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Clinical Microbiology Newsletter



Vol. 28, No. 1

January 1, 2006

Laboratory-Acquired Infections: Are Microbiologists at Risk?

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Abstract

Exposure of laboratory workers to infectious agents in the clinical microbiology laboratory continues to be an occupational risk. This risk is mitigated by the application of safety guidelines issued by regulatory agencies and professional organizations. The Clinical and Laboratory Standards Institute (formerly NCCLS) published a guidance document (M29-A3) in 2005 on the risk of transmission of infectious agents in the laboratory, preventative measures to reduce risk, and management of exposure to infectious agents. The key to a safe workplace is employees who are knowledgeable of the routes of transmission of infectious agents in the laboratory setting and apply safety principles and work practices to reduce the risk.

Introduction

The Occupational Safety and Health Act of 1970 provided the regulatory basis for ensuring that all workers in the United States have a safe and healthy work environment. Laboratory management is responsible ultimately to implement the procedures and work practices necessary to ensure a safe work environment and to adequately train and educate their employees in laboratory safety. This is a challenging task for clinical microbiology laboratories as globalization increases the dispersion of infectious agents throughout the world, climate changes expand the endemic ranges of some microbial pathogens and their vectors, new microbial pathogens are recognized, antimicrobial resistance increases, acts of bioterrorism are threatened, and new technologies and tests are introduced into the laboratory. These events expand the potential exposure of clinical microbiologists and other health

care workers to infrequently encountered infectious agents. Considering all of these factors, it is increasingly difficult for regulatory agencies and professional organizations to provide detailed up-to-date safety guidelines for all new situations. The Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) recently published guidelines for the protection of laboratorians from occupationally acquired infections (1). A portion of this report is a review of the safety recommendations outlined in that document.

What Is the Risk?

For the past 35 years, there has been general agreement that clinical microbiologists are at risk from laboratory acquired infections (LAIs) but that the risk cannot be accurately quantitated due to the lack of a systematic reporting system and adequate screening of workers for occupationally-acquired infections. The exception has been the national reporting of occupationally acquired HIV infections to the Centers for Disease Control and Prevention (CDC). For other LAIs, risk is estimated based on historic data, case reports, periodic surveys of laboratories, and personal communications (2). The his-

torical data published by Pike (3,4) were instrumental in identifying the risk associated with working in clinical and research laboratories and documenting the common routes of transmission (Table 1). However, these data were published in the 1970s and are not reflective of modern laboratories, due in part to the implementation of many safety procedures and work practices based on Pike's observations. Today, the general consensus is that LAIs are infrequent but occur most often in individuals who work in the clinical microbiology laboratory (5,6). Wilson and Reller (7) estimated that the annual rate of LAIs in the U.S. is approximately 1 to 5 infections per 1,000 employees.

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Accepting the premise that clinical microbiologists are at risk for a LAI, the goal of laboratory management (and the laboratory worker) is to minimize that risk. To achieve that goal, a risk assessment of all work practices should be an integral, on-going part of laboratory operations. A risk assessment is simply a series of actions taken to recognize or identify hazardous conditions in the laboratory and to measure or estimate the risk or probability that an untoward consequence will occur because of the hazard. The severity of the consequence of infection (morbidity and mortality) is also factored into the assessment of risk.

Factors that influence risk include the prevalence of the agent in the community, the route of transmission (e.g., aerosols, contact, ingestion, and percutaneous inoculation), laboratory procedures that produce aerosols or splashes (e.g., centrifugation, mixing, or pipetting), the morbidity and mortality associated with the infection (e.g., HIV or *Salmonella*), amplification of the agent in the specimen or culture, culture volume, and availability of a vaccine or adequate postexposure therapy.

The prerequisites for performing a risk assessment include knowledge and application of safety principles, the pathogenicity and mode of transmission of infectious agents, laboratory practices that generate unsafe conditions, and availability of medical surveillance or postexposure prophylaxis. In short, identify the hazard, determine the degree of risk associated with the hazard, and employ procedures to mitigate the risk. Risk assessment is the easy part; ensuring that laboratory workers use safe work practices at all times is more difficult to achieve.

