Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

8 Safety Precautions

A pathology department can be a dangerous place to work. Hazards include physical injury (scalpel cuts, needle sticks), infectious disease, radioactivity, and noxious chemical fumes. Although we all take risks when we work with specimens from patients, these risks can be minimized for both ourselves and our coworkers by following the procedures outlined in this section.

INFECTIOUS DISEASE: THE BAD NEWS

The incidence of infectious diseases, particularly those that are incurable or difficult to treat, is on the rise. In a study of patients undergoing major surgery in New York, 5.2% were HCV positive, 1.4% HBV positive, and 1.6% HIV positive (or 6.7% with one or more of these viruses).[1] Often, the presence of infection is unknown or unreported to the pathology department. Healthcare workers are at risk for contracting these diseases by working with patients. The risk is lower for pathology personnel, but exposure can occur by aerosolization of tissues, needlestick injury, scalpel wounds, and mucocutaneous exposure during the processing of pathology specimens (Box 8-1).

Other types of infectious agents (e.g., other types of bacteria or fungi, *Pneumocystis jiroveci*, other viral agents) are also potential dangers, particularly to immunocompromised healthcare workers, but transmission is very rare and has not yet been reported.

INFECTIOUS DISEASE: THE GOOD NEWS

The actual incidence of transmission of infectious agents from **unfixed surgical specimens** to pathology department personnel is extremely low. There are only three reported cases, all involving conversions to positive tuberculin skin tests after using an aerosolized gas coolent to freeze a tissue block during an intraoperative consultation.[2,3] However, transmission of other types of infectious disease is theoretically possible and has occurred for HBV, HIV, and TB during the performance of autopsies.

The good news is that pathology personnel can take action to protect themselves: by educating themselves about risks, taking physical precautions to protect themselves and others, avoiding the use of hollow-bore needles, and making sure they are vaccinated for HBV (Table 8-1). Personnel who are themselves immunocompromised must be especially vigilant.

BOX 8–1. Diseases that have been transmitted to healthcare workers

- Hepatitis B, C, and A
- Tuberculosis (including strains resistant to multiple drugs)
- HIV
- Syphilis
- Creutzfeldt-Jakob disease
- *Coccidioides immitis* (risk is primarily from cultures of the fungus in microbiology laboratories); if this infection is suspected all specimens must be labeled appropriately
- Also parvovirus, *H. pylori*, *Cryptosporidium*, scabies, pertussis

Hepatitis B Virus (HBV)

The CDC estimated that 18,000 healthcare workers whose jobs entailed exposure to blood became infected with HBV each year prior to widespread vaccination. Of these, 200 to 300 died of complications of HBV infection. Prior to widespread vaccination, 25% to 30% of pathologists were positive for HBV with their exposures likely due to the performance of autopsies. However, the incidence of HBV infection has sharply declined with vaccination, and all pathology department workers who come into contact with tissue should be vaccinated. OSHA bloodborne standards require that employers offer the vaccine at no cost to all employees at risk.

Seroconversion is 30% after a needle stick from HBeAg-positive blood and <6% after HBeAg-negative blood in nonvaccinated individuals. Mucocutaneous exposure can also occur.

Postexposure prophylaxis with HBV hyperimmune globulin and vaccine is suggested for nonvaccinated individuals or in vaccinated persons with low antibody titers. Treatment provides about 75% protection from infection if instituted within a week.[4,5]

Hepatitis C Virus (HCV)

The seroprevalence in healthcare workers has ranged from 0% to 1.7% in multiple studies. Occupational infections in pathology personnel have not been reported. Eighty percent to 90% of infections will become chronic with risk for the development of chronic hepatitis, cirrhosis (3% to 20% of patients), and hepatocellular carcinoma. HCV has also been linked to cryoglobulinemia and many other immune system–related diseases.

