory technologists, and practicing physicians—so that they may learn from the mistakes of others and not make new mistakes of their own. If the specific errors described in this book were all reduced in frequency by more than 90%, there would be a tremendous improvement in patient outcome and a substantial reduction in the cost of health care.

Michael Laposata, MD, PhD
CHAPTER 5
Clinical Microbiology
CHARLES W. STRATTON

PREANALYTIC ERRORS IN THE CLINICAL MICROBIOLOGY LABORATORY

Clinical microbiologists are well aware of the adage first coined by computer programmers, “garbage in, garbage out,” but for their profession have renamed it “quality in, quality out.” Their adage refers to the fact that the quality of the clinical specimen received by the clinical microbiology laboratory is a key factor in the optimal use of clinical microbiology. For serological testing, the timing of the serum collection may be an equally critical factor for optimal use. Unfortunately, the clinicians often do not have the tools, interest, training, access to data, or time to determine optimal use of the clinical microbiology laboratory for their patients. This chapter discusses common preanalytic medical errors in the clinical microbiology laboratory.

FAILURE TO CONSIDER INFECTION

Failure to consider infection is actually a more common problem than one might think. It seems to center around surgical procedures where a malignancy is suspected. Thus, oncologists and surgeons must be alert and always consider the possibility of infection even when malignancy is their first concern.
Not sending material from a clinical specimen to the clinical microbiology laboratory for culture or other microbiological testing may result in this type of preanalytic medical error. This is a very subtle type of medical error and is considered an individual type of error that is not easily rectified by a systems approach. Bone marrow aspirations and biopsies are often done to rule out malignancy; cultures may not be requested on the aspirate/biopsy as the clinicians are focused on malignancy and not thinking about infection. Oncologists and surgeons must be alert and always consider the possibility of infection even when malignancy is their first concern.

For example, failure to consider infection may occur when evaluating a patient with neck mass and/or cervical lymphadenopathy in which lymphoma or metastatic carcinoma is the working diagnosis. Because lymph node biopsy is often reserved for situations in which a malignant process is suspected, the clinician may not think to order cultures. Biopsy for asymptomatic cervical lymphadenopathy of greater than three weeks’ duration is a common situation in which metastatic carcinoma is suspected, particularly in patients over 40 years of age. These enlarged cervical lymph nodes thus are usually excised or biopsied, and the lymphatic tissue is sent to the surgical pathology laboratory. If cultures are desired, the surgeon must send part of the lymphatic tissue to the clinical microbiology laboratory. Lymphatic tissue sent to the surgical pathology laboratory is fixed in formalin, which precludes additional tests such as tissue cultures when the hematoxylin and eosin (H&E) examination reveals lymphadenitis. Failure to send part of the lymphatic tissue to the clinical microbiology laboratory for culture is a particular problem in children, in whom nontuberculous cervical lymphadenopathy is more commonly seen. Infections that may present with cervical lymphadenopathy include cervical mycobacterial infections (Mycobacterium tuberculosis [MTB] and Mycobacterium avian complex), cat scratch...
disease (*Bartonella henselae*), histoplasmosis, and toxoplasmosis.

Biopsy of indeterminate mediastinal masses, which is often done in order to evaluate the mediastinal mass/lymph nodes for malignancy, presents another example. When histopathologic examination reveals no malignancy, the opportunity for culture has passed. The demonstration of microorganisms by special stains may provide the diagnosis. Tuberculosis is an unusual cause of mediastinal mass in an infant, but in contrast, histoplasmosis as a cause of mediastinal mass in an infant or in a child has been reported on many occasions. These cases of mediastinal histoplasmosis in children were sometimes mistakenly diagnosed as lymphoma. There is a significant risk for medical errors in cases involving a mediastinal mass in a child if infection is not considered.

Lung infections mimicking malignancy are another relevant presentation that is well described in the medical literature. An important reason for this is that both pulmonary infections and pulmonary malignancies are initially detected by a radiologic diagnostic procedure such as a chest radiograph x-ray or a chest computed tomography scan. Radiologic features suggestive of a pulmonary malignancy include a parenchymal mass with speculated margins, microlobulations, thick-walled cavity, cavity showing nodular margins, and chest wall invasion. These findings, however, are not specific and can be seen with pulmonary infections. If the possibility of an infection is not considered, the diagnostic procedures done may not include those measures such as culture that are necessary to detect infection. In one large series of over 2,000 patients who underwent a lung biopsy with a presumed diagnosis of malignancy, 37 (1.3%) of these cases were found to have infection rather than malignancy. Fungal infections accounted for 46% of the infections diagnosed in this series. Thus, the clinician must keep in mind the possibility of infection when initiating diagnostic procedures to confirm a presumed pulmonary malignancy.
STANDARDS OF CARE

- Failure to consider infection can result in a medical error when material from biopsy specimens is not sent to the clinical microbiology laboratory because malignancy is considered the most likely diagnosis; when the tissue turns out to not be malignant, the lack of a culture result may result in harm to the patient.
- Conversely, sending material for culture from a tissue biopsy specimen that ultimately turns out to be malignant is not considered a medical error; the culture will not grow and no harm to the patient will result.
- Oncologists and surgeons, in particular, must remember that infections are able to mimic malignancy; therefore, obtaining cultures of biopsy tissues should be carefully considered when biopsies are being done to rule out or confirm suspected cancer.

FAILURE TO CONSIDER UNCOMMON INFECTIONS

Failure to consider uncommon infections is another common medical error seen in infectious diseases and clinical microbiology. This type of error is best avoided by obtaining consultation (informal or formal) from infectious disease clinicians and/or the clinical microbiology laboratory director.

Consider the example of failure to consider an uncommon infection such as ehrlichiosis/anaplasmosis in the differential diagnosis of a febrile patient with “summer flu.” This error may, at best, delay the diagnosis of this infection, which can cause significant morbidity and mortality if not suspected and treated promptly. Recognition of ehrlichiosis/anaplasmosis as a possible diagnosis requires the treating clinician to have knowledge about tickborne illnesses, which are an emerging infectious threat. Alternatively, consultation with an infectious diseases clinician may avoid such a medical error. Serologic testing does not
usually help in the diagnosis of acute ehrlichiosis, as seroconversion may not occur until three weeks into the illness. Treatment thus should be initiated based on the clinical presentation and not based on the results of laboratory testing. A polymerase chain reaction (PCR) assay for ehrlichiosis is an alternative method for diagnosing this illness and is more likely to be positive. The availability of a PCR assay for ehrlichiosis depends on the capabilities of an individual clinical microbiology laboratory. Even if the PCR assay is available, treatment for ehrlichiosis should be initiated before the PCR result is available. Finally, making a PCR assay for ehrlichiosis available for a more rapid diagnosis may require costly upgrading of the molecular diagnostic capabilities of the clinical microbiology laboratory.

Another uncommon infection is Rocky Mountain spotted fever (RMSF), which is similar to ehrlichiosis/anaplasmosis in a number of ways. In both cases, initial failure to consider a tickborne illness in summer months can result in a delay in the diagnosis and treatment of an infection. With RMSF, a potential outcome is rickettsial meningoencephalitis resulting in death. RMSF is still the most lethal tickborne illness in the United States. Pitfalls related to the evaluation of the patient with possible RMSF include (a) waiting for the rash to develop, (b) misdiagnosing the febrile illness as another infection such as gastroenteritis, (c) discounting the diagnosis in the absence of history of tick bite, (d) using an inappropriate geographic exclusion, (e) using an inappropriate seasonal exclusion, (f) failing to treat on clinical suspicion, (g) failing to elicit an appropriate history, and (h) failing to treat with doxycycline. The diagnosis of RMSF has been, and continues to be, problematic. The most widely used diagnostic tool is serologic testing, which is not useful during active infection. Seroconversion of RMSF infection may not occur until three weeks into the illness. PCR assays for diagnosing RMSF have been developed, but to date these assays have not been fully evaluated in the clinical setting. A critical issue in their usefulness...
would be the length of time that *Rickettsia rickettsii* would remain in the blood. Combined PCR and electrospray ionization mass spectrometry method may be able to detect both *Ehrlichia* species and *R. rickettsii*. The diagnosis and empirical doxycycline therapy of RMSF is particularly difficult in children as pediatricians, family physicians, and/or emergency room physicians may not appreciate that RMSF is seen in children or be aware that the appropriate treatment strategy requires doxycycline treatment before the rash is seen. Finally, it should be noted that a newly recognized tickborne spotted fever group rickettsiosis has been described. The cause of this tickborne escar-associated spotted fever group rickettsiosis is *Rickettsia parkeri*, which originally was thought to be nonpathogenic in humans. Clinically, this rickettsiosis presents in a manner that is very similar to RMSF with symptoms of fever, fatigue, myalgia, headache, and a generalized rash; in addition, patients describe a “sore” or “pimple” at the site of a tick bite. This escar typically precedes the onset of fever by several days. This illness, like RMSF, is mostly seen in the southeastern United States. As with RMSF, empirical therapy with doxycycline should be initiated in patients with this constellation of symptoms.

Babesiosis is another tickborne infection seen during summer months that can be particularly difficult to identify unless it is considered in the differential diagnosis. Clinically, babesiosis resembles malaria and is endogenous to the United States. Observing intraerythrocytic ring-forms in a blood smear can quickly make the diagnosis if the clinician requests such smears. Otherwise, multiple episodes of a febrile illness may go undiagnosed until a routine blood smear and/or an alert medical technologist allow the diagnosis of babesiosis to be made. Patients may require the review of multiple thin and thick blood smears to make a diagnosis. Diagnosis may be made serendipitously on a routine blood smear; however, autoanalyzers or a less observant medical technologist might miss this diagnosis, and multiple blood smears and/
or thick smears may be required. A careful review by a medical technologist or pathologist of abnormal red blood cell images stored in current blood autoanalyzers is the best way to make a diagnosis of babesiosis, as there are far more red blood cells screened and abnormal red blood cells stored as an image than is possible with a blood smear. Finally, PCR methods have been described, but are not widely available. Moreover, the diagnosis must be considered before a PCR assay can be ordered.

Lyme disease represents another case in which failure to consider an uncommon tickborne infection may lead to diagnostic confusion. Tickborne infections should be considered in the differential diagnosis for a febrile illness in a patient with thrombocytopenia, especially in a patient presenting in summer. Early Lyme disease is particularly difficult to diagnose and empirical antimicrobial therapy should be considered with the appropriate clinical situation. Antigenic stimulus due to *Borrelia burgdorferi* infection is known to cause a blastoid transformation of B and T lymphocytes that can result in cerebrospinal fluid (CSF) cytology mimicking central nervous system malignancy.

**STANDARDS OF CARE**

- Failure to consider uncommon infections clearly can result in harm to a patient; it may be less clear that a medical error has occurred although the patient and/or a lawyer would likely consider such a failure to be a medical error.
- Failure to consider uncommon infections as a source of medical errors can be avoided by a number of mechanisms; these include use of the medical literature, use of the Internet (e.g., PubMed or *UpToDate*), consultation with the clinical microbiology laboratory director, and consultation with an infectious diseases clinician.
- Tickborne infections are an emerging infectious threat and cause uncommon infections that must
be considered in the differential diagnosis of febrile patients seen during summer months in order to avoid medical errors.

