Nebraska Isolation and Quarantine Manual
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Laboratory Operations

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Background

Laboratory safety represents one of the more difficult challenges associated with isolation and quarantine care. In these situations, laboratory managers and the isolation/quarantine team must balance the safety of laboratorians and health care workers with the ability to provide diagnostic and other clinical laboratory data that may be critical for clinical or public health decisions. With appropriate planning, both considerations can be adequately addressed.

An asymptomatic individual placed in quarantine following exposure to a high-risk pathogen may not require laboratory support during the infectious agent’s incubation period. Exceptions might include serological testing to assess the individual’s immune status, bloodwork to assess response to an experimental vaccine or other postexposure prophylactic, or baseline assessment of a number of parameters (blood counts, chemistries, liver functions, banked serology) for future comparison if illness were to occur. Additionally, an asymptomatic person in quarantine may need some laboratory support for an underlying condition that requires routine monitoring (i.e., the monitoring of glucose levels in a diabetic patient or the exclusion of other potential comorbid events). For most highly hazardous communicable diseases (HHCDs), specimens from
exposed patients without symptoms can be handled in a standard biosafety level 2 clinical laboratory using routine biosafety practices without enhanced precautions.

Once a person becomes symptomatic or is suspected of being capable of shedding infectious agent, the risk calculation changes and their disease becomes potentially communicable. They are then placed in isolation and reclassified as a person under investigation (PUI) for a high-risk pathogen, and specimens will be collected and handled following in-house protocols developed for a PUI in consideration of guidance from the Centers for Disease Control and Prevention (CDC). The periods of communicability (and the specimens at highest risk for transmission of infection in the laboratory) for various HHCDs warranting isolation (and potentially quarantine) are described in table 17.1.

Incubation periods differ among various diseases, but the contagious period for most pathogens generally begins after disease signs or symptoms are present. This principle is well established for the viral hemorrhagic fevers (VHFs). Influenza is a notable exception to this rule, and research has shown that influenza virus shedding and infectivity may occur 24 hours prior to the onset of symptoms. For other pathogens (SARS and MERS coronaviruses, for example) insufficient evidence is available to definitively establish the window of infectivity.

Specimens collected after the onset of signs and symptoms may carry a concentration of the pathogen that could result in infection of laboratorians from specimen collection, transport, analysis, and disposal. Exposure can occur through direct contact with mucus membranes, a sharps injury, or from inhaling an aerosol. Laboratorians should recognize, on a case-by-case basis, that certain specimens are riskier to handle than others. For example, respiratory specimens from an individual with a severe acute respiratory infection, such as coronavirus or avian influenza virus, will contain a higher concentration of virus than other body site specimens, whereas a patient infected with Ebola virus or Marburg virus may have extremely high concentrations in the blood, depending on the period of illness. Laboratorians, however, should recognize that any specimen could potentially contain a viable pathogen. For example, studies have identified virus in a variety of body fluids in patients with
Ebola virus disease, and virus shedding in stool was linked to clusters of SARS transmission during the 2003 outbreak.

Preanalytical Processes

As noted above, risk assessment for collection and transport of patient specimens is pathogen-specific. Specimens from asymptomatic persons in quarantine may be handled and analyzed in a manner identical to routine specimens, with the exception of novel influenza virus or other pathogens with potential for presymptomatic infectivity. Communication between the medical care team and laboratory personnel is essential during this observational period, as the situation could change rapidly and alter the risk dynamics. Assurances also need to be made to laboratory personnel that any specimen sent to the clinical laboratory will be appropriately labeled for tracking if an HHCD is subsequently identified. When a quarantined individual becomes symptomatic (now classified as a PUI), the laboratory protocol for collection and transport of specimens from this patient will need to be activated following communication between clinicians and the laboratory.

Laboratories are required to follow the appropriate local, state, or federal guidelines for specimen transport and surveillance reporting, which are dependent on the agent suspected. Facilities should plan and exercise collection and movement of specimens within the facility as well as packaging and shipping specimens for diagnostic testing outside of the facility, that is, to a Laboratory Response Network facility or to the CDC. All isolation unit and laboratory staff should be trained on US Occupational Safety and Health Administration (OSHA) Bloodborne Pathogens Standard (29 CFR 1910.1030), and personnel responsible for packaging and shipping potentially hazardous specimens should be proficient in US Department of Transportation Hazardous Materials Regulations (HMR) 49 CFR 171-180.