TABLE 8–1. RISK OF EXPOSURE TO COMMON INFECTIOUS AGENTS

AGENT	% OF HOSPITAL PATIENTS	RISK OF INFECTION AFTER PERCUTANEOUS INJURY*	RISK AFTER MUCOCUTANEOUS EXPOSURE	RISK OF ENVIRONMENTAL EXPOSURE	POST-EXPOSURE PROPHYLAXIS AVAILABLE
HIV	~ 0.2 - 14%	0.3%	0.09%	Possible, but very rare	YES – effective
HCV	~ 2 - 5%	1.8%	Rare	Yes, but rapidly degrades	NO – not shown to be effective
HBV	~ 2%	30%	Yes, probably high	Occurs, can be found in dried blood ~ 1 week	YES – effective
TB	~ 10%	Yes – risk not quantified	Yes – risk not quantified	Yes	NO – treatment initiated only if skin test converts

*Percutaneous injury: needlestick injury (majority) or other penetrating injury with a sharp object (e.g., scalpel, broken glass).

The risk is about 1.8% for HCV transmission after a needle stick. Risk after skin or mucous membrane exposure is likely to be very low.

Postexposure treatment has not been shown to be effective. If there has been a potential exposure, the person should be monitored for infection in order to start treatment as early as possible.[4-6]

Human Immunodeficiency Virus (HIV)[7-15]

As of 2001, 57 healthcare workers had developed HIV infection following documented occupational exposure and an additional 138 workers were considered possible cases. Most exposures (88%) were percutaneous involving hollow-bore needles, scalpels, and broken vials. 20% occurred during the disposal of sharp objects. Mucous membrane and skin exposure were responsible in about 10% of cases. The source in almost all cases was infected blood (86%). The risk is increased with the volume of blood, the depth of the injury, and the viral titer of the patient (with an increased risk with patients close to death).

A pathologist was infected by HIV after a scalpel wound to the hand during an autopsy.[10] Surgical specimens containing blood could also potentially transmit the virus, if an injury occurs. HIV can be cultured from cadavers hours to days after death. The effect of fixation has not been studied but would presumably lower or eliminate risk.

Approximately 0.3% of persons will seroconvert after a needle-stick exposure to HIV, 0.1% after mucocutaneous exposure, and <0.1% after skin exposure.

Postexposure treatment with antiviral agents can decrease the risk of seroconversion by 81%. Treatment should be started as soon as possible, as it may be less effective after 2 to 3 days. Additional agents used in combination for prophylaxis may be more effective, as the source patients for occupational cases have a high prevalence of drug-resistant HIV. There have been 21 cases of healthcare personnel becoming infected with HIV despite postexposure prophylaxis.

Tuberculosis

The risk of transmission of tuberculosis to autopsy personnel during the performance of necropsies is well documented. TB can be transmitted as an aerosol but also percutaneously.[16] It must be kept in mind that many cases of TB are first diagnosed after death. Multiple individuals had skin test conversions after the autopsy of an infected person.[17]

The three cases of conversion to positive skin tests after frozen sections previously mentioned were associated with use of an aerosolized coolant. This method of cooling should not be used.

Healthcare workers also have a significant risk of contracting multiple-drug-resistant tuberculosis. Although healthcare workers have been infected by drug-resistant TB, no fatal cases have been reported (yet!) if the worker did not have an underlying immunodeficiency disorder.

Mycobacteria can survive in tissue fixed in formalin. Of 138 autopsy cases with histologically documented acid-fast bacilli, 12 (8.7%) grew mycobacteria, including three cases of *M. tuberculosis*.[18] Thus, even fixed tissue must be regarded as potentially infectious.

Special respiratory protective devices are recommended for personnel that may be exposed to tuberculosis.

If an exposed person does not develop a positive skin test, no treatment is necessary. Converters and persons who are immunocompromised should be treated.

Hospital workers are required to undergo yearly TB testing.

Severe Acute Respiratory Syndrome (SARS)

SARS was first identified in China in late 2002. It is caused by SARS-associated coronavirus (SARS-CoV). Spread is via respiratory droplets contacting the mucous membranes of a second person. Occupationally-acquired cases have occurred among healthcare workers. The risk to surgical

pathology personnel is likely to be low, as most patients will not undergo surgical procedures. However, autopsies may be performed.