- Broad-spectrum empirical antimicrobial therapy may be needed while the differential diagnosis is being developed and the results of diagnostic testing are pending; this is particularly true for tickborne infections where only babesiosis can be quickly diagnosed.

### FAILURE TO APPRECIATE THE PROPER TIMING FOR SEROLOGY TESTS

Failure to appreciate the proper timing for serology is another common medical error and leads to confusion when the “obvious” diagnosis is “ruled out” by the serologic test. Consultation with the laboratory can assist with this problem.

Acute West Nile encephalitis presents a case illustrating the need for proper timing of serologic testing. Acute West Nile encephalitis is a serious public health issue in the United States with over 700 cases reported to the Centers for Disease Control and Prevention (CDC) in 2009. The CDC recommends that West Nile virus immunoglobulin M (IgM) detection by an IgM capture enzyme-linked immunosorbent assay (ELISA) in serum or CSF should be the major laboratory tool used to identify symptomatic patients with acute West Nile virus infections. This test has a sensitivity approaching 100% in appropriately timed samples. In early symptomatic infections, the West Nile virus can be detected by PCR in serum or CSF. However, levels of West Nile virus RNA typically peak before symptoms appear and then rapidly decline as IgM antibody production begins. Thus, there is a limited window for RNA detection. Once IgM antibodies for West Nile virus appear, they remain detectable for several months after the acute illness. Although most patients
with West Nile virus encephalitis present late in their illness, some patients seeking medical assistance within a week of symptom onset may still be in the RNA-positive/antibody-negative window and the infection may be missed if only IgM testing is done. To avoid missing cases of acute West Nile infection, both West Nile virus RNA testing and West Nile virus IgM testing may be required. However, as there is no current antiviral therapy for West Nile virus encephalitis, a delay in the diagnosis may not present a therapeutic problem.

Proper timing is also relevant in the serologic diagnosis of Lyme disease. Serology may not allow the diagnosis of early Lyme disease. Suspicion of Lyme disease based on erythema migrans is sufficient reason to begin empiric antimicrobial therapy.

Leptospirosis presents another infection where the timing of testing is relevant. Leptospirosis is a zoonotic disease caused by the spirochetes of the genus *Leptospira* and is considered to be one of the most common zoonoses in the world. In the past decade, leptospirosis has been recognized as an emerging public health problem that occurs in urban and rural areas of developing and developed countries. Humans are accidental hosts and become infected through exposure to environmental sources contaminated by the urine of chronically infected mammals. In the United States, the most common sources of exposure are dogs, livestock, and wild animals, especially rodents. Outbreaks of leptospirosis have been reported and are often due to natural disasters such as floods. Leptospirosis is also recognized as an infection seen in travelers returning from the tropics. Patients hospitalized with leptospirosis may have mortality rates as high as 25%; this is, in part, related to a delay in diagnosis. The majority of leptospirosis cases are diagnosed by serology. The current standard is the microscopic agglutination test, which involves the reaction of antigens in the form of live *Leptospira* organisms with the antibodies found in the patient’s sera. A positive reaction results in agglutination of the *Leptospira* that can be seen microscopically. The IgG
antibody response to leptospirosis for this test takes about two weeks and can be delayed by antimicrobial therapy. New serologic methods are commercially available; some of these tests measure an IgM response and may thus allow more rapid results. PCR testing is also being developed and should allow the most rapid means of diagnosis.

STANDARDS OF CARE

- Certain infectious diseases such as many viral infections, as well as infections involving *Mycoplasma*, *Leptospira*, *Borrelia*, *Treponema*, *Coxiella*, and *Chlamydia*, often require a serologic diagnosis; appreciation of the time required for an antibody response to the acute infection is important when obtaining such serologic tests.
- Failure to appreciate the proper timing for serology tests can result in harm to a patient even though the correct diagnosis was considered, and an appropriate serology test was ordered; failure to appreciate the proper timing for serology tests is a subtle but real form of medical error.
- Unlike failure to consider infection or failure to consider uncommon infections, in this situation the correct infection was considered; using empirical antimicrobial therapy when applicable can avoid this type of medical error.
- Appreciating the appropriate timing of serology tests may result in repeating a serology test that is initially negative; empirical antimicrobial therapy as mentioned earlier prevents harm to the patient.

FAILURE TO APPRECIATE THE SENSITIVITY OR SPECIFICITY OF MICROBIOLOGY TESTS

Failure to appreciate the sensitivity or specificity of microbiology tests is another common problem and can lead
to medical errors. This problem often can be avoided by consultation with the laboratory.

The need to understand the sensitivity and specificity of specific microbiology tests was illustrated vividly during the spring and summer of 2009, when a novel influenza A virus of swine origin, H1N1, emerged in humans in North America. The sensitivity of rapid diagnostic tests for influenza during the peak influenza season is approximately 60%; a lower prevalence of influenza at other times of the year will result in a lower sensitivity for rapid influenza testing. Nasopharyngeal swabs are preferred over buccal swabs. Empiric antiviral treatment should be based on the clinical picture rather than the results of rapid influenza testing. The Infectious Diseases Society of America Clinical Practice Guidelines currently recommend early treatment (ideally within 48 hours) with oseltamivir or zanamivir for persons in whom influenza virus infection is highly suspected. Unfortunately, such treatments were not recommended by the CDC in early summer of 2009.

Cryptococcal meningitis is another case where use of a sensitive culture method is critical to accurate diagnosis. Cryptococcal antigen and cryptococcal CSF cultures are both of limited value, and BACTEC Myco/F Lytic bottle is more sensitive. In particular, capsule-deficient isolates of Cryptococcus neoformans are known to cause difficulty in diagnosing chronic cryptococcal meningitis using the CSF cryptococcal latex agglutination test. In nonimmunosuppressed patients, the delayed diagnosis of cryptococcal meningitis is a recognized problem that has increased the morbidity and mortality of this condition. False-positive cryptococcal antigen testing has been reported and must be considered in such antigen testing.

Diagnosis of Legionella infection is also limited by the nonspecific nature of clinical features and the shortcomings of diagnostic tests. Legionella species are important causes of pneumonia in humans. Currently, of the more than 50 species of Legionella, at least 24 are
associated with human disease. Although *Legionella pneumophila* appears to be more pathogenic to humans and causes the majority of human disease, other species clearly can infect humans. Importantly, cavitary pulmonary infection has been associated with *Legionella bozemanii*. *Legionella micdadei* and *Legionella longbeachae* are other common etiologic agents causing human infection. Unfortunately, no single microbiology test is able to diagnose *Legionella* infection in a timely fashion with a high degree of sensitivity and specificity. Although *Legionella* culture remains the most useful single test, culture diagnosis requires special media, adequate processing of specimens, and technical expertise. The standard medium used to culture *Legionella* species is buffered charcoal yeast extract (BCYE) agar. Supplementation of BCYE agar with bovine serum albumin will enhance the growth of some *Legionella* species such as *L. bozemanii* and *L. micdadei*; in contrast, addition of cefamandole to this agar, as is often done, will inhibit growth of these two species. Despite the appropriate use of BCYE agar for sputum cultures, the sensitivity of expectorated sputum cultures ranges from 10% to 80% as fewer than half of patients with *Legionella* pneumonia produce sputum. Bronchoscopy or pulmonary biopsy specimens are more likely to yield positive cultures than are expectorated sputum samples. The detection of soluble *Legionella* antigen in urine specimens has become a rapid and reliable tool for the diagnosis of *L. pneumophila* infections. These urinary antigen tests have sensitivities in the range of 70% to 100% but are only able to detect *L. pneumophila* serogroup 1. Other species of *Legionella* are not reliably detected. False-positive results for the *Legionella* urinary antigen have been reported as well. Serologic testing for *Legionella* infection is hampered by the delay in seroconversion, which may take several weeks, as well as by the inability of serologic testing to accurately detect all *Legionella* species and subgroups. Clearly, there remains a role for *Legionella* cultures obtained by bronchoscopy or pulmonary biopsy.
STANDARDS OF CARE

- Failure to appreciate the sensitivity or specificity of microbiology tests can result in harm to a patient even though the correct diagnosis was considered, and an appropriate microbiology test was ordered; failure to appreciate the sensitivity or specificity of microbiology tests is a subtle but real form of medical error.
- The sensitivity and specificity of antigen testing in clinical microbiology is particularly important; both false-negative and false-positive test results are factors in such antigen testing and must be appreciated.
- Consultations with the clinical microbiology laboratory and/or the infectious diseases unit are excellent ways to avoid this potential error.

FAILURE TO SUBMIT A SUITABLE MICROBIOLOGY SPECIMEN

Failure to submit suitable microbiology specimens is unfortunately a common problem that can lead to medical errors in infectious diseases and clinical microbiology. Consultation with the clinical microbiology laboratory regarding suitable specimens is the best way to avoid this error.

Skin and soft tissue abscesses present an area where suitable specimen collection may be crucial. Areas of debate here include the usefulness of cultures and empiric treatment with antimicrobial agents. The increasing incidence of community-associated methicillin-resistant staphylococcus aureus (CA-MRSA) has intensified this debate. Nocardia species, for instance, often take five days or longer to grow on sheep blood agar, so a “no growth” culture result after 48 hours would not assist in the care of such a patient. Holding the culture longer than two days may allow the diagnosis and appropriate therapy. If this infection is not diagnosed, the Nocardia infection may eventually progress to involve deeper
tissues and bone in the foot; a type of infection known as “Madura foot,” for example, is very difficult to treat and often leads to amputation of the infected foot.

The value of sputum Gram stain and culture in the diagnosis of community-acquired pneumonia is another area of considerable debate. Obtaining a good-quality sputum specimen is difficult in young, nonexpectorating children with pneumonia. Routine sputum collection and analysis has not been recommended in children with community-acquired pneumonia for a number of reasons. Among these cogent reasons are that viral pneumonia is the most common cause of community-acquired pneumonia during the first two years and that young children cannot easily expectorate sputum. Moreover, empiric therapy with newer cephalosporins generally has proven effective in situations in which clinicians suspect a bacterial cause of community-acquired pneumonia in a child. Resistance to newer cephalosporins can result in treatment failure leading to readmission to the hospital. Collection of sputum in children or in adults is likely to be very important in the near future when traditional diagnostic methods are supplemented with PCR-based methods in order to increase the microbiological yield for the etiology of community-acquired pneumonia.