Table 1. Common laboratory routes of exposure to infectious agents

Route	Microbiological practices/accident
Inhalation	Procedures that produce aerosols: Centrifugation Mixing, sonication, vortexing, blending Spills and splashes Pouring/decanting culture fluids Manipulation of inoculating loop
Inoculation	Needlestick Lacerations from sharp objects (e.g., blades, broken glass)
Ingestion	Splashes to the mouth Placing contaminated articles/fingers in mouth Consumption of food in the laboratory Mouth pipetting
Contamination of skin and mucous membranes	Splashes Contact with contaminated fomites

Exposure Risks

Infectious agents include all pathogenic bacteria, fungi, viruses, and parasites that may be transmitted to laboratorians through exposure to body secretions, fluids, and tissues, and work procedures and practices used in the laboratory. Bacteria cause most LAIs, while parasites are infrequent causes. For an infectious risk to be present, there must be a susceptible host, a route of transmission, and a concentration of the infectious agent sufficiently to cause infection. Organisms that pose the greatest risk to laboratorians include the bloodborne pathogens (BBP) (e.g., HIV, hepatitis C virus [HCV], and hepatitis B virus [HBV]), because of the severity of infection and lack of curative therapy; new or emerging agents (e.g., West Nile virus [WNV], and severe acute respira-

tory syndrome-coronavirus [SARS-CoV]); due in part to a lack of knowledge and experience handling these organisms; and some bioterrorism agents, because identification is often delayed or is incorrect. Other potential exposure risks for which there are little published safety data include the introduction of new methods and instrumentation prior to performing a risk assessment and the increasing prevalence of multidrug-resistant organisms (MDRO) recovered in the laboratory.

The key to prevention is understanding the exposure risk. Historical data have clearly identified four common routes of transmission in the laboratory: (i) percutaneous inoculation (e.g., needles, scalpels, and broken glass), (ii) inhalation following aerosolization of pathogen (e.g., centrifugation, mixing,

flaming loops), (iii) cutaneous exposure through splashes or contact with contaminated fomites, and (iv) ingestion by placing contaminated objects in the mouth (Table 1). Although most agents are associated with a primary route of transmission (e.g., BBP and percutaneous inoculation), they can be transmitted in the laboratory by multiple routes. For example, the primary mode of transmission for *Mycobacterium tuberculosis* is by inhalation, but cutaneous infection has occurred following percutaneous inoculation (8). Therefore, safety procedures and programs should focus on work practices, containment equipment, and facilities that interrupt the transmission of agents by all routes and therefore protect against all LAIs.

Laboratory-Acquired Infections

The following section contains examples of infectious agents that may cause or pose a risk of infection to workers in a clinical microbiology laboratory. The degree of risk varies from high for the BBP to unknown for SARS-CoV. The brief summary for each agent identifies the laboratory hazards and recommended precautions to prevent or reduce the risk of infection and is, in large part, compiled from references 1 and 9). A more complete listing of infectious agents that pose a risk to laboratorians is found in *Biosafety in Microbiological and Biomedical Laboratories* (9).

Bloodborne viruses

Occupational exposure to the BBP, specifically HIV, HCV, and HBV, was recognized early as a significant risk to laboratory workers, as well as other health care providers who handle or are exposed to blood and other potentially infectious material from infected patients. The number of infected individuals in the U.S., the severity of infection, and the lack of adequate therapy resulted in the passage of a federal regulation addressing occupational exposure to BBP (10). The risk from these agents to the exposed health care worker is influenced by the prevalence of the virus in the population, the concentration of virus in the blood or body fluid, the volume of blood or body fluid involved in the exposure, and whether postexposure treatment is administered in a timely fashion (1).

Laboratory Hazards

All three viruses are found primarily in blood and body fluids but may be present in a number of other body substances (1). The primary hazards are percutaneous inoculation, splashes to the mucous membranes, and contact exposure with non-intact skin.

Recommended Precautions

Biosafety Level (BSL) 2 practices, containment equipment, and facilities are recommended for all procedures involving blood and other potentially infectious material. Facial protection should be worn when performing activities that may result in splashes. Aerosol transmission does not appear to be a significant risk. All laboratory workers must be offered the HBV vaccine.

Neisseria meningitidis

Laboratory-acquired meningococcal disease is a documented but infrequent hazard to laboratory workers (6). Meningococcal isolates recovered from sterile sites (e.g., blood and cerebrospinal fluid [CSF]) may have increased risk of infection for clinical microbiologists. There appears to be little risk to other laboratory workers who do not work on cultures.