There are no reported cases of transferring SARS via the handling of pathology specimens. However, as there is little experience with this virus, all cases from patients with known or suspected SARS may best be handled as for cases of HBV. All tissue should be promptly fixed and the cryostat decontaminated if necessary.[19]

Creutzfeldt-Jakob Disease

The only cases of infection in laboratory personnel from **fixed tissue** are due to Creutzfeldt-Jakob disease. As of 1995, 24 healthcare workers had developed Creutzfeldt-Jakob disease including two histotechnologists and one pathologist. Infectious units are present in fixed and paraffin-embedded tissue for years. Any adult patient with a rapidly progressive dementia, myoclonus, and nonspecific neurologic findings should be considered as potentially having the disease.

Any tissues from affected patients are potentially infectious. The virus is not inactivated by standard formalin fixation or boiling water. Tissues should be fixed in formalin for 24 hours, then in 95% formic acid for one hour followed by formalin fixation for one day.[20,21]

BIOLOGIC TERRORISM

Hopefully, pathologists will not receive specimens from acts of biologic terrorism, but if such an event occurs, pathologists can aid in recognizing the disease and the likely method of infection (Table 8-2).[22-31] The first anthrax case in 2001 was suspected when typical organisms were seen on a Gram stain of CSF. The autopsy determined that the mode of exposure was inhalational and this finding helped direct investigators to search for possible sources of airborne spores.

In the event of an actual or threatened bioterrorist attack, local health and law enforcement agencies should be contacted and additional information can be found at www.bt.cdc.gov/emcontact/index.asp or the CDC Emergency Response Hotline 770-488-7100.

The CDC recommends saving tissue from autopsies (and other specimens) from possible victims of biologic terrorism:

- Fixed tissue: Histologic examination for patterns of tissue damage and special stains for identification of organisms. IHC and DFA assays are available at the CDC and most can be performed on fixed tissue.
- Blood, cerebrospinal fluid, tissue samples, or swabs for bacterial and viral culture. Mucosal swabs for cases of possible botulinum toxin inhalation.
- Serum for biologic and serologic assays
- Frozen tissue for PCR
- Fixed tissue (glutaraldehyde) for electron microscopy to identify viral particles.

Laboratory Response Network

The Laboratory Response Network (LRN) is a partnership of local, state, and federal public health laboratories, and veterinary, food, and environmental laboratories, the CDC, the Food and Drug Administration, the Environmental Protection Agency, the US Army Medical Research Institute of Infectious Diseases, and other Department of Defense laboratories (see www.bt.cdc.gov/lrn/biological.asp). The network functions to channel specimens from sentinel laboratories to advanced laboratories for confirmation and final identification of pathogens. Specimens from suspected biologic terrorism-related cases can be submitted to the state public health laboratory. Contact information for all state laboratories is included in the CDC guidebook listed in the resources. If the suspected agent is smallpox, the state laboratory should be notified as such specimens may be transported directly to the CDC.

Risks to Pathology Personnel

All of the infectious agents listed in Table 8-2 could potentially be transmitted to personnel during the performance of an autopsy or by handling fresh tissue, except for botulinum toxin. Smallpox, tularemia, and viral hemorrhagic fevers have been transmitted to persons performing autopsies. Biologic terrorism raises an additional risk of surface contamination by the agent (e.g., powders used to transmit anthrax or botulinum toxin). Because of the incubation period, it is likely victims will have changed clothes and bathed and such contamination, in most cases, will likely be minimal. Standard universal safety precautions should be used for all and should be protective.

Cadavers of patients dying of *B. anthracis*, *Y. pestis*, or botulinum toxin are unlikely to pose a threat to nonautopsy personnel (e.g., funeral home workers). However, smallpox virus and hemorrhagic fever viruses could be transmitted and should only be handled with safety precautions. In general, such bodies should not be embalmed as this might impose increased risk.

Sending Specimens to Reference Laboratories

Detailed descriptions for the packaging and shipping of specimens to reference laboratories are available at the CDC website. In general, such specimens must have three levels of containment and must be marked with an "Infectious Substance" label. The laboratory director of the state health department should be contacted before shipping a specimen with a suspected biologic agent.