Malaria evaluation is another case in which the failure to submit a suitable microbiology specimen may be problematic. Peripheral blood examinations performed using automated equipment may be inadequate. The number of fields scanned by a technologist on these smears using automated equipment is quite low, and thus failure to pick up a light malarial parasitemia is not unusual. More extensive scanning of the blood fields stored in automated blood equipment by a pathologist is, however, an excellent way to make a diagnosis of malaria. The initial key to the diagnosis of malaria is travel history (e.g., South America) as the incubation period can be variable for all strains of malaria. Indeed, fever in a returned traveler must always raise the possibility of malaria in the differential diagnosis.
In addition, imported malaria in visitors to the United States must also be considered in febrile patients with vague and nonspecific clinical presentations of malaria who may be seen in emergency rooms. Thin and thick smears for malaria should be ordered as the parasitemia may be missed with routine complete blood counts done on automated instruments. Thrombocytopenia is the most common laboratory abnormality encountered with malaria, seen in approximately 60% of cases regardless of the type of malaria, and should also prompt a blood smear. Hyperbilirubinemia is also seen in approximately 40% of malaria cases, and anemia is seen in approximately 30%. The presence of thrombocytopenia and hyperbilirubinemia alone has a positive predictive value of 95% in the presumptive diagnosis of malaria in the febrile traveler returning from a part of the world where malaria is endemic. It is important to understand that babesiosis can also present with fever, thrombocytopenia, hyperbilirubinemia, and anemia and also may require thin and thick blood smears for diagnosis; routine complete blood counts on automated instruments may miss this diagnosis for the same reason that malaria can be missed. Clearly, not sending blood for parasite analysis (i.e., malaria and babesiosis) can represent a failure to submit a suitable specimen in a febrile patient.

Mycotic infections provide yet another example of the importance of collecting suitable specimens. Chromoblastomycosis is a chronic mycotic infection caused by pigmented saprophytic molds of the Dermatiaceae family ubiquitous in the environment. The members of the Dermatiaceae family are dimorphic filamentous fungi with melanic-type pigment in the cell wall. Clinically, the infection usually follows traumatic inoculation through penetrating thorn or splinter wounds and is characterized by the development of chronic verrucose lesions at the inoculation site. *Phialophora richardsiae* is a recognized cause of chromoblastomycosis in humans and can cause osteomyelitis. Puncture wounds of the foot can result in serious complications such as osteomyelitis. For this reason,
puncture wounds may require wound enlargement and a search for a retained foreign body. Imbedded rubber foreign bodies from footwear and thorn or wood splinters are recognized risk factors for infection. Biopsy with appropriate cultures should be done initially rather than relying on empiric antimicrobial therapy. Gram-negative bacteria such as *Pseudomonas aeruginosa* can cause osteomyelitis following puncture wounds of the foot. However, other microorganisms including fungi or mycobacteria can also cause osteomyelitis of the calcaneus secondary to a puncture wound. It thus is important to realize that when cultures are ordered in calcaneal osteomyelitis following a puncture wound, bacterial, fungal, and mycobacterial cultures should be specified on the requisition.

Infection with *Staphylococcus aureus* and MTB may also cause osteomyelitis. If bone cultures for *Mycobacterium* are not done, and granulomatous inflammation without demonstrable acid-fast bacilli is seen, there are two potential solutions. The first solution is to recut the formalin-fixed, paraffin-embedded tissue for additional acid-fast staining. Additional sections cut for acid-fast staining will sometimes identify acid-fast bacilli not seen in the first cuts. The second solution is to use molecular detection methods such as PCR testing for *M. tuberculosis*; these are done on the formalin-fixed, paraffin-embedded tissue, and have proven successful in such situations. Such testing is best done in consultation with the clinical microbiology laboratory. In general, bone specimens from patients with vertebral osteomyelitis should include bacterial, fungal, and mycobacterial cultures in order to avoid this type of medical error. Molecular testing is a reasonable adjunct test when mycobacterial cultures have not been done or are negative.

**STANDARDS OF CARE**

- Failure to submit a suitable microbiology specimen or any microbiology specimen at all even though
infection is suspected may happen for a number of reasons and can be another subtle form of medical error.

- If unusual microorganisms are suspected, the clinical microbiology laboratory should be consulted as special media and/or incubating the cultures for a prolonged period of time might be necessary; such consultation may also result in assistance in terms of what type of cultures should be ordered on specimens from a febrile patient.

- Consultation with infectious diseases clinicians is also useful in determining what type of cultures should be obtained in a febrile patient.

- Fever in returning travelers or foreign travelers visiting the United States should raise the diagnostic possibility of malaria; thick and thin blood smears for malaria are indicated in this situation.

- Mixed infections with dissimilar microorganisms such as bacteria and fungi or bacteria and mycobacteria do occur; specimens sent to the clinical microbiology laboratory must specifically request bacterial, fungal, and mycobacterial cultures in order to ensure that all are done.

- Molecular diagnostic techniques now may offer a “second chance” to make the correct diagnosis if appropriate cultures are not requested on the specimen initially sent to the clinical microbiology laboratory.

- The pathophysiology of a suspected infection may provide insight on additional tissue that can be biopsied for culture and/or PCR testing when initial testing is nonrevealing.

**FAILURE TO PROPERLY IDENTIFY PATIENT, SPECIMEN, OR TEST ORDER**

Failure to properly identify patient, specimen, or test order is a common issue in all laboratories. Attention to detail and electronic bar code labeling can assist with this problem.
Rejection and recollection of a specimen once mislabeling is detected is the most suitable approach to managing this issue; that is, the microbiology technologist may call the emergency room so that the person who obtained a blood culture that appears mislabeled may come to the microbiology laboratory and properly label the bottles. This solution may not be possible, however, if antimicrobial agents have been initiated. An unlabeled blood culture bottle might appear to be a minor issue that is easily resolved, but this type of preanalytic phase medical error is extremely common and has great potential for becoming a major issue. Consider a case, for instance, in which there is more than one unlabeled set of blood culture bottles, each set from two separate patients. Assume also that these were received in the microbiology laboratory at the same time. Properly labeling these two sets of blood culture bottles would become a major problem.

The preanalytic phase of laboratory testing is manually intensive and thus prone to having the highest error rate. Blood collection is a particularly error-prone portion of the total laboratory testing process. Among the common preanalytic phase errors are mistakes in tube filling, inappropriate containers, inappropriate requesting procedures, and identification errors (i.e., misidentification). Indeed, misidentification has been identified as a major problem in the preanalytic phase of laboratory testing with the following causes being the most problematic: (a) physician ordering a laboratory test on the wrong patient, (b) incorrect or incomplete computer entry of patient’s data, (c) collection of a specimen from the wrong patient, (d) inappropriate labeling of the specimen, (e) lost identification (label or requisition) for the specimen, and (f) incorrect entry of the patient’s results in the computer database.

Clearly the preanalytic phase of laboratory testing is vulnerable to errors; most of these errors result from system flaws and insufficient audit and control of the operators involved in specimen collection. A number of factors must be considered in order to deal with
these types of preanalytic errors. The first factor to consider is prediction of accidental events, which is accomplished by the following processes: (a) exhaustive process analysis, (b) reassessment and rearrangement of quality requirements, (c) dissemination of operating guidelines and best-practice recommendations, (d) reduction of complexity and error-prone activities, (e) introduction of error-tracking systems, (f) continuous monitoring of performance, and (g) root cause analysis of any errors identified to ensure that any systems flaws can be addressed.

The next factor to consider is an increase in and diversification of defenses, which is accomplished by the application of multiple and heterogeneous systems to identify nonconformities. The final factor to consider is a decrease in vulnerability, which is accomplished by implementation of reliable and objective detection systems, causal relation charts, and education/training. These factors taken together constitute a systems approach for solving the problem of preanalytic errors.

**STANDARDS OF CARE**

- The preanalytic phase of laboratory testing is manually intensive and prone to system flaws and operator error; a systems approach is required to avoid these kinds of errors.
- Failure to properly identify a patient, specimen, or test order can be considered a “misidentification” error and is actually a common preanalytic error in laboratory testing that can result in minor inconvenience (e.g., redrawing or relabeling) or in serious consequences (e.g., wrong patient or delay in diagnosis); the “paperwork” must be considered an integral and important part of patient care.
- Quality programs developed around the preanalytic phase of laboratory testing are required to avoid preanalytic errors; when errors occur, a root cause analysis must be done to identify any systems flaws that may contribute to such errors.
In contrast to preanalytic errors in laboratory testing, analytic errors have been carefully addressed in both the clinical microbiology laboratory and in the laboratory as a whole. Bartlett et al. have comprehensively reviewed the process of managing quality in the clinical microbiology laboratory, and this review continues to serve as an ongoing template for a systems approach to quality. This does not mean that the analytic phase of testing in the clinical microbiology laboratory is error-free. Indeed, the detection and prevention of clinical microbiology laboratory–associated errors have been recognized and addressed by the American Society for Clinical Microbiology in their *Cumitech* series. The *Cumitech* series is designed to provide consensus recommendations regarding the judicious use of clinical microbiology and immunology laboratories; each series is written by a team of clinicians, laboratorians, and other knowledgeable stakeholders to provide a broad overview of various important aspects of infectious diseases testing. The discussion of analytic error that follows is based on the medical literature as well as the personal experience of the author and illustrates common medical errors that may occur in the clinical microbiology laboratory.

**MISREADING OR MISINTERPRETATION OF GRAM STAIN OR OTHER STAINS**

Misreading or misinterpretation of Gram stain or other stains is not a common problem in most clinical microbiology laboratories, but this error does occasionally happen. Technical issues usually contribute to this problem when it happens. These technical issues should be understood.

The well-recognized difficulty of diagnosing cryptococcal meningitis provides a useful example
of cases where a misread Gram stain of the CSF may contribute to diagnostic confusion. The Gram stain of CSF is recognized as critical in the diagnostic evaluation of a patient with suspected meningitis, and positive Gram stains revealing microorganisms are used to direct initial therapy. Clinicians and laboratory personnel usually do not consider a false-positive Gram stain from CSF to be a potential problem. However, it must be appreciated that such false-positive Gram stains can occur.

In general, the microscopic examination of CSF in the diagnosis of meningitis is quite sensitive, ranging from 67% to 92%. It is rare for CSF examinations to incorrectly suggest the presence of microorganisms. C. neoformans is known to be confusing on Gram stain; both gram-positive and gram-negative misidentification is reported. A high index of suspicion for cryptococcal meningitis along with the use of the cryptococcal antigen test is a key factor in the diagnosis of such cases and will help avoid delays in treatment.

Clearly, the rapid and accurate detection and characterization of microorganisms encountered in purulent CSF from patients with meningitis are important. Quality assessment programs in the clinical microbiology laboratory include both internal and external proficiency testing as well as the testing of microbiology technologists for colorblindness. Such competency assessment in the clinical microbiology laboratory is an important, ongoing function that prevents such errors. In addition, most clinical microbiology laboratories routinely have a senior microbiologist review any positive Gram stains from CSF. Other causes of false-positive Gram stains from CSF are not infrequently described and do not include misreading the Gram stain. Instead, contamination with nonviable bacteria from various products used in the process is the cause of such false-positive Gram stains of CSF.

Factitious meningitis due to nonviable bacteria in commercial lumbar puncture trays was first reported in the mid-1970s and still occurs. The medical
products industry has effectively ensured the sterility of commercial medical devices, but the procedures used to sterilize these products do not prevent the presence of nonviable microorganisms. Therefore, physicians and laboratory personnel must be aware that such false-positive Gram stains may occur. Although specimen tubes in lumbar puncture trays are the most common cause of factitious meningitis, other sources of nonviable microorganisms such as cytocentrifuge funnels and Gram-stain reagents may be a source. The laboratory must review any specimen showing microorganisms on direct smears that fail to grow. If factitious organisms are suspected, the physician should be notified. If possible, a repeat CSF specimen should be obtained using new, clean, and sterile glass tubes. Any cluster of such cases should be reported to the Food and Drug Administration (FDA).

