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.

Safety precautions

8

A pathology department can be a dangerous place to work. Hazards include physical injury (scalpel cuts, needlestick injuries), 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 below.

INFECTIOUS DISEASE: THE BAD NEWS

The incidence of infectious diseases, particularly those that are incurable or difficult to treat, is rising. In a study of patients undergoing major surgery in New York,[1] 5.2% were HCV positive, 1.4% HBV positive, and 1.6% HIV positive (or 6.7% with one or more of these viruses). Often, the presence of infection is unknown or is not reported to the pathology department. Healthcare workers are at risk for contracting these diseases when working with patients (Box 8-1). 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.

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

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* (the risk arises primarily from cultures of the fungus in microbiology laboratories); if this infection is suspected, all specimens must be labeled appropriately
- Parvovirus and *H. pylori* infection, cryptosporidiosis, scabies, pertussis

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 conversion to positive tuberculin skin tests after use of an aerosolized gas coolant to freeze a tissue block during an intraoperative consultation.[2,3] However, transmission of other types of infectious disease is theoretically possible: transmission of HBV, HIV, and TB has occurred 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 immunocompromised must be especially vigilant.

Hepatitis B virus[4,5]

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, their exposure likely being due to the performance of autopsies. However, the incidence of HBV infection has sharply declined with vaccination. 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. (http://www.osha.gov).

After a needlestick injury, the seroconversion rate is 30% from HBeAg-positive blood and <6% from HBeAg-negative blood in non-vaccinated individuals. Mucocutaneous exposure can also occur.

Table 8.1 Risk of exposure to common infectious agents

AGENT	PERCENTAGE OF HOSPITAL PATIENTS	RISK OF INFECTION AFTER PERCUTANEOUS INJURY[a]	RISK AFTER MUCOCUTANEOUS EXPOSURE	RISK OF ENVIRONMENTAL EXPOSURE	POSTEXPOSURE 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

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

Postexposure prophylaxis with HBV hyperimmune globulin and vaccine is suggested for non-vaccinated individuals or vaccinated persons with low antibody titers. Treatment provides approximately 75% protection from infection if instituted within a week.

Hepatitis C virus[4-6]

The seroprevalence of HCV 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.

The risk is approximately 1–8% for HCV transmission after a needlestick injury. The 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.

Human immunodeficiency virus[5,7-10]

As of 2001, 57 healthcare workers had developed HIV infection following documented occupational exposure; an additional 138 workers were considered possible cases. Most exposures (88%) were percutaneous and involved hollow-bore needles, scalpels, and broken vials: 20% of exposures 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.[11] 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.[12] The effect of fixation has not been studied but would presumably lower or eliminate risk.

Approximately 0.3% of persons will seroconvert after a needlestick 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.[13] There have been 21 cases of healthcare personnel becoming infected with HIV despite postexposure prophylaxis.

Tuberculosis

The risk of transmission of TB to autopsy personnel during the performance of necroscopies is well documented. TB can be transmitted not only as an aerosol but also percutaneously.[14] It must be kept in mind that many cases of TB are first diagnosed after death. Multiple individuals had conversion to a positive skin test after the autopsy of an infected person.[15] Exposure can be diminished by wearing special respiratory protection.

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 case has yet been reported in the absence of an underlying immunodeficiency disorder.

There are no definitive studies on the survival of mycobacteria in fixed surgical specimens.[16,17] Formalin probably kills mycobacteria, but the time required for it to do so is unknown.

Special respiratory protective devices are recommended for personnel who 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[18]

Severe acute respiratory syndrome (SARS) was first identified in China in late 2002. It is caused by SARS-associated coronavirus (SARS-CoV) and spreads 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 SARS being transferred 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.

Creutzfeldt–Jakob disease[19,20]

The only cases of infection in laboratory personnel from *fixed tissue* are due to Creutzfeldt–Jakob disease (CJD). As of 1995, 24 healthcare workers had developed CJD, 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.

All tissues from affected patients can potentially cause infection. 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.

BIOLOGIC TERRORISM[21-27] (Table 8-2)

It is to be hoped that pathologists will not receive specimens from acts of biologic terrorism, but, should such an event occur, pathologists can aid in recognizing the disease and the likely method of infection. 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 inhalation 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. 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, CSF, 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 EM to identify viral particles.

The 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. The network functions to channel specimens from sentinel laboratories to advanced laboratories for confirmation and final identification of pathogens. Specimens from cases suspected to be related to biologic terrorism 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 so that such contamination, in most cases, will likely be minimal. Standard universal safety precautions should be used in all cases and should be protective.