TRANSMISSION OF TUMORS

In general, malignant tumors do not pose a risk to people other than the patient. However, malignancies can be transferred from a graft to organ transplant recipients.[32]

TABLE 8–2. AGENTS MOST LIKELY TO BE USED FOR BIOLOGIC TERRORISM (CATEGORY A AGENTS)

AGENT ***MODE OF TRANSMISSION***	CLINICAL SYNDROME	PATHOLOGIC FINDINGS	AVAILABLE TESTS[a]/ APPEARANCE OF ORGANISM	TREATMENT/PROPHYLAXIS
Smallpox virus (variola major) *Inhalation – aerosols* *Direct contact with lesions or contaminated surfaces* *Person to person spread*	Diffuse rash (including palms and soles): deep-seated, firm/hard, round well circumscribed vesicles or pustules, all in same stage of development Hemorrhage into skin and GI tract	Early vesicles are multilocular (but coalesce in later stages), ballooning degeneration of epithelial cells (not multinucleated), eosinophilic intracytoplasmic viral inclusions (Guarnieri bodies)	IHC EM: fluid from vesicles can be used to detect viral particles PCR: viral DNA.	Vaccine available[b]. Routine vaccination in the US ended in 1972. Persons with remote vaccination probably have some, but not complete, immunity.
Bacillus anthracis (anthrax) *Direct contact with spores (skin or ingestion)* *Inhalation of spores* *No person-to-person spread*	Cutaneous – eschar with hemorrhage, edema, necrosis, perivascular infiltrate, vasculitis Gastrointestinal – hemorrhagic enteritis, hemorrhagic lymphadenitis, mucosal ulcers with necrosis in the terminal ileum and cecum, peritonitis Inhalational - hemorrhagic mediastinitis, hemorrhagic lymphadenitis, hemorrhagic pleural effusion CNS – hemorrhagic meningitis	Skin: edema, focal necrosis, vasculitis, acute inflammation, ulceration. Organisms only rarely seen by H&E. Lymph nodes: hemorrhage, necrosis After antibiotic treatment, organisms may only be visible by silver stains and IHC	Gram, silver stains: Large broad (3 × 5 μm × 1 × 1.5 μm) encapsulated Gram pos bacilli with flattened ends in short chains India ink: shows capsule in blood and CSF IHC – sensitive and specific DFA (but cannot be used on formalin fixed tissue) PCR: formalin or fresh tissue	Vaccine available[b] Antibiotic prophylaxis available
Yersinia pestis (plague) *Flea bites* *Inhalation – aerosols* *Person-to-person spread*	Bubonic – acute lymphadenitis with surrounding edema (a bubo is a local painful swelling) Pneumonic – severe, hemorrhagic bronchopneumonia, often with fibrinous pleuritis, diffuse alveolar damage (ARDS), sepsis with DIC CNS - meningitis	Lung: severe, confluent, hemorrhagic, necrotizing bronchopneumonia, often with fibrinous pleuritis Lymph nodes: necrosis – preferred for histologic examination and culture	Gram, silver, Giemsa stains: Short fat Gram neg bacilli IHC DFA	Vaccine available (but does not protect against pneumonia)[b] Antibiotic prophylaxis available
Clostridium botulinum toxin (botulism) *Ingestion or inhalation of preformed neurotoxin* *No person-to-person spread*	CNS – hyperemia and microthrombosis of small vessels associated with symmetrical, descending pattern of weakness and paralysis of cranial nerves, limbs, and trunk	No specific findings for cases due to ingestion or inhalation of preformed toxin Swabs of mucosal surfaces or serum may be used for the botulinum toxin mouse bioassay Samples should be taken prior to the use of antitoxin	Gram-positive bacteria – however organisms unlikely to be present in a terror attack	Antitoxin available