*Streptococcus pneumoniae* is a common cause of community-acquired meningitis in pediatric patients, but *Acinetobacter baumannii*, which is a short, plump, gram-negative rod that is difficult to destain, may also be misidentified as a gram-positive *Diplococcus*. Broad-spectrum antimicrobial therapy will provide coverage against this isolate. *A. baumannii* rarely causes community-acquired meningitis, although it has been reported as a cause of community-acquired pneumonia. When *A. baumannii* is seen as a cause of meningitis in a child, it usually follows a neurosurgical procedure and is multidrug resistant.

An issue with the Gram stain that is well known to microbiologists but not to physicians is Gram stain variability in select bacteria, including *Bacillus* species. *Bacillus* infections have been reported in orthopedic trauma cases. *Bacillus* species including *Bacillus cereus* are known to be gram-variable and can stain as gram-negative bacilli as well as gram-positive filamentous forms that show beading and can be confused with *Nocardia* species. *B. cereus* produces multiple beta-lactamases, which include a metallo-beta-lactamase. These beta-lactamases are
very potent against beta-lactam agents, including the third-generation cephalosporins. Imipenem and other carbapenem agents seem to be active against *B. cereus* despite the presence of this metallo-beta-lactamase. However, carbapenem-resistant strains of *B. cereus* have been reported. Vancomycin or clindamycin are preferred choices for therapy of *B. cereus* infections.

Morphologic changes can sometimes be seen in gram-negative bacilli that are exposed to certain beta-lactam agents; for example, piperacillin interacting with penicillin-binding proteins may result in cell elongation without division. These filamentous forms may appear by Gram stain to be a fungal pathogen.

Prompt Gram staining of positive blood cultures is recognized as an important factor in directing antimicrobial therapy and has been shown to decrease mortality. As mentioned earlier, physicians rarely question the accuracy of such Gram stains. Yet, the exigencies of the staining properties of certain species of bacteria as well as human interpretive error can result in misinterpretation of a Gram stain from a positive blood culture. Indeed, misinterpretation of Gram stains from positive blood cultures has been reported for certain species of bacteria as well as for instances of under- or overdecolorization of the Gram stain. In one report, two systematic errors were noted. In 11 cases, *Bacillus* species were read as gram-negative bacilli (this is known to be a problem with this species), and in five cases, *Acinetobacter* species were read as gram-positive cocci or gram-positive bacilli (also a known problem with this species).

Underdecolorization and overdecolorization of the Gram stain are related to the use of acetone and isopropanol in the decolorization step. Acetone is too strong a decolorizer and isopropanol is too weak a decolorizer for gram-positive microorganisms. Therefore, most Gram stain kits use a mixture of one part acetone to three parts of isopropanol. The decolorization step should be done until the solvent running from the slide is colorless. Safranin or fuchs
is used as a counterstain and should be applied for 30 to 60 seconds. Prolonged application may cause gram-positive microorganisms to appear gram negative, while short application may cause gram-negative microorganisms to appear gram positive. The timing and the acetone/isopropanol ratio as well as the species of microorganism all are important factors in the Gram stain. For Gram stains of clinical specimens that include polymorphonuclear cells in the background, a good quality-control indicator is that occasionally the nucleus of a polymorphonuclear cell should stain purple. If most of the nuclei are staining purple, the stain is underdecolorized. If no purple nuclei can be seen after reviewing multiple fields, the stain is overdecolorized. If a Gram stain is considered under- or overdecolorized, the slide can be washed with xylene and the stain repeated.

Clearly, the answer to the question, “Can we always trust the Gram stain?” is “No.” Misread Gram stains from positive blood cultures are generally recognized within one to two days when the microorganism grown on plates is recognized as being inconsistent with the Gram stain report; an amended report should be done. In addition, the physician should be notified by telephone.

Artifacts and organism mimickers can pose many problems in the diagnosis of infection. Of these problems, fungal elements from contamination during slide preparation are the most difficult to deal with because these will stain with Gomori methenamine silver (GMS) and periodic acid-Schiff (PAS) stains. Pathologists and microbiologists must assess the tissue inflammatory response when fungal elements are seen; if the cellular response is inconsistent, fungal contamination during slide preparation must be considered. An additional mimicker of fungal yeast elements can be seen in H&E stains from dermal lesions in which there is inflammation and plasma cells. This mimic is Russell bodies, which are intracytoplasmic immunoglobulin bodies in plasma cells. Russell
bodies have been reported to cause confusion with blastomycosis as well as other pathogenic fungi such as *Histoplasma*, *Cryptococcus*, and *Candida* species that have yeast forms. Russell bodies are of variable size and lack the budding characteristics of these pathogenic fungi. Although Russell bodies are positive with PAS stains, they stain brown-gray with GMS, not black as would be expected.

The evaluation of frozen sections also poses certain problems with speciation. Even with special GMS or PAS stains, identifying a specific fungal microorganism from tissue may be difficult even for experienced pathologists and microbiologists. Morphologic identification can be a useful tool for the preliminary diagnosis of fungal infection, but culture remains the gold standard for speciation. All should be used concurrently to ensure that an accurate diagnosis is made. For example, lack of budding in a frozen section stain can make *Blastomyces dermatitidis* difficult to distinguish from Coccidioides. Moreover, empty, overlapping spherules in Coccidioides can mimic budding yeast and be mistaken for *B. dermatitidis* broad-based yeast in the process of budding. The Alcian blue or an acid-fast stain can be used to distinguish between Coccidioides and Blastomyces; Coccidioides is negative and Blastomyces is weakly positive. Some recommend identifying the presence of at least one intact spherule containing endospores before making a diagnosis of Coccidioides in tissue. Other special stains can be used to distinguish Blastomyces from Cryptococcus. Cryptococcus usually will stain strongly with mucicarmine; the occasional capsule-deficient forms of cryptococci stain with melanin. In contrast, the cell wall of Blastomyces is only weakly positive when stained with mucicarmine and negative with melanin.

### STANDARDS OF CARE

- Gram stains or other stains can be misread and/or misinterpreted due to a number of technical
reasons; these reasons are understood by clinical microbiologists and pathologists, but may not be understood by physicians taking care of the patient.

- When misreading and/or misinterpreting a stain occurs and is recognized, a corrected report must be entered into the health record; moreover, the clinicians involved should be called and told of this error.

- A root cause analysis should be done for misreading and/or misinterpreting a stain in order to determine if there are any recurring systems issues that can be corrected.

- Because many errors caused by misreading and/or misinterpreting a stain cannot be completely avoided due to technical reasons, it is important that microbiologists/pathologists maintain clear communication channels with clinicians in order to quickly resolve and correct such errors when they occur.

### MISIDENTIFICATION OF MICROORGANISM

**Misidentification of a microorganism does not occur frequently, but can happen. Often there are technical issues that must be appreciated. Correction of the misidentification in the medical record and timely communication of the misidentification are important.**

Automated identification systems are known for misidentification of isolates of the *Burkholderia cepacia* complex (BCC), and molecular methods for confirmatory identification of BCC are highly recommended, such as amplification and sequencing of a 500-bp fragment of the 16S rRNA gene.

*Burkholderia pseudomallei* is the cause of melioidosis, a serious infection common in Southwest Asia. Treatment of any infection caused by *B. pseudomallei* is difficult, and there is a high rate of relapse if prolonged therapy is not completed. Generally, two weeks of intravenous therapy with ceftazidime or a carbapenem is given followed by at least four months of oral
sulfamethoxizole/trimethoprim. Such cases also raise issues regarding the safety of laboratory personnel exposed to the pathogen. Automated systems for identification and antimicrobial susceptibility testing of bacterial isolates, such as the BD Phoenix Automated Biology System, have become standard in most clinical laboratories. Identification of bacterial isolates is dependent on the database of the automated system; *B. pseudomallei* is not in the database of the Phoenix System. Currently, the most rapid and accurate identification method for *B. pseudomallei* is a manual method that uses the API 20NE system combined with a noncommercial latex agglutination test. Molecular methods are accurate, but they take more time. The limitations of automated systems must be understood by clinical microbiologists in order to avoid this type of identification error.

Other identification methods are known to have difficulty distinguishing *Streptococcus constellatus* and other members of the *Streptococcus anginosus* (also known as *Streptococcus milleri*) group from group C streptococci (*Streptococcus equisimilis*). Many clinical microbiology laboratories presumptively identify beta-hemolytic streptococci on the basis of Lancefield group- ing. Some of the group C streptococcal bacteremia cases reported in the medical literature may actually represent bacteremia by members of the *S. anginosus* group. Differentiation of group C streptococci from members of the *S. anginosus* group is best accomplished by the Voges-Proskauer (VP) test; members of the *S. anginosus* group produce acetoin whereas *S. equisimilis* does not. The Phoenix Automated Microbiology System cannot be expected to detect diacetyl (caramel odor); moreover, the Phoenix Streptococcal Panel does not include the VP test.

Isolation of a member of the *S. anginosus* group from a blood culture is a “sentinel result,” because these pathogens can be associated with abscesses and/or suppurative thrombophlebitis. It is important that clinical microbiologists appreciate and alert clinicians
to the potential pathogenicity of \textit{S. anginosus}. This type of sentinel result has been termed a “vital value”; alerting clinicians regarding such a result can promote patient safety by preventing a medical error and is an example of “enhanced clinical consulting.”

Another issue arises with misidentification of \textit{Mycobacterium abscessus}, which may result in a substantial delay in the administration of optimal antimicrobial therapy against this pathogen. \textit{M. abscessus} is a member of the rapidly growing mycobacteria that are unusual causes of endocarditis. Rapidly growing mycobacteria can easily be misidentified as \textit{Nocardia} spp. or \textit{Corynebacterium} spp. In a European quality control report, \textit{Mycobacterium fortuitum} specimens labeled as “pus from an abscess” were sent to 50 clinical microbiology laboratories for proficiency testing. Only 13 of the 50 laboratories correctly identified \textit{M. fortuitum}. These specimens were misidentified as \textit{Nocardia} spp. (23 laboratories) or \textit{Corynebacterium} spp. (14 laboratories). Acid-fast staining of gram-positive bacilli should be routinely included in the identification procedure; if acid-fast staining results are positive, isolates should be sent to a reference laboratory for definitive identification as well as for susceptibility testing.

Conventional diagnosis of mycobacterial infection uses acid-fast staining, culture, and phenotypic characterization of culture isolates; cultures may require weeks or months before results are available. Accordingly, nucleic acid probe- and amplification-based molecular methods have been developed for identification of mycobacterial culture isolates as well as for direct detection of mycobacteria in clinical specimens. These molecular methods have greatly reduced the time to diagnosis of tuberculosis. However, molecular methods have their own set of problems, such as the potential for misidentification of a microorganism owing to a false-positive result from a molecular amplification test for tuberculosis. The Gen-Probe Amplified \textit{Mycobacterium tuberculosis} Direct (MTD) test is a rapid molecular test that uses
isothermal transcription-mediated amplification and a hybridization protection assay to detect nucleic acid from *M. tuberculosis* complex in clinical specimens including lymph nodes. False-positive results may lead to a misdiagnosis of tuberculosis and weeks of unnecessary antituberculous therapy. A high concentration of *Mycobacterium leprae* in a clinical specimen, for example, can lead to a false-positive result for tuberculosis with the Gen-Probe MTD test.