Laboratory Hazards

The agent is present in pharyngeal exudates, blood, and CSF. Infectious aerosols, droplet exposure to mucous membranes, and percutaneous inoculation are the primary hazards to laboratory personnel.

Recommended Precautions

BSL2 practices, containment equipment, and facilities are recommended for all activities involving potentially infectious body substances and cultures. Activities that may produce aerosols or splashes (e.g., subculturing of blood bottles and preparing bacterial suspensions) should be performed in a biological safety cabinet (BSC) or behind a splashguard with appropriate personal protective equipment (PPE), such as a mask. Vaccination should be considered for personnel regularly working with infectious material. Antimicrobial prophylaxis should be available to laboratory workers who inadvertently manipulate invasive *N. meningitidis* isolates on an open bench without effective protection from droplets or aerosols (6).

Francisella tularensis

Although fewer than 200 cases of tularemia are reported annually in the U.S. (11), *F. tularensis* has been the third most common LAI over the past 35 years, occurring primarily in individuals who work in research laboratories. Few infections have occurred in clinical laboratory workers, most likely related to the low prevalence of the disease in the U.S. However, risk is always present because of delayed recognition of the organism by many clinical microbiologists (12). The delayed identification results in manipulation of the culture on an open bench, increasing the unnecessary exposure of laboratory personnel to potential aerosols. *F. tularensis* is a select agent because of its potential use as an agent of bioterrorism (<http://www.bt.cdc.gov>; www.cdc.gov/od/sap).

Laboratory Hazards

F. tularensis is recovered from a variety of specimens, such as blood, body fluids, skin lesion exudates, CSF, respiratory secretions, and urine. Infection may result from direct skin/mucous membrane contact with cultures, ingestion, parenteral inoculation, and exposure to aerosols or splashes. Manipulation of cultures on an open bench presents the greatest risk to laboratory personnel. The infectious dose by aerosol is approximately 10 to 50 organisms, while approximately 10⁸ organisms are required by ingestion (<http://www.usamrid.army.mil/education/bluebook.html>).

Recommended Precautions

BSL2 practices, containment equipment, and facilities are recommended for transport and plating of clinical specimens. BSL3 practices, containment equipment, and facilities are recommended for all activities involving manipulations of cultures. Vaccination for *F. tularensis* is available and should be considered for personnel who routinely work with infectious material or cultures.

Brucella spp.

Brucellosis is an uncommon disease in the U.S. where 100 to 200 cases are reported annually. However, *Brucella* spp. are highly infectious because the infectious dose by an aerosol is only 10 to 100 organisms (<http://www.usamrid.army.mil/education/bluebook.html>). All *Brucella* spp. have been implicated in

LAI, and they may account for up to 2% of all LAIs (13).

Laboratory Hazards

Brucella spp. are present in blood, bone marrow, CSF, tissue, semen, and occasionally other specimens. Aerosols created during manipulation of cultures are the primary mode of transmission in the laboratory. Other routes include parenteral inoculation and splashes to eyes and mucous membranes.

Recommended Precautions

BSL2 practices are recommended for handling clinical specimens. BSL3 practices, containment equipment, and facilities are recommended for all manipulations of cultures. No licensed vaccine is available in the U.S.

Mycobacterium tuberculosis

Acquisition of tuberculosis is a recognized risk for laboratory workers who must handle clinical specimens and cultures containing *M. tuberculosis*. The magnitude of the risk is dependent on the prevalence of tuberculosis in the community, the number of patients treated for the disease, working in specific areas of the laboratory (e.g., morgue or mycobacteriology laboratory), and the effectiveness of control measures. The infectious dose for *M. tuberculosis* is believed to be 1 to 10 organisms (14). In the most recent published data from the 1980s, the rates of infection in laboratory personnel ranged from 0.3 to 0.5 per 1,000 persons and an unbelievable 26.3 per 1,000 persons who processed specimens in anatomical pathology (14).

Laboratory Hazards

The agent can be recovered from sputum, urine, gastric lavage specimens, CSF, other body fluids, and tissues. The greatest risks to laboratory workers are from aerosols generated from activities involving manipulations of cultures, preparation of frozen sections, or performing an autopsy on an infected individual.