continued

TABLE 8–2. AGENTS MOST LIKELY TO BE USED FOR BIOLOGIC TERRORISM (CATEGORY A AGENTS)—cont'd

AGENT *MODE OF TRANSMISSION*	CLINICAL SYNDROME	PATHOLOGIC FINDINGS	AVAILABLE TESTS[a]/ APPEARANCE OF ORGANISM	TREATMENT/PROPHYLAXIS
Francisella tularensis (tularemia) *Tick bite* *Direct contact with infected fluids or tissues* *Ingestion of infected meat* *No person-to-person spread*	Ulceroglandular – skin ulcer with associated suppurative lymphadenitis Glandular – suppurative necrotizing lymphadenitis without associated skin ulcer Oculoglandular – eyelid edema, acute conjunctivitis and edema, small conjunctival ulcers, regional lymphadenitis Pharyngeal – exudative pharyngitis or tonsillitis with ulceration, pharyngeal membrane formation, regional lymphadenitis Typhoidal – systemic involvement, DIC, focal necrosis of major organs Pneumonic – acute inflammation, diffuse alveolar damage	Ulcer with a nonspecific inflammatory infiltrate and a granulomatous reaction. In some cases, large necrotizing granulomas with giant cells may be present. Lymph nodes: extensive necrosis, irregular microabscesses and multiple granulomas with caseous necrosis. Lung: necrotizing pneumonia with abundant fibrin, acute inflammation	Small encapsulated Gram-negative coccobacilli - difficult to see with histochemical stains IHC DFA	Antibiotic prophylaxis available
Hemorrhagic fever viruses, including: -Filoviruses (including Ebola and Marburg viruses) -Arenaviruses (e.g., Lassa fever) *Close personal contact with infected person, blood, tissue, or body fluids*	Diffuse rash, massive hepatocellular necrosis, extensive necrosis in other major organs, diffuse alveolar damage	Massive hepatic necrosis with filamentous viral inclusions in hepatocytes, extensive necrosis of other organs	IHC EM: viral inclusions PCR	No specific treatment

ARDS: acute respiratory distress syndrome, DIC: disseminated intravascular coagulopathy, IHC: immunohistochemistry; DFA: direct fluorescent assay.
[a]IHC and DFA tests for each of these organisms are available at the CDC. Consult their website to determine how to decide if a specimen is appropriate for testing and how to send such a sample: call the CDC at 404-639-3133 or fax the CDC at 404-639-3043, for more information.
[b]Vaccination is not currently recommended for individuals without a known exposure. Vaccination for smallpox may be considered for selected personnel who would be a first responder for the examination of the remains or specimens from patients dying of smallpox.

Benign and malignant tumors can be transferred among dogs and wolves and among Tasmanian devils by contact. The transfer of these tumors has been species-specific.

There has been one case of a sarcoma transferred to the hand of a nonimmunocompromised surgeon after a scalpel injury.[33] Thus, although the risk is extremely small, tumors (and all human tissue) must be handled with appropriate safety precautions.

GUIDELINES FOR PROCESSING SPECIMENS WITH KNOWN/PROBABLE INFECTIOUS DISEASE

Specimens from patients with infections not posing a risk to immunocompetent individuals (e.g., routine bacterial and fungal infections, opportunistic pathogens) can be processed as for other pathology specimens using universal precautions. Specimens from patients with infections (or suspected infections) posing a greater risk to pathology personnel (TB, HBV, HCV, HIV, Creutzfeldt-Jakob disease) must be handled with special precautions. All specimens must be fixed as soon as possible and stored in rigid leakproof containers. Gloves must always be worn when handling specimens.

Fresh tissues are potentially infective and all specimens are placed in fixative as soon as possible. Formalin is effective for inactivating viruses (including HIV and HBV) and will reduce the infectivity of mycobacteria. Procedures that could aerosolize an infectious agent (e.g., cutting a specimen with a bone saw) should not be performed. Creutzfeldt-Jakob disease requires special procedures for handling it safely (see specific section).

Small specimens (e.g., colon biopsies and open lung biopsies) are usually of immediate diagnostic importance and can be processed as usual as long as the specimens fix in formalin for at least four to six hours.

Larger specimens, if of no immediate diagnostic importance (e.g., a placenta from a normal delivery or a colon resection for trauma) can be sectioned thinly and placed in an adequate volume of fixative (1:10 specimen/formalin fixative ratio) for 72 hours before submitting for histologic processing. If the specimen is of immediate diagnostic importance, small sections can be cut for blocks and fixed as above before processing.

Potentially infectious cases are not photographed in the fresh state. If it is an especially interesting case, pictures after fixation may be taken if special precautions are used in order not to contaminate surfaces or the camera.