The Roche COBAS AMPLICOR system is a fully automated RNA and DNA amplification and detection system for routine diagnostic PCR. The menu of this system includes selected members of the *Mycobacterium* family, including *M. tuberculosis*, *M. avium*, and *Mycobacterium intracellulare*. Use of this system has also resulted in false-positives for *M. tuberculosis*.

The presence of *M. leprae* in clinical specimens tested by two different molecular assays can result in misidentification for other species of *Mycobacterium*. Clinical microbiologists should be aware of this potential for this type of misidentification of *M. leprae* using commercially available MTB molecular assays.

Another well-known problem with PCR testing in the clinical microbiology laboratory is PCR amplification carryover contamination and subsequent false-positive results. The procedure for the PCR assay for HSV-1 may be modified to include a repeat assay for any positive results. This will not prevent PCR amplification carryover contamination but will reduce the likelihood of a false-positive result being reported. Over the past two decades, PCR assays and other DNA/RNA amplification techniques have been utilized in clinical microbiology laboratories. Unfortunately, the exquisite sensitivity of these assays makes them vulnerable to contamination. Potential sources of contamination include large numbers of target microorganisms/virions in clinical specimens as well as repeated amplification of the same target sequence, leading to accumulation of amplification product in the laboratory environment. The accumulation of amplification product is a critical issue and,
if uncontrolled, will lead to contamination of laboratory reagents, equipment, and even the ventilation system. Accordingly, clinical microbiology laboratories utilizing PCR for diagnostic purposes have established protocols to minimize this problem. Nevertheless, false-positive results from PCR amplification carryover contamination in molecular assays continue to occur occasionally despite the best efforts of a laboratory. When a false-positive result is recognized, a corrected report should be issued. In addition, a root cause analysis should be done to be sure that there is no recurring systems issue that can be corrected. Finally, communication with clinicians about amplification carryover contamination in a PCR assay is very important; many clinicians do not fully understand this issue and may attribute such false positives to technologist error.

STANDARDS OF CARE

- Misidentification of microorganisms can occur for a number of technical reasons; microbiologists are familiar with these technical reasons for misidentification, but clinicians may not understand these issues.
- When misidentification occurs and is recognized, a corrected report must be entered into the health record; moreover, the clinicians involved should be called and told of this error and why such errors occur despite best efforts to prevent them.
- A root cause analysis should be done for misidentification in order to determine if there are any recurring systems issues that can be corrected.
- Molecular methods such as PCR can assist in the correct identification of microorganisms, but may require additional time; moreover, PCR methods have their own set of problems with false-positive results due to PCR amplification carryover contamination being the most critical problem.
- Because some errors caused by misidentification cannot be avoided due to technical reasons,
it is important that microbiologists/pathologists maintain clear communication channels with clinicians in order to quickly explain and resolve such errors when they occur.

**SUSCEPTIBILITY TESTING ERROR**

Susceptibility testing error does not occur frequently in the clinical microbiology laboratory, but such errors can happen. Often there is a technical reason for such errors; automated susceptibility testing systems have been involved in such errors.

Most clinical microbiology laboratories today rely on automated systems such as the Phoenix Automated Microbiology System for identification and susceptibility testing. Such systems can give inaccurate results for selected antimicrobial agents and microorganism combinations; aminoglycoside resistance and susceptibility testing errors for *A. baumannii* is one of these combinations. It is recommended that confirmation by a manual method be done for this combination.

The performance of susceptibility testing in a clinical microbiology laboratory depends on robust methodology, good laboratory practices, and clearly delineated antimicrobial breakpoints. Moreover, routine susceptibility testing must be checked with both internal and external quality control programs. At one time, the results of susceptibility testing were so disconnected from actual clinical outcomes that one microbiologist was compelled to ask “In vitro Veritas?” Fortunately, this message was heard and improvements were implemented. Today, susceptibility testing has been greatly improved thanks to organizations such as the National Committee for Clinical Laboratory Standards (NCCLS), which has been renamed the Clinical Laboratory Standards Institute (CLSI). The published standards/guidelines from the NCCLS/CLSI provide the basis for uniform susceptibility testing procedures in the clinical microbiology laboratory.
Although there are still occasional errors, these errors should be recognized and quickly corrected.

Both clinicians and the clinical microbiology laboratory face uncertainty when the results of a susceptibility test are not consistent with the established susceptibility patterns for a particular species. The availability and reflex use of a confirmation test may be critical for directing proper antimicrobial therapy. For example, the CDC recommend that clinical microbiology laboratories perform a modified Hodge test or use PCR testing to confirm the presence of KPC carbapenemases in isolates with reduced susceptibility to carbapenems. Clinical microbiology laboratories must take an aggressive approach to detecting carbapenemases in order to provide clinicians with clinically relevant susceptibility results.

One of the critical functions of the director of a clinical microbiology laboratory is to select and monitor the susceptibility testing procedures and results so that these provide clinicians with relevant information. As resistance is constantly changing, the director must be aware of newly emerging resistance mechanisms and utilize new molecular technologies to detect such mechanisms.

STANDARDS OF CARE

- Susceptibility testing errors can occur for a number of technical reasons; microbiologists are familiar with these technical reasons for susceptibility testing errors, but clinicians may not understand these issues.
- When a susceptibility testing error occurs and is recognized, a corrected report must be entered into the health record; moreover, the clinicians involved should be called and told of this error.
- A root cause analysis should be done for susceptibility testing errors in order to determine if there are any recurring systems issues that can be corrected.
Molecular methods such as PCR are being evaluated in place of phenotypic susceptibility testing methods, but are not yet widely used; it should be anticipated that PCR methods also would have their own set of problems.

Because some errors caused by susceptibility testing cannot be avoided due to technical reasons, it is important that microbiologists/pathologists maintain clear communication channels with clinicians in order to quickly resolve such errors when they occur.

POSTANALYTIC ERRORS IN THE CLINICAL MICROBIOLOGY LABORATORY

The postanalytic phase in laboratory testing includes the reporting of the laboratory result to the clinician as well as the clinician’s interpretation of that result. Reporting of laboratory results has received a great deal of attention since the early 1970s when the concept of critical values in laboratory medicine was first introduced. This concept has been expanded to include a “vital value.” A vital value is defined as a laboratory result that is just as important as a critical value, but one for which timing is not as crucial. Many of the test results from the clinical microbiology laboratory logically can be defined as vital values. Microbiology test results that are of vital value require timely notification of the health care provider; most microbiology laboratories call nurses or physicians for such results.

Notification of the health care provider for critical values has become an established laboratory policy in all medical centers. Indeed, physician communication has become a focal point in efforts to promote patient safety by preventing medical errors. Timely communication of important laboratory data has long been recognized as essential for providing optimal health care.

The responsibility for interpretation of laboratory data has not been as clear as the reporting of these data.
The role of surgical pathology in the interpretation of histopathologic results has long been recognized. However, similar interpretation of laboratory data by the clinical pathologist has been less clear, and this concept is only recently coming to the forefront. The responsibilities of clinical pathologists, like the surgical pathologist, should extend into the postanalytic phase of the laboratory testing to assist clinicians in reviewing and understanding the results, and often providing an interpretation and/or recommending a future course of action. Failure to provide such information may result in a postanalytic error. The discussion of postanalytic error that follows is based on the medical literature as well as the personal experience of the author and includes common postanalytic medical errors from the perspective of the clinical microbiology laboratory.

**FAILURE OF CLINICIANS TO CONSIDER AND/OR CORRECTLY INTERPRET MICROBIOLOGY RESULTS**

Failure of clinicians to consider and/or to correctly interpret microbiology results is not a frequent cause of medical errors, but the problem does occur. Consultation with infectious disease clinicians and/or the clinical microbiology laboratory director can help avoid such errors.

The diagnosis of Lyme disease can be difficult; overdiagnosis and overtreatment of Lyme disease is a recognized problem. In one notable case, a patient died from a complication of her chronic indwelling central venous catheter, which had been placed for prolonged intravenous antimicrobial therapy for chronic Lyme disease. The diagnosis of chronic Lyme disease, however, was not fully documented. The chronic symptoms of this patient were nonspecific, and the results of her diagnostic evaluation for Lyme disease did not support this diagnosis. In this case, the diagnosis of Lyme disease was based on the result of
one positive PCR assay out of a total of 11 PCR assays done on this patient; this finding may have been the result of PCR amplification carryover contamination. Another similar case with false-positive results for PCR testing for Lyme disease has been reported in the medical literature. Sequential testing with enzyme immunoassay antibody assay for *B. burgdorferi* and confirmation by Western blot is the most accurate method for ruling in or out the possibility of Lyme disease.

Diagnosis of Whipple’s disease may pose similar difficulties, such as contradictory results between PAS staining of duodenal biopsies and PCR techniques. The problem of false-positive PCR results for Whipple’s disease is also well known. Contradictory results warrant antimicrobial therapy with oral sulfamethoxazole/trimethoprim or oral tetracycline as this therapy can result in rapid improvement of the clinical status. Critical review of the diagnostic results, including meticulous re-evaluation of all specimens and repeated sampling, is warranted. Careful review of previous culture results is always advisable, as is telephone notification of this result to the clinicians caring for this patient.

In another case, a patient was preoperatively suspected of having a brain tumor based on imaging findings but was eventually diagnosed with a brain gumma based on brain histopathology and CSF analysis. However, this patient’s medical history revealed that she had been engaged in prostitution in the past; a serum Venereal Disease Research Laboratory (VDRL) result was positive, as was a fluorescent treponemal antibody-absorption (FTA-ABS) IgG test. Based on this serologic information and the imaging studies of the brain, neurosyphilis and a brain gumma should have been considered. If neurosyphilis had been suspected, the diagnosis could have been made by analysis of the CSF; this analysis includes a CSF VDRL and FTA-ABS IgG test.

Related problems may arise in diagnosing acute HIV infection as this infection is characterized by a
negative or weakly positive ELISA test for HIV, a negative or indeterminate Western blot analysis for HIV-1, and high-level viremia detected by nucleic acid testing. Quantitative testing for HIV-1 nucleic acids may be needed to make this diagnosis. The fact that an ELISA test for HIV is weakly positive and the Western blot analysis for HIV-1 is negative should not prevent the correct test from being done.

Acute HIV-1 infection is also a recognized cause of a mononucleosis-like syndrome and should be considered in the differential diagnosis for patients presenting with a classic mononucleosis-like triad of fever, sore throat, and lymphadenopathy. The diagnosis of acute HIV-1 largely depends on quantitative testing for HIV-1 nucleic acids. Finally, acute HIV-1 infection presenting as a mononucleosis-like syndrome also must be considered in adolescents as up to half of all new HIV-1 infections occur in this age group.

Diagnosing even a relatively common infectious disease such as mononucleosis may be difficult when the clinical presentation is not what is usually seen.