Cadavers of patients dying of *B. anthracis, Y. pestis*, or botulinum toxin are unlikely to pose a threat to non-autopsy personnel (e.g., funeral home workers). However, smallpox virus and hemorrhagic fever viruses could be

Table 8.2 Agents most likely to be used for biologic terrorism (category A agents)

AGENT *MODE OF TRANSMISSION*	CLINICAL SYNDROME	PATHOLOGIC FINDINGS	APPEARANCE OF ORGANISM/ AVAILABLE TESTS[a]	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)	Viral inclusions present in cytoplasm 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) encapsulated Gram-positive 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-negative 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

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	APPEARANCE OF ORGANISM/ AVAILABLE TESTS[a]	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) and 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	Viral inclusions in hepatocytes IHC EM: viral inclusions PCR	No specific treatment

ARDS, acute respiratory distress syndrome; DFA, direct fluorescent assay; DIC, disseminated intravascular coagulopathy; IHC, immunohistochemistry.

[a] IHC and DFA tests for each of these organisms are available at the CDC. Consult the CDC 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 first responders for the examination of the remains or specimens from patients dying of smallpox.

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 instructions for the packaging and shipping of specimens to reference laboratories are available at the CDC website (www.cdc.gov). 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 a specimen with a suspected biologic agent is shipped.

TRANSMISSION OF TUMORS

In general, malignant tumors do not pose a risk to any person other than the patient. However, malignancies can be transferred from a graft to an organ transplant recipient.[28]

There has been one case of a sarcoma transferred to the hand of a non-immunocompromised surgeon after a scalpel injury.[29] 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 OR 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, CJD) must be handled with special precautions. All specimens must be fixed as soon as possible and stored in rigid leak-proof 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 effectively inactivates viruses (including HIV and HBV) and reduces the infectivity of mycobacteria. Procedures that could aerosolize an infectious agent (e.g., cutting a specimen with a bone saw) should not be performed. Tissue from a CJD patient requires special procedures for handling it safely (see "Creutzfeldt–Jakob disease," above).
- **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 are fixed in formalin for at least 4 to 6 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. Placentas and products of conception must be fixed for 7 days before processing. If such a specimen is of 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 may be taken after fixation 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. Most injuries and exposure to blood and other body fluids can be prevented if the following guidelines are followed:

Gloves

- All fresh and fixed tissues must be handled with gloves. The use of two pairs of gloves is recommended as small tears in gloves are common. Metal mesh and Kevlar cloth type gloves are available and should be worn if puncture injuries are possible.
- Latex gloves protect against biohazards but not against fixatives. Nitrile gloves 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 leak-proof.

Protective clothing

- 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 handling large specimens.
- Protective clothing, including gloves, must be removed and disposed of properly before leaving the surgical cutting or OR consultation rooms.

Sharps

- 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. OCT blocks are not removed from the chuck with a razor blade. Holding the stem for a few seconds will melt the OCT 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 of into designated containers.
- The most common site of an injury is the nondominant hand.
- Reusable but contaminated equipment should be decontaminated with bleach.

Tissue fixation

- All tissues are fixed as soon as possible. Unfixed specimens must be kept in leak-proof 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 non-reusable material contaminated by any body fluid or tissue, must be disposed of in labeled hazardous waste containers (containers with red bags and biohazard symbols). Urine, blood, and feces may be disposed of directly into the municipal sewerage system.

Eye protection

- 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 the specimen near a 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

- 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 of 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.

RECOMMENDATIONS FOR POSTEXPOSURE TREATMENT AND INCIDENT REPORTING

Unfortunately, accidents will occasionally occur. First aid is administered at the site. Bleeding injuries are allowed to bleed liberally. The site should be cleaned with soap and water. If there has been an eye or mucous membrane exposure, these sites are liberally flushed with water.

All exposures involving percutaneous inoculation or contact with an open wound, non-intact skin (e.g., chapped, abraded, weeping, or dermatitic), or mucous membranes by blood or tissue should be seen by a physician. The exposed person should record the name of the patient and the surgical specimen number and file an incident report.

The exposed individual should be informed of current recommendations for postexposure prophylaxis (HIV and HBV). The exposed individual should be counseled on the relative risks and benefits of this treatment, if available.

The blood of the source individual can only be tested for HIV after appropriate consent is obtained. The results of such a test may be made available to the exposed individual after he or she is made aware of applicable laws and regulations concerning disclosure of the identity and infectious status of a source individual and after signing a confidentiality statement.

RADIATION

Radioactive substances are widely used in the evaluation of patients and may be present in tissues submitted to pathology departments. In some cases patients have been injected with radioactive agents for the purpose of localizing and surgically removing a lesion (e.g., sentinel nodes, octreotide-positive lesions). Little published information is available about the incidence of such specimens and the risk to pathology personnel.[30] In general, patients are injected with small amounts (<5 millicuries) and typical half-lives are short. Specimens should have minimal residual radioactivity and can be generally handled and disposed of without special precautions. However, radiation safety personnel should be consulted for unusual cases or unusual isotopes.

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