Frozen sections on potentially infectious cases may be performed but should be avoided if cytologic preparations can be used or an intraoperative diagnosis is not necessary. Freezing does not inactivate infectious agents. If an infectious case is cut in a cryostat, the cryostat should be decontaminated. Pressurized sprays should not be used as this can aerosolize infectious agents. Air-dried slides should be considered potentially infectious and are not saved or submitted to the histology laboratory. Any smears submitted for special stains must be fixed in methanol.

PREVENTION OF INJURIES AND EXPOSURES

Prevention of injuries and exposures is the goal of all pathology personnel. The most common injury is to the nondominant hand. Most injuries and exposure to blood and other body fluids can be prevented if the following guidelines are followed:

- Gloves must be worn when handling fresh and fixed tissues. Two pairs of gloves are recommended for hazardous specimens, as small tears in gloves are common. Metal mesh and Kevlar cloth type gloves can help prevent puncture injuries
- Latex gloves will protect against biohazards but not fixatives. Nitrile gloves will also provide protection from fixatives. Some individuals (5% to 10%) have or develop allergic reactions (usually dermatitis but sometimes asthma or anaphylaxis) to latex antigens.
- Do not touch objects in general use (door handles, telephone, computer, etc.) with contaminated gloves.
- Hands must always be washed after handling specimens and after leaving a specimen handling area because gloves are not completely leakproof.
- Protective clothing, including gloves, must be removed and disposed of properly before leaving the surgical cutting or OR consultation rooms.
- Scrub suits or disposable jumpsuits are recommended if large bloody specimens need to be processed.
- Aprons must be worn when handling many specimens (e.g., at a cutting bench) or for handling large specimens.
- If lab coats are worn while working in the surgical cutting room, they cannot be worn outside of this area.
- Any person using a scalpel blade, razor blade, or syringe needle is responsible for disposing of it properly. Scalpel blades are removed from the handle with extreme caution after gross blood and tissue have been removed. Frozen section blocks are not removed from the chuck with a razor blade. Holding the stem for a few seconds will melt the embedding medium sufficiently for removal with a fingertip. Syringe needles are never recapped. All blades, needles, and disposable scissors must be discarded into impervious labeled sharps containers. Broken glass slides and coverslips must also be disposed into designated containers.
- Reusable but contaminated equipment should be decontaminated with bleach.
- All tissues are fixed as soon as possible. Unfixed specimens must be kept in leakproof containers and stored in an appropriate biohazard refrigerator or freezer.
- Always dispose of all blood and tissue fragments before leaving a worksite. All tissues, or nonreusable material contaminated by any body fluid or tissue, must be disposed in labeled hazardous waste containers (containers with red bags and biohazard symbols). Urine, blood, and feces may be disposed directly into the municipal sewerage system.
- Areas contaminated after handling a known infectious case should be immediately cleaned with dilute bleach.

- Eye protection should be worn when cutting into large specimens. Cysts may feel deceptively solid when filled with fluid. Such fluid may be under pressure and can travel several feet when the cyst is opened (this has been documented by many pathologists!). Place near sink on a surgical drape or blue barrier and make a small nick near the bottom in order to let fluid slowly drain out of the cyst.
- Food or beverages must not be consumed, or brought into, the cutting room or the OR consultation room. Foods cannot be stored in refrigerators used to store specimens. Food or food containers (e.g., an empty coffee cup) cannot be disposed into containers in these areas as this may be used as evidence that food consumption is occurring in these areas. Evidence of food consumption is monitored by OSHA and can be grounds for penalties or closure.

RADIATION[34-39]

Radioactive substances are widely used in the evaluation of patients and may be present in tissues submitted to pathology departments. In some cases, patients will have been injected with radioactive agents for the purpose of localizing and surgically removing a lesion (e.g., sentinel nodes, octreotide-positive lesions). In general, patients are injected with small amounts (<5 millicuries) and typical half-lives are short (e.g., the half-life of ^{99m}technetium used for sentinel lymph nodes is 6 hours). Specimens should have minimal residual radioactivity and can be generally handled and disposed without special precautions. However, radiation safety personnel should be consulted to determine the appropriate procedures for the techniques used in individual institutions.

Federal law allows routine methods of solid medical waste disposal for radioactive specimens after decay in storage, which requires the lapse of 10 half-lives. Thus, specimens containing technicium can be disposed using normal methods 60 hours after the time of surgery.

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