As a rule, specimens should be packaged for transport inside the isolation unit using redundant and shatterproof containment and surface decontamination, whether destined for the in-house laboratory or for an outside diagnostic facility. Procedures should minimize direct con-
tact with specimen containers, facilitate rapid movement of specimens from isolation unit to destination, and minimize the number of people involved in the chain of movement. CDC guidelines for packaging and transport of a specimen that contains or may contain Ebola virus provide a reasonable general guide and can be accessed at https://www.cdc.gov/vhf/ebola/laboratory-personnel/specimens.html.

**Analytical Processes**

Safe handling and testing of specimens from a patient with the potential to have an HHCD in the clinical laboratory present particular laboratory biosafety challenges, and plans and procedures should be worked out in advance to enable safe operations and provide confidence for facility staff and the community at large. As with other activities in the isolation unit, the hierarchy of controls provides a framework for safe laboratory operations.

Ideally, facility plans can minimize or even eliminate the involvement of the main clinical laboratory in specimen processing and analysis. In many cases, point-of-care and small benchtop analyzers can facilitate bedside and satellite laboratory testing within the isolation unit itself, negating the need to move specimens outside of containment. In some cases, a small automated blood culture system within the isolation unit satellite lab are used.

In the event that bedside or in-unit laboratory testing is not feasible, utilization of the clinical laboratory should weigh the value of clinical laboratory information to be garnered from analysis with the risk presented to laboratory staff. Basic clinical laboratory testing, such as blood counts and chemistries, are critical in providing appropriate clinical care for patients with HHCDs, many of whom may be critically ill. The CDC’s recommended test menu for the care of patients that are infected with Ebola virus can be accessed at https://www.cdc.gov/vhf/ebola/laboratory-personnel/safe-specimen-management.html.

Risk to staff can be mitigated through engineering and administrative controls that confine sample handling and testing to a remote or contained area of the laboratory with dedicated staff and equipment. If present, a clinical biosafety level 3 laboratory, such as a mycobacteriology
or mycology laboratory section, provides preexisting controls that may be leveraged. Temporary containment structures that provide negative air pressure with HEPA-filtered exhaust can be purchased commercially. Specimens also could be processed and tested at off hours, allowing all unnecessary staff to vacate the lab and any cleaning or decontamination processes to occur prior to reinitiating normal laboratory shift work. Ideally, processing and testing should occur in automated and completely closed-loop analyzers and avoid procedures (such as centrifuging) with potential for aerosol generation. Laboratory staff should thoroughly investigate manufacturer guidance for the specific equipment located in the laboratory to understand any potential risk for aerosol generation and recommended decontamination procedures.

Finally, laboratory personnel handling HHCD specimens should wear appropriate personal protective equipment (PPE) for the specific pathogen in question. While some high-risk pathogens may present low epidemiological risk for aerosol transmission in the clinical setting (such as the filoviruses), certain laboratory procedures can create a higher chance for aerosolization. Aerosol protection with N-95 respirators or powered air-purifying respirators (PAPRs) is therefore generally recommended for laboratory staff working with specimens from a patient with an HHCD.

**Postanalytical and Other Processes**

Timely and accurate reporting of results closes the loop for clinical laboratory testing. To limit opportunities for communication breakdown, standard reporting processes should be used when possible. For security or other reasons, facilities may choose not to use standard health system inpatient or outpatient medical record systems for quarantined persons or patients in isolation. This situation will require precise communication between the medical care team and the laboratory, and alternate reporting systems should be planned and exercised in advance.

For clinical and public health applications, excess clinical material from specimens that have been collected from a person in isolation or quarantine should be appropriately stored if the need for additional testing is anticipated. Many high-risk pathogens are on the select agent list, and their handling is therefore subject to rules and regulations of
the US Federal Select Agent Program (42 CFR Part 73). While clinical specimens are generally exempt from the requirements of select agent regulations, specimens from which a select agent has been confirmed are subject to these regulations 7 days after the conclusion of patient care. Any identification of a select agent from a clinical specimen should be reported to appropriate authorities immediately, and laboratory directors should contact the Division of Select Agents and Toxins at the CDC for specific guidance on handling these specimens. More information can be obtained at the program website: https://www.selectagents.gov/index.html.