A final case illustrating incorrect interpretation of microbiology results involves lack of recognition of *Staphylococcus lugdunensis* as a pathogen. *S. lugdunensis* is a member of the coagulase-negative staphylococci and, as such, may not be considered a pathogen. However, *S. lugdunensis* has become recognized as an atypically virulent pathogen with a unique clinical profile. For instance, although coagulase-negative staphylococci are rarely found in a breast abscess, such infections do occur. Serious consequences may occur if an *S. lugdunensis* isolate is in endocarditis. Although rare, *S. lugdunensis* is now a recognized cause of endocarditis and can cause destructive native valve endocarditis. Because *S. lugdunensis* isolated from blood cultures in children or adults may indicate infectious endocarditis, coagulase-negative staphylococci from blood cultures should be speciated.
STANDARDS OF CARE

- Failure of clinicians to consider and/or correctly interpret microbiology results is less likely in an age of electronic information when the medical literature is available on one’s telephone; given this fact, this type of error is less forgivable.
- When clinicians do fail to consider and/or correctly interpret microbiology results, it is likely to be an oversight; attention to detail is important when considering the volume of information generated by a medical evaluation.
- Newer molecular tests and/or newer antigen tests are perhaps easier to misinterpret, in part, because of their newness; their sensitivity and specificity may still be evolving.
- Recognition of the pathogenesis and virulence of microorganisms are constantly evolving; do not assume that a microorganism is not a pathogen simply because it was not recognized as such in the past.

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CHAPTER 6
Laboratory Management

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ACCREDITATION AND REGULATORY COMPLIANCE

Laboratory services are regulated at the federal level, and in many cases, by one or more state agencies as well. If state regulations are more stringent than federal, then the state regulations supersede federal. In addition, there are federally designated, nongovernment agencies that conduct periodic and unannounced on-site inspections of laboratories. These inspections serve to document performance compliance with standards and thereby accredit the laboratory to receive or maintain a federal license to operate. This federal license is referred to as a “Clinical Laboratory Improvement Amendments (CLIA)” license as laboratory licensure was deemed a regulatory requirement with the enactment of the CLIA of 1988.

Good management requires that the leadership team understand both the federal and state laws as well as the accreditation standards established by the inspecting agencies. It is the leadership team’s responsibility to ensure that actual laboratory practice complies with both legal regulations and accreditation requirements. Failure to do so may lead to consequences ranging from almost nothing to the catastrophic for the laboratory service: for example, from a substandard performance that requires a repeat inspection to unacceptable performance with suspension of license and testing.
UNDERSTAND REQUIREMENTS OF STATE REGULATIONS

The management team must be aware of government (federal, state, and local) regulations, accreditation standards, and institutional policies. These performance requirements apply to a broad range of laboratory activities, including personnel, safety, reports and records, claims billing, and waste disposal.

PREPARE FOR INSPECTION

Unannounced inspection for licensure is a routine practice. At a moment’s notice, the laboratory management team must produce numerous test procedures and quality report records that demonstrate performance over a two-year period. This requires a standard practice for documenting and maintaining records of test and instrument performance, quality control, written procedures, and reviews, so that these can be readily produced at the time of inspection.

COLLABORATE WITH INSTITUTIONAL DEPARTMENTS

There are accreditation standards and regulations that define key data elements that must appear on a test results report. However, the laboratory test report is also a medico-legal record. As such, all test results and comments are subject to interpretation in any legal proceeding.

STANDARDS OF PERFORMANCE

Laboratory management should verify and understand regulatory requirements at all levels of government: federal, state, and local. Federal regulations, including CLIA, routinely state that the
federal requirements are a minimum performance standard and do not supersede more stringent standards from state and local government agencies. It is also important to know the performance standards for any other regulatory agency, such as the College of American Pathologists, The Joint Commission, and the American Association of Blood Banks, that has accreditation oversight of the laboratory. The laboratory’s procedures and policies must meet the most stringent requirements imposed by the applicable regulatory entity or accrediting agency.

While laboratory inspectors arrive unannounced, they are fully prepared and expect to complete all aspects of inspection within a specific time frame for that site. It is imperative that the management team has defined a standard process for maintaining necessary and complete documents and records, so that these can be readily produced at the time of inspection.

The laboratory test result report is a medico-legal document and this applies to all information contained on the report, not just the test results. Statements that are simple and clear in everyday communication may not meet those legal standards in a court of law. As test result reports are created or revised, the management team is responsible for ensuring that these documents are properly reviewed and approved.

**PATIENT SAFETY**

The Institute of Medicine report published in 2000 clearly documented an unacceptable number of negative outcomes for patients. One of the key factors contributing to the problems in patient care is the failure of health care providers to define safe practice standards
and consistently enforce compliance. This report led to the development of the patient safety standards by numerous agencies, including The Joint Commission and the College of American Pathologists.

A key patient safety standard for the laboratory is to ensure positive patient identification (PPID). It is a required practice that PPID must use two unique patient identifiers. These identifiers usually include the patient’s complete name and one or more of the following: medical record number, complete birth date, or Social Security number. Once a specimen has been received in the laboratory and is in process, a common practice is to assign a unique accession number that may be used in conjunction with the patient’s name during the testing process.

The PPID practice is a critical step in the preanalytic phase of laboratory testing. Some accrediting agencies require that at the time of specimen collection, health care providers must use both “active and passive” identification methods. Passive identification requires the health care provider to verify the printed patient identifiers (on specimen labels, test requisitions, or computer screen) with a patient identification armband that must be attached to the wrist or ankle of an admitted patient. For active identification, the employee is required to engage the patient to verbally confirm his or her identity. A common practice is to request the patient to state his or her complete name, spell his or her last name, and provide his or her complete date of birth. The employee must verify that the patient’s responses match the printed identifiers (on specimen labels, test requisitions, or computer screen).

During the analytic phase, many test methods require manual processes. It is necessary to design workflow to ensure that the patient identity is correctly maintained with the specimen throughout testing.

Likewise, in the postanalytic phase, there are some circumstances that may warrant providing a verbal result to the clinician. It is imperative that this communication between both parties occurs with the use of PPID.
Regardless of the accuracy of the test method, a correct result provided for the wrong patient can have dire consequences, including loss of life. Laboratory leadership is responsible for defining clear procedures for patient safety, training staff to ensure competency, and consistently maintaining accountability for compliance by all staff at all times.

**PERFORM PROPER SPECIMEN COLLECTION**

When performing PPID, the phlebotomist often has multiple computer-generated labels that will be applied to each test tube. It is necessary to verify the patient identifiers on each printed label, not just on the first label.

In the outpatient setting, patients present for specimen collection, but do not receive a patient identification arm band. However, the patient does have a physician’s written test order with the patient’s complete name. A common practice is to use this document in lieu of the identification band. When performing passive and active patient identification, it is incumbent upon the phlebotomist to verify all computer-generated labels and the patient’s verbal identification with the written test order.

In addition to performing both passive and active patient identification, another requirement of PPID is to label all specimen containers at the patient’s side. This practice minimizes the risk of error that a label could inadvertently be applied to a specimen collected from another patient.

**VERIFY PATIENT IDENTIFICATION IN THE ANALYTIC PHASE**

Many test methods require that an aliquot of the specimen be manually transferred from the original specimen container to another container (tube, well, plate, cassette) for testing. It is absolutely necessary to verify the patient identification
on the original specimen container with the patient identification on the test container. Standard procedure is to perform this specimen transfer process on a one-by-one basis. The employee should only work with one patient at a time when transferring specimens from one container to another. This practice reduces the risk of erroneously transferring a sample from one patient to a container identified for another patient.

To minimize the amount of blood collected from a patient, it is common practice to use one tube of blood or body fluid for tests that are performed in multiple departments. The usual practice is to properly label new test containers and then aliquot samples from the original specimen. Patient identifiers on the original tube and aliquot tubes should be verified as the samples are dispensed.

If the initial test result is positive and the method requires a repeat test to validate an original positive result, it is recommended to obtain the original specimen container, if possible, and perform the repeat test with a sample from the original specimen container.

The importance of performing specimen transfer on a one-by-one basis cannot be overemphasized. It is analogous to the patient safety standard that requires that all specimen containers are labeled at the patient’s side. Both of these practice standards are intended to ensure that the specimen material in the container actually belongs to the patient identified on the container.

CONFIRM PATIENT IDENTITY WHEN PROVIDING VERBAL RESULTS

In the vast majority of patient care situations, information technology enables the clinician to have ready electronic access to test results. However, there are circumstances where a patient is in critical condition and the provider does not have immediate electronic access to results. The clinician will then call the laboratory and request a verbal report of
the results. At any given time, the laboratory is performing tests on dozens if not hundreds of patients. Patients with the same or very similar names can be undergoing testing in the same time frame. It is still necessary to obtain patient identifiers to ensure that the correct results will be provided on the correct patient.

STANDARDS OF PERFORMANCE

- The laboratory service is unlike any other health care service in that testing is performed in the absence of the patient. Thus, it is absolutely imperative to define procedures to ensure that both patients and patients’ specimens are accurately identified throughout the testing process. Staff must consistently comply with key performance standards for PPID.
- At the time of collection, a health care provider must perform both active and passive identification. In those circumstances where the patient cannot communicate, the laboratory should define appropriate actions in consultation with risk management. All labels must be applied to specimen containers in the presence of the patient.
- During the analytic phase, it is particularly important to design manual work processes to minimize the risk of erroneously placing patient specimens in an incorrectly labeled test container.
- All verbal communication must include unique patient identifiers. This will reduce the risk of confusing information about two different patients with the same or similar names.

QUALITY MANAGEMENT AND PERFORMANCE IMPROVEMENT

A defined quality management (QM) program is an essential tool to measure the success of clinical testing
services. A QM program must evaluate the production of test results across the entire performance spectrum: the preanalytic stage, the analytic stage, and the postanalytic stage.

The clinical leadership is responsible for identifying specific performance indicators to monitor against defined performance thresholds. Generally, tests are selected for monitoring based on the potential impact to patient care. “High volume” tests are those for which errors would affect a large number of patients. “High risk” tests are those for which errors would produce serious negative outcomes, including loss of life or limb. Performance indicators should include appropriate activities across the preanalytic, analytic, or postanalytic phases.

Performance thresholds may be defined in several ways. A common practice is to base a threshold on the required outcomes for patient care, such as a turnaround time (TAT) of 40 minutes for test results ordered on stroke patients for whom timely therapeutic drug intervention is required. Some performance benchmarks are determined by the accreditation standards, for example, the presence of two unique patient identifiers on specimen containers.

There are some tests that largely serve an outpatient population. In this setting, it is necessary to understand the industry standards established in the commercial marketplace such as acceptable wait times for patients in an outpatient phlebotomy service.

COLLECT AND ANALYZE DATA TO SUPPORT PATIENT OUTCOMES

To effectively evaluate routine performance of a test at any phase, one must first measure the activity and then define the performance standard. It is often necessary to conduct several observations and measure the time to complete the procedure from start to finish. Once the performance standard is
determined, then the performance threshold can be defined. Generally, an acceptable performance threshold is reported as the ability of the laboratory to complete the procedure and meet the performance standard with a high rate of success. A poorly defined performance threshold or inadequate data collection will lead to a failure to identify problems with the procedure, and thereby pose an undue risk to patient care.

**DEFINE PERFORMANCE STANDARDS**

When there is a failure to accurately define a performance standard, then it will not be possible to identify problems and take corrective action. Various performance indicators can be monitored such as the TAT for test results or patient wait times. A threshold must be appropriately defined for each performance indicator. The actual performance can then be compared to the threshold and evaluated as to whether the actual performance is acceptable or unacceptable.