Recommended Precautions

BSL2 practices, containment equipment, and facilities are adequate for non-aerosol-generating activities involving manipulations of clinical specimens. All aerosol-producing procedures must be performed in a BSC. The propagation and culture of *M. tuberculosis* must occur in a BSL3

facility, using BSL3 practices and containment equipment. All personnel should be tested at least annually for exposure to *M. tuberculosis* (15).

SARS-CoV

Following the 2003 outbreak of SARS-CoV, there were two reports of infections in research laboratory workers. To date, there have been no reports of infections in clinical laboratory workers, but until more experience is gained in handling clinical specimens and viral cultures, appropriate precautions should be employed.

Laboratory Hazards

The virus is present in blood, feces, urine, upper and lower respiratory tract specimens, body fluids, and tissues. Airborne dissemination is thought to occur most often by respiratory droplets, possibly by aerosols, contact with contaminated fomites, or by some unknown route (16-18).

Recommended Precautions

BSL2 practices, containment equipment, and facilities should be used for activities involving manipulation of clinical specimens. All aerosol-generating activities should be performed in a BSC, and the appropriate PPE should be worn (gloves, gown, eye protection, and a N95 mask). Centrifugation of potentially infectious material should be performed in a sealed rotor. The propagation of the virus should occur in a BSL3 facility. A medical surveillance plan should be used for employees who handle SARS-CoV specimens or cultures. No vaccine is currently available.

VHF viruses

The sporadic outbreaks of viral hemorrhagic fever (VHF) viruses (e.g., Marburg virus) in Africa raise the possibility of encountering an infected patient in the northern hemisphere. The VHF viruses are recovered from blood, respiratory and throat secretions, urine, semen, and tissues. Some agents may be transmitted through aerosols or droplets, parenteral inoculation, and contact with contaminated materials. When a patient is infected or believed infected by a VHF virus, the CDC should be contacted prior to collection of specimens. Specimens that may have been collected and all cultures should be placed in a BSL3/BSL4 facility until they can be forwarded to the CDC or

destroyed. All activities involving specimen handling and cultures should be performed in a BSL4 facility. All personnel with exposure to the material should be placed in a medical surveillance program. No vaccine is available. Guidelines for handling unknown or suspected VHF viruses are available (www.asm.org; www.bt.cdc.gov).

WNV

In 1980, the Subcommittee on Arbovirus Laboratory Safety reported 15 cases of LAIs, one of which was due to aerosol exposure. Two recent cases resulted from percutaneous inoculation during work with infected animals (19).

Laboratory Hazards

WNV is present in the serum, blood, tissue, and CSF of infected humans. Percutaneous inoculation with infectious material is probably the greatest risk to laboratory workers. Other potential risks include contact exposure of nonintact skin and aerosols.

Recommended Precautions

BSL2 work practices and facilities are recommended for handling specimens. Manipulation of material containing a high concentration of virus (e.g., material from a fatal case) and aerosol-generating procedures should be performed in a BSC. BSL3 facilities and practices should be employed for WNV viral cell cultures. There is no available immunization against WNV infection.

Stool pathogens

It is estimated that 38 to 211 million cases of acute gastrointestinal illness occur annually in the U.S. (20). Of the bacterial pathogens, *Salmonella* spp., *Shigella* spp., Shiga toxin-producing *Escherichia coli*, and *Campylobacter* spp. are more frequently involved in gastrointestinal disease, probably related to the low infective dose (100 to 1,000 organisms) needed to cause infection (20).

Laboratory Hazards

The agents are present in feces and are rarely recovered in urine, blood, or other body fluids. Ingestion is the primary mode of transmission, and parenteral inoculation is a potential risk. Ingestion can occur from splashes or any activity that results in a contaminated article (e.g., finger or pencil) being placed in the mouth.

Recommended Precautions

BSL2 working practices, containment equipment, and facilities are recommended for activities involving manipulations of clinical specimens and cultures.