Any laboratory supporting isolation and quarantine units should maintain a staff monitoring program to identify individuals who may have handled specimens from isolation patients or a quarantined individual, should this individual become ill from a high-risk pathogen. This will require that an occupational health program be implemented to allow monitoring of laboratorians and other individuals handling the specimens for the complete period of incubation (similar to what may be done for clinical providers exposed to patients with potentially hazardous infections), starting on the day with the last exposure to the specimen.

Finally, any HHCD that is thought to be from a potential deliberate exposure will be subject to investigation by appropriate law enforcement and counterterrorism authorities. In these cases, additional protocols for handling of specimens, such as maintenance of a chain-of-custody, may need to be implemented in conjunction with law enforcement protocols.

**Conclusion**

Laboratorians recognize the risks involved in handling human specimens on a routine basis. These personnel use appropriate PPE and follow the standard biosafety practices developed for the laboratory handling of specimens on a daily basis, which should facilitate planning for handling specimens from isolation or quarantine units. Nevertheless, high-risk pathogens present special challenges for laboratory operations, and a detailed plan and regular training will be critical in preventing laboratory-acquired infection. Communication between the medical care team and the clinical laboratory during periods of quarantine and, if applicable,
Table 17.1. Quarantinable Diseases and Their Periods of Contagion\(^a\)

<table>
<thead>
<tr>
<th>Disease(s)</th>
<th>Incubation period (days)(^b)</th>
<th>Start of contagious period (days)(^c)</th>
<th>Specimens of Highest Risk(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza(^e)</td>
<td>2–4</td>
<td>One day prior to symptoms</td>
<td>Respiratory secretions</td>
</tr>
<tr>
<td>Pneumonic plague</td>
<td>1–3</td>
<td>Onset of disease symptoms</td>
<td>Respiratory secretions</td>
</tr>
<tr>
<td>Monkeypox</td>
<td>7–17</td>
<td>Appearance of rash</td>
<td>Body fluids, lesions</td>
</tr>
<tr>
<td>MERS</td>
<td>2–14</td>
<td>Onset of disease symptoms</td>
<td>Respiratory secretions</td>
</tr>
<tr>
<td>SARS</td>
<td>2–14</td>
<td>Onset of disease symptoms</td>
<td>Respiratory secretions</td>
</tr>
<tr>
<td>Smallpox</td>
<td>10–14</td>
<td>Appearance of rash</td>
<td>Body fluids, lesions</td>
</tr>
<tr>
<td>Viral hemorrhagic fevers(^f)</td>
<td>6–21</td>
<td>Onset of disease symptoms</td>
<td>Blood, other body fluids(^g)</td>
</tr>
</tbody>
</table>

MERS = Middle Eastern respiratory syndrome; SARS = severe acute respiratory syndrome

\(^a\)The contagious period and transmission routes for the various diseases are not always well defined and continue to raise uncertainties. Laboratory personnel use blood and body fluid precautions as a standard of practice.

\(^b\)Time between exposure to a pathogen and symptom onset.

\(^c\)When a person becomes contagious and most likely to transmit disease. Fever is the most common primary symptom recognized.

\(^d\)Specimen(s) that are most likely to contain a concentration of the pathogen capable of transmitting disease in the laboratory.

\(^e\)Includes any novel influenza virus that could cause a pandemic.

\(^f\)Includes but not limited to South American hemorrhagic fevers, Crimean-Congo hemorrhagic fever, Ebola virus disease, Hendra virus disease, Lassa fever, Marburg hemorrhagic fever, Nipah virus encephalitis, and Rift Valley fever.

\(^g\)Any specimen containing blood should be considered capable of transmitting disease in the laboratory, i.e., bloody sputum.

after the onset of signs and symptoms is a major component in the care of a quarantined individual or isolation patient. Regular interaction in planning and training will help provide for a safe environment for all individuals involved in the care of these unique cases.