**STANDARDS OF PERFORMANCE**

- Laboratory performance must be measured to ensure that the service meets or exceeds the defined standard. An appropriate performance threshold must be defined for the performance indicator.
- Measuring performance indicators requires that a representative sample must be collected for data analysis. Therefore, it is necessary to understand the unique characteristics that are associated with a particular test or procedure.
- It is important to consider the most applicable unit of measure when reporting a performance indicator. Many accrediting agencies frequently define acceptable performance as the ability to meet the performance standard at least 80% of the time.
- Generally, reporting an absolute number for performance indicators is an appropriate measure to
use where errors can have significant consequences such as an incorrect blood transfusion.

FINANCIAL MANAGEMENT

Provision of laboratory services requires resources: staff, equipment, and supplies. The leadership is responsible for acquiring resources and managing expenses in both the operating and capital budgets. It is also necessary to manage the revenue stream so that billing claims are submitted correctly and timely to maximize payment for services.

When assessing the expansion of an existing laboratory service or implementation of new test programs, the financial impact of the operating costs (if necessary, capital expenses as well) must be calculated. This financial analysis should also consider other factors. The opportunity cost of not choosing to pursue new or expanded programs must be assessed. This evaluation should include the impact on patient care such as a decreased length of stay (LOS) by decreasing result TAT. A financial assessment should also consider the pros and cons of “make versus buy” and determine whether it is cheaper and more efficient to “make” the test in the laboratory or “buy” it from a vendor.

Operating expenses should be routinely monitored on a monthly basis. Supervisory staff should review budget reports for actual expenses and confirm that both staff salary and supply costs are correct. It is important to engage staff so that they can contribute to controlling supply expense. Employees should understand that payment for services is not provided until 45 days or more from the date when the claim is submitted. Defined processes for inventory management should be structured to minimize unnecessary overstocking on supplies.

Conversely, billable test volume and revenues must be regularly reviewed as well. Management
oversight should include verification that the correct Current Procedural Terminology (CPT) codes are submitted on claims. The timeliness of claim submissions should be monitored as well to minimize the risk of nonpayment for services rendered.

**MONITOR SUPPLY EXPENSES**

Supply inventory should be managed so that reasonable quantities are maintained on site. Excessive supply inventory ties up financial resources that could be better spent on salaries, capital equipment purchase, new or expanded programs, and infrastructure needs.

The management team must routinely review actual expenses that are charged to the operating budget. Although much of the purchasing and accounts payable functions are electronically processed, there are still opportunities for error.

**MANAGE REVENUE**

In those few situations when a new test method is released with a new CPT code, it is important to verify that insurers will reimburse payment for the new test. However, there are circumstances when an existing test with a CPT code will be recommended as part of a new protocol for patient care diagnosis or treatment. This situation also warrants a review to determine that insurers will reimburse payment for the new use of the test.

Managers should use financial reporting tools to monitor the revenue cycle. A commonly used report is one that monitors the number of denied claims. This report can indicate problems that require the manager to investigate and take action to ensure that payments are received. Claims may be denied due to delays in submitting claims, incorrect CPT codes or modifiers, missing or incorrect diagnosis, and many other causes.
ASSESS PROGRAM OPPORTUNITIES

When evaluating the financial impact of a test, the potential effect on patient care must be considered as well. Upon initial examination, a test may have a modest financial impact on the laboratory budget. However, the results may allow providers to initiate treatment so that it substantially benefits both patient care and the institution’s financial picture.

STANDARDS OF PERFORMANCE

- Managers should routinely monitor supply expense and inventory. In addition, all laboratory staff must participate in effectively managing supplies to better control operating expenses. For every dollar in operating cash spent on supplies, one dollar less is available for salaries and capital equipment.
- The need to obtain the best price for supplies should be balanced with maintaining a reasonable inventory. Generally, payment for testing services is not received until 45 days or longer after the service has been performed. Thus, there is little benefit to investing operating cash to purchase a product that could last for many months or years.
- Operating budget reports should be reviewed monthly to ensure that appropriate supply expenses are documented. This includes verifying that all lease payments or reagent rental fees are correct, as per the contracts.
- Product inventory should be monitored and this includes those test supply items that are provided to clients. For those supplies that are provided to clients, there should be a reasonable association between the test volumes returned to the laboratory with supply items delivered to the client.
- Operational processes should support accurate and timely billing and claims submission to ensure that the full revenue payment is received for services
rendered. When implementing new test programs it may be necessary to confirm that insurers will provide reimbursement for a new service.

- Automated electronic billing must be used as new tests are added to the test order menu. This will ensure that claims are consistently and correctly submitted within contractual requirements.
- Financial management reports should be monitored to identify any problems with claims submissions and payment denials. The manager is responsible for taking corrective action to ensure that claims are accurate, complete, and meet contractual deadlines.
- The laboratory leadership is responsible for recognizing the larger impact of the laboratory service on patient care. There may be circumstances when incurring additional costs to provide a laboratory service is more than offset by an enhanced outcome for patient care.

## STAFF MANAGEMENT

The laboratory leadership is responsible for ensuring that qualified staff are hired and properly trained to provide accurate test results. Building a team of competent employees starts with the proper selection of candidates.

A well-defined training program is necessary to ensure consistent performance by all new employees. Orientation training must also include competency assessments to objectively measure actual task performance relative to the procedure standard.

Management must also define and communicate objective performance standards to staff. Employees should receive periodic reports so that they can clearly understand how they are completing their work as compared with the standard.
SELECT QUALIFIED CANDIDATES

The selection process starts with a well-defined job description that includes required education, experience, and skills. It is necessary to interview candidates and thoroughly assess their capabilities to meet the job requirements. However, it is equally important to evaluate the candidate’s interpersonal communication skills with other employees and to obtain objective references from the candidate’s current and previous employers.

DEFINE STANDARDS AND MEASURE ACTUAL PERFORMANCE

Performance standards should be clearly defined and communicated to staff so that they understand what is required to successfully accomplish tasks. It also enables coworkers to form a stronger sense of team since their work is measured based on objective standards and not subjective perception.

ADDRESS COMPENSATION ISSUES

Many factors can impact the ability to hire and retain staff. A competitive salary is one of the key elements for attracting and retaining employees. Laboratory management must identify those circumstances that can create a noncompetitive position with salaries. It is also important to engage the human resources staff to assist with collecting data and, if necessary, finding solutions.

ASSESS STAFFING LEVELS AND WORKLOAD

It is important to monitor test volume activity and identify when new staff are required. This allows the laboratory to continue to meet performance standards and minimize any disruption in service.
STANDARDS OF PERFORMANCE

- Evaluating candidates should include an assessment of their clinical expertise and their communication and interpersonal skills. When possible, candidates should be interviewed by colleagues and subordinates as well as by superiors.
- It is recommended that references are obtained from both current and previous employers when an applicant is the preferred candidate for a position.
- Clearly define objective and quantifiable performance measures for employees. This allows employees to understand what is expected and enables the laboratory to dependably support patient care.
- Identify conditions in the marketplace that can affect salaries and impact an employer’s competitive position. The human resources staff can provide the necessary data to justify appropriate actions to recruit and retain staff.
- Monitor test activity to determine staffing needs. When appropriate, analyze data and define when staffing coverage should be assigned.

LABORATORY SAFETY

The laboratory leadership team must ensure that the work environment complies with safety standards as defined by government regulations, accreditation standards, and institutional policies. In addition to implementing procedures, the staff must be educated to properly perform safety procedures and comply with them.

DEFINE PROCEDURES AND MONITOR COMPLIANCE

Since the mid-1980s, the Occupational Safety and Health Administration (OSHA) has required that personal
protective equipment must be used in all situations where there is a risk of biohazard exposure. In the laboratory, all staff are required to wear laboratory coats and gloves when handling specimens and performing tests.

Laboratory management must have defined written procedures for laboratory safety and must monitor compliance with these procedures. Staff are required to comply with all safety procedures, and laboratory leadership is responsible for holding staff accountable to properly perform work in accordance with the safety standards.

STANDARDS OF PERFORMANCE

- Laboratory management is obligated to implement defined procedures that meet safety requirements and monitor staff compliance with safety standards. Appropriate staff resources within the laboratory and from outside departments should be actively engaged with defining, implementing, and monitoring laboratory safety matters.

- Safety practices are applicable to all employees who perform those tasks that are covered by government regulations or institutional policies. As new safety initiatives are implemented, staff should be trained in proper practice and understand that there are consequences for noncompliance. It is management’s responsibility to monitor compliance and provide a mechanism to allow staff to report safety failures without fear of retaliation.

SPECIMEN LOGISTICS

An important step in the preanalytic process is the transport and delivery of specimens to the laboratory bench. It is imperative to understand the regulations that govern specimen transport and ensure that the actual practice is in compliance. The transport process must be designed to minimize the risk of losing
specimens as they are moved from the collection site to the laboratory bench.

There are Department of Transportation regulations that define numerous standards for transporting biohazardous materials. These regulations apply to both internal transport within the hospital from the patient “bedside” to the laboratory and external transport by courier services from an outside facility to the laboratory. A health care facility is accountable for contracted vendors. Therefore, it is incumbent upon the laboratory management to ensure that its contract with an outside courier service requires vendor compliance with regulations. The laboratory will be liable should a contracted courier service fail to meet Department of Transportation standards.

There should also be an efficient process to ensure that specimens are moved from the collection site to the laboratory bench. This process should be designed to move the specimens in a timely manner. Within a health care facility, it is generally easy to accomplish timely transport through the use of pneumatic tube transport systems. The widespread adoption of computerized provider order entry enables the laboratory to better manage pending test orders with the receipt of patient specimens. However, this process design is more challenging when moving specimens from satellite collection facilities to the laboratory.

**TRANSPORT SPECIMENS FROM SATELLITE SITES**

Specimens must be transported, at all times, in a manner that complies with all safety standards and minimizes risk of exposure to biohazardous materials. A process for “handing off” specimens from one location to another must be defined for both routine and nonroutine circumstances. Any number of communication tools (verbal, written, or electronic) can be appropriately applied to the situation in an effort to minimize the risk of losing specimens.
DEFINE EFFICIENT WORKFLOW PROCESS

Workflow should be designed so that staff can complete tasks with consistent efficiency. When possible, nonvalue-added tasks should be removed from the work process.

STANDARDS OF PERFORMANCE

- All specimen transport activities must comply with government regulations to ensure that there is minimal risk of biohazardous exposure or contamination. Laboratories are responsible to ensure that both their employees and contracted vendors acceptably perform these duties.
- The procedure for transporting specimens should be designed to ensure that there is documentation of a specimen’s location as it moves through the “transport system.” Documentation can be either electronic or paper and, when necessary, may need to include verbal communication as well.
- The workflow process should be efficiently designed to move the specimen from the preanalytic step to the bench for analysis. Nonvalue-added tasks should be removed and reassigned to designated staff.