Multidrug-resistant organisms

The emergence of vancomycin-resistant and vancomycin-intermediate *Staphylococcus aureus* (VRSA and VISA) and other MDRO is another potential safety challenge for clinical microbiologists. There are published data that document the survival of vancomycin-resistant enterococci and methicillin-resistant *S. aureus* in the inanimate hospital environment (21). However, only indirect evidence suggests that contaminated fomites lead to increased nosocomial infections (21). There are no published reports of the transmission of or colonization or infection by MDRO among laboratory workers, but there is excellent documentation that contamination of laboratory surfaces occurs (22) and may pose a risk to laboratory workers. Therefore, it is prudent to decontaminate work surfaces at least daily, practice proper hand hygiene, and when appropriate, use barrier precautions to reduce skin and nasal colonization or infection. Similarly, VISA or VRSA cultures should be manipulated in a BSC to prevent accidental transmission to a laboratory worker.

Prevention of Laboratory Acquired Infections

Many LAIs occur because laboratory personnel do not appreciate the increased exposure risk associated with an incorrect or delayed identification of a highly infectious agent (e.g., *Brucella* spp. or *F. tularensis*) that often leads to performing aerosol-producing procedures outside of the BSC. The keys to the prevention of LAIs are knowledgeable personnel who are aware of the potential hazards, understand the various modes of transmission within the workplace, and are proficient in safe microbiological practices and techniques, and a laboratory-specific safety manual (Table 2). Ideally, the microbiological characteristics of BSL3 organisms that commonly cause LAIs should be added to the routine bench procedures as a constant reminder to the laboratory worker (12).

Laboratory safety should focus on

Table 2. Topics for employee safety training

Epidemiological characteristics of infectious agents (especially BSL3 agents)
Standard precautions and hand hygiene
Criteria for BSL1 to BSL4
Use of a biological safety cabinet
Use of personal protective equipment
Safe work practices and aseptic technique
Disposal of biohazardous waste
Safe use of laboratory equipment (e.g., centrifuge, autoclave)
Disinfection and sterilization
Postexposure management

Table 3. Examples of safe work practices and procedures

Provide annual safety training for all laboratory workers
Process specimens in a biological safety cabinet
Use appropriate containment equipment for aerosol-generating work practices
Practice standard precautions and hand hygiene
Use personal protective equipment when appropriate
Dispose of sharps and biohazardous material safely
Enforce safety policies and procedures
Decontaminate work surfaces daily

training employees to practice standard precautions at all times, process specimens in a BSC, use appropriate containment equipment and safety barriers when necessary, decontaminate work surfaces at least daily and following a spill, and properly dispose of hazardous waste (Table 3).

Standard precautions

Standard Precautions dictate that all patients and their specimens (except sweat) be handled as if they were infectious and capable of transmitting disease. This concept is fundamental to safety in the microbiology laboratory and, if practiced, will prevent or reduce the contact of potentially infectious material with the skin or mucous membranes of laboratorians (1). Two key components of laboratory safety are proper hand hygiene (23) and the use of gloves when performing routine laboratory work with blood or other potentially infectious material or contacting surfaces potentially contaminated with these materials (1). Frequent hand hygiene is extremely important, and the hands should be washed with soap and

water (or an alcohol-based product) after removal of gloves, after accidental skin contact with potentially infectious material, or after a break in a glove. Soap and water should be used when hands are visibly contaminated with potentially infectious material. Whether gloves should be required for routine bench work in the microbiology laboratory is a question that has been discussed for years. There is no doubt that laboratory surfaces are contaminated, (22) but to my knowledge, there is no specific regulation that requires the use of gloves while manipulating cultures. However, clinical microbiologists should be given the option of wearing gloves, if they choose.

Laboratory practices and techniques

The routine and special practices and techniques used in the microbiology laboratory have been described for BSL1 through BSL4 (9). Most routine clinical microbiology laboratories use BSL2 techniques and practices. If the laboratory performs cultures for BSL3 agents (e.g., *M. tuberculosis*), BSL3 practices and facilities should be

employed. Laboratory workers in a BSL2 facility should be suspicious of bacteria that are difficult to identify and that exhibit characteristics of *Brucella* spp. or *F. tularensis*. Activities involving manipulations of these organisms should be conducted in a BSC or behind other containment equipment. The workup of the occasional BSL3 organism (e.g., *Brucella* spp.) must be performed in a BSC.

Acknowledgements

I am indebted to the other authors of M29-A3; Kevin E. Bove, Donald R. Callihan, Martin S. Favero, Harvey T. Holmes, Beverly M. Kovanda, Michael A. Noble, and Randy A. Taplitz, and to the staff at CLSI.

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