TEST UTILIZATION

In the ongoing national debate concerning the growing consumption of health care services, increased expenditures for laboratory tests, particularly molecular diagnostics, face continued scrutiny to control costs. Evaluating test utilization should cover both inpatient and outpatient activity as well as those tests that are performed in the laboratory and those sent to an outside vendor.
Effectively managing test utilization produces both operational and financial benefits. By reducing excessive orders for tests, there is available capacity, with both staff and instruments, to implement new tests as the need arises and to absorb increased volume. It will also increase the net revenue margin for test services that are reimbursed through capitated payments.

CREATE PARTNERSHIPS WITH KEY CLIENTS

In its effort to appropriately manage test orders, the laboratory leadership should consider engaging external resources. These resources can include practicing physicians who are “thought leaders” within a medical specialty, information technology tools that can monitor activity, or consultative expertise from other areas such as finance, compliance, legal, or risk management.

MANAGE TEST UTILIZATION

Inappropriate utilization of some tests may occur because there is a poor understanding of the appropriate clinical indications. The laboratory clinical leaders can actively manage appropriate test utilization and constructively support the providers.

STANDARDS OF PERFORMANCE

- Patient care providers can obtain large amounts of diagnostic information from numerous tests. Whenever appropriate, the laboratory leadership should engage technology to assist in appropriately directing the selection and ordering of tests.
- Laboratory management must be effective stewards of its employees, instruments, and supplies. Test order patterns should be periodically monitored to
identify any excessive or unnecessary utilization. Appropriate test order activity will ensure that laboratory resources are efficiently supporting patient care and that there is available capacity to manage increased volume and implement new tests.

COMPETITIVE PERFORMANCE IN THE OUTREACH MARKET

Hospital laboratories have long recognized the opportunities of testing services in the outpatient market. The hospital has the capital infrastructure and capacity in the off-hour shifts that coincidentally is the time frame when most outreach testing is performed. A hospital laboratory also has an existing relationship with the physicians who admit patients and can build on that relationship.

Hospital laboratory leadership must recognize that performance standards in the outreach market are decidedly different from those for their inpatients. To succeed in outreach, the hospital laboratory must compete with commercial laboratories and at least meet, if not exceed, the performance standards in the outpatient marketplace. It is imperative to understand the service standards, conduct a SWOT (strengths, weaknesses, opportunities, and threats) analysis, and implement the necessary processes to meet the clients’ service expectations.

UNDERSTAND SERVICE REQUIREMENTS

The laboratory management team often attempts to capitalize on its “strength” of clinical expertise. Frequently though, the laboratory fails to adequately evaluate the clients’ service needs or provide the clinical consultation most needed by the ordering physician.
MANAGE STAFF PERFORMANCE TO SUPPORT OUTREACH MARKET

There are many service demands in the outreach market that do not coincide with service demands for inpatients and hospital unit staff. It is incumbent upon the laboratory leadership to understand the outreach service requirements, educate the staff, and implement any necessary workflow changes to support the clients’ service needs.

DEFINE INFRASTRUCTURE REQUIREMENTS

Hospital laboratories can engage support for the outreach market from a broad array of services provided by other departments such as finance and marketing. It is management’s responsibility to constructively engage colleagues in other departments and clearly communicate service needs and to assist with development and implementation.

STANDARDS OF PERFORMANCE

■ Once the specific laboratory services for the outreach market have been identified, it is imperative to evaluate the service requirements as defined by the clients. Service requirements can be very broadly defined from ease of test ordering and availability of specimen collection supplies to complete and comprehensive reports that are consistently delivered in a timely manner.

■ Management must ensure that there are adequate resources, both instrument and staff, so that clients’ service needs are reliably met.

■ The management team must educate staff to understand that the service needs for the “outreach” market are different, and problems must be appropriately addressed. When there is a failure at any step in the process (preanalytic, analytic, or postanalytic phases), there should be a defined procedure
that directs staff to notify the appropriate individuals who can assist with troubleshooting and problem resolution.

Competing in the “outreach” market often requires infrastructure support outside of traditional hospital laboratory operations. The laboratory manager must enlist key departments, such as finance, IT, and marketing, and engage them so that they fully understand the performance requirements to meet the clients’ service needs. Laboratory leadership should maintain constructive and ongoing communication with these external departments so that they can continue to support the service demands for the “outreach” clients.

**SELECTION AND MANAGEMENT OF REFERENCE LABORATORIES**

The volume of tests sent to reference laboratories generally comprises a relatively small percentage of total ordered tests. However, the expenses incurred for reference laboratory services often constitute a significant portion of the supply budget. With the introduction of molecular diagnostic tests, the costs for reference laboratory testing have been growing exponentially for more than a decade. Laboratory leadership must be actively engaged in the selection of vendors for reference testing service and the providers’ utilization of this resource.

**MONITOR UTILIZATION OF REFERENCE LABORATORIES**

For hospital-based laboratories, there are regulatory requirements that stipulate that the selection of reference laboratories must be determined jointly by the laboratory leadership and
the hospital’s medical staff. It is necessary for laboratory leadership to actively engage in the selection and use of reference laboratory facilities. The laboratory management team possesses the expertise to carefully evaluate the clinical quality, suitability of the test menu to meet patient needs, and service performance of the various vendors. These factors, in addition to cost, must be assessed when selecting a reference laboratory.

**EVALUATE VENDORS’ FULL SCOPE OF PERFORMANCE**

Given the explosive growth in molecular testing, managers are finding that costs for reference testing can consume 10% or more of total supply costs. It is certainly essential to consider costs when evaluating vendors for reference laboratory testing. However, clinical quality and service performance must also be considered. The vendor must meet defined clinical and service criteria so that the patient care needs are appropriately provided. Also, regulatory requirements hold the hospital laboratory accountable for any subcontractor’s performance.

**STANDARDS OF PERFORMANCE**

- Even when a contract is in place with a vendor, the cost for reference testing can spiral out of control when providers are given carte blanche to both order tests and select the reference testing site. Laboratory leadership must monitor “leakage” of tests to noncontracted vendors and, where appropriate, engage the clinicians and redirect the tests.

- Common business practice does require a competitive bid for those services that incur significant expense. However, the selection of a reference laboratory service should be evaluated on clinical performance and service requirements as well as cost. Consideration of these three elements can better ensure that the necessary diagnostic needs for patient care are addressed in addition to the business need to effectively control costs.
INSTRUMENT SELECTION FOR THE CLINICAL LABORATORY

The diagnostic laboratory industry is composed of manufacturers who compete in both the national and global marketplace. There are a large number of instruments available to meet the needs of both commercial and hospital-based laboratories of all sizes. It is imperative to clearly understand patient care needs in order to properly select instruments. Selection criteria should include clinical method evaluation, reagent stability, throughput capacity, ease of use and process control, and documented instrument performance and vendor service record.

UNDERSTAND PATIENT CARE NEEDS

The acquisition of any major instrument requires a thorough consideration of both current patient care needs and any new programs. Failure to do so may create a situation where the laboratory is unable to properly support patient care needs over the life of the instrument.

EVALUATE COMPETITIVE PRODUCTS

Many laboratory instruments are offered by manufacturers who compete in the global marketplace. As in any industry, these competitive forces drive manufacturers to continuously enhance their instruments and reagents. Laboratory management should engage in a competitive evaluation of products to ensure that it is providing the latest technology that best meets patient care needs and optimizes the efficient use of resources.

STANDARDS OF PERFORMANCE

The acquisition of new instrument technology must consider the current and future patient care
needs. Laboratory managers should collaborate with key departments, such as finance, business development, and marketing, to identify programs planned for future implementation that will require support from the new instrument. Clearly defining current and anticipated patient testing needs can improve the instrument selection process by providing for discounted costs triggered by volume targets and enhanced performance requirements from the vendor.

- An instrument reaching the end of its useful life presents an opportunity to comparatively assess new technology and select an instrument and reagent system that can best support patient care. Many instruments have a useful life of 5 to 7 years or sometimes more. However, the competitive forces in the marketplace drive technological innovations during that same period of time. These innovations can benefit patient care and laboratory operations and should be evaluated.

- Clinical performance is crucial to evaluating instruments. However, many other factors must be considered as well. Methods should be assessed to ensure that staff can work efficiently and in a manner that minimizes the risk of errors. The financial assessment should identify “hidden” costs that may be associated with quality control, instrument maintenance, or other factors such as a renovation expense that may be required for installation.

### SELECTION AND UTILIZATION OF A LABORATORY INFORMATION SYSTEM

The laboratory information system (LIS) represents a strategic investment in data management capabilities and capital funds. These laboratory test results provide essential information to providers for the diagnosis
and treatment of patients in both inpatient and outpatient settings. Therefore, the selection and ongoing operation of an LIS requires participation from a broad array of users, clients, and key stakeholders.

When selecting an LIS, the users, both pathologists and technologists, must identify performance requirements such as capabilities for managing and processing test orders, interfacing with various instruments and other software information systems, manipulation of data to support numerous requirements for results reporting, and supporting ancillary functions such as billing, client services and QM, and process control. A dedicated team from across the clinical and anatomical pathology services should define and rank the performance requirements. These criteria can serve as an objective tool to evaluate each LIS application.

Laboratory clients include physicians and nurses. They may have test order or result report needs for patient care that should be considered when assessing LIS applications.

Key stakeholders include other departments that must interact on some level with the LIS. For example, the information technology group provides services such as network support or interface design and maintenance associated with other software applications. Finance is another department that may rely on the LIS for obtaining coding data and completing claims submission. It is necessary to engage these key stakeholders and assure that the LIS will not compromise any necessary operational processes with external departments.

Lastly, the management team must understand the level of staff expertise that is required to support the LIS, including adequate staff coverage and the necessary training of users.

**DETERMINE STAFF SUPPORT FOR LIS**

The laboratory leadership should manage the LIS installation so that its performance is optimized to support data
management. When extensive custom modifications are required for the software, management should understand and plan for the necessary support resources.

CONFIRM COMPATABILITY WITH OTHER SOFTWARE APPLICATIONS

There are a number of software applications that must be interfaced to an LIS. The “owners” of these external information systems should participate in evaluating the new LIS products to ensure that there is an acceptable degree of compatibility. Failure to do so can create unnecessary problems.

SUPPORT CLIENTS’ SERVICE EXPECTATIONS

Periodically, a laboratory will expand its test menu. When providing a new service, it is important to understand the service requirements that clients may have for these result reports.

STANDARDS OF PERFORMANCE

- It is the responsibility of laboratory leadership to understand and define the resources required to support the LIS. Resource needs can vary depending on the complexity of the LIS. A highly customized LIS will require staff with programming expertise, whereas a simple “turnkey” application will require vendor-trained staff.
- The LIS provides critical support for data management of test orders and results. Given the laboratory’s key role in patient diagnosis and treatment, it is absolutely essential that the LIS can effectively communicate with various independent software applications. The laboratory leadership is responsible for engaging key stakeholders of external software applications and ensuring that all necessary performance requirements can be met.
When selecting a new LIS, a laboratory team should be formed with representation from across numerous subspecialties. The team should define and prioritize performance requirements that can then be used as an objective tool to measure capabilities of various LIS applications.

Clients’ needs for test ordering or result reporting should be solicited. They should be engaged when evaluating a new LIS and also when there is a service update.

**BIBLIOGRAPHY**

A number of textbooks are available that can provide a more extensive discussion of management concepts and practices that are applicable to the laboratory setting. The following is a brief list of resources for the interested reader:


