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Proposal of the Autopsy Guideline for Infectious Diseases: Preparation for the Post-COVID-19 Era (abridged translation)

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ABSTRACT

With the rapidly spreading coronavirus disease 2019 (COVID-19) pandemic over the past few months, the world is facing an unprecedented crisis. Innumerable lives have been lost to this novel infectious disease, the nature of which supersedes conventional medical understanding. The COVID-19 pandemic is not just a global health crisis, several aspects of life in the post-COVID-19 era are also being contemplated. Experts in unison are warning that the upcoming changes in all areas of life could potentially be far more drastic than ever experienced in the entire human civilization. The medical community is no exception, and therefore, personnel involved in forensic medicine also need to be adequately prepared for the future. Forensic medicine is a branch of medicine dedicated to one of the most important stages of the human lifecycle and has always been at the forefront in times of unprecedented social change. The autopsy, one of the most important tools of forensic medicine, is also useful to infectious diseases because it identifies the causal relationship between death and infection, reveals medical and epidemiological knowledge, and provides objective evidence for legal disputes. We present new autopsy guidelines in forensic medicine, formulated based on the various infectious diseases that we presently live with and may encounter in the future. In formulation of these guidelines several considerations have been taken into account, namely, the role forensic pathologists should play in the post-COVID-19 era and the necessary preparations as well as the support needed from society to fulfill that role. The present COVID-19 outbreak should be a starting point for formulating improvements in current practices in forensic science, including autopsy biosafety practices and the medicolegal death investigation system.

Keywords: Autopsy; Infectious Disease; Guideline; COVID-19; Forensic Medicine

Author Contributions

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I. INTRODUCTION

Despite the development of medical science, as the complexity of our society increases, various microorganisms that have the potential to be infectious agents constantly threaten humanity. Through accumulated mutation, even well-known microorganisms are becoming new species, resulting in stronger transmission or higher number of fatalities. Korea is also in a situation where management is required of both the interior spread and the foreign inflow of various infectious diseases. For examples of the former in Korea, there are respiratory-mediated infectious diseases, such as tuberculosis, which is known to be endemic, and blood-mediated infectious diseases, such as hepatitis B, hepatitis C, and acquired immune deficiency syndrome (AIDS), which need continuous monitoring.^{1,2} Numerous foreign infectious diseases are newly emerging as a result of changes in climate and biological distribution due to environmental degradation, and the collapse of interspecies barriers. As international exchange increases, they can flow into other countries at any time.³

Recently, several respiratory diseases caused by novel viruses, such as severe acute respiratory syndrome (SARS) in 2002, novel influenza A (H1N1) in 2009, and Middle East respiratory syndrome (MERS) in 2015, were introduced worldwide. This year, on March 11, the World Health Organization (WHO) declared a global pandemic of coronavirus disease 2019 (COVID-19). A “highest” level of crisis alert was issued in Korea on February 23 based on the judgment that the spread of the disease within the local community had begun. As of May 27, 2020, about 5 million COVID-19 patients had been reported in 215 countries, resulting in 348,836 deaths, while 11,265 patients and 269 deaths had been reported in Korea.⁴

In a situation where enormous social and economic losses are caused by the periodic outbreak of novel infectious diseases, the national quarantine system requires improvement to cope with the public health crisis. We believe that autopsy can provide the basic data for establishing appropriate quarantine and preventive measures. The autopsy is the most direct approach to a disease or other medical abnormalities. Historically, a wide range of information on pathogenesis, epidemiology, and the natural course of numerous diseases has been collected through autopsy, leading to the development of medicine. Also, the autopsy identifies legal problems related to death and prevents potential disputes, the necessity for which has been recognized across many sectors of society. It should be considered more important in a death related to an infectious disease.

While the clinical environment is ready for infectious diseases under administrative and financial support, the death investigation system in Korea does not seem to be comparable. Although many infectious diseases are diagnosed only postmortem through autopsy, the personnel related to the autopsy are exposed to the risk of infection, due to insufficient clinical information, lack of facilities or equipment for protection, and injury accidents.

Therefore, a guideline for the standard autopsy for infectious diseases is stated here, which aims to: 1) provide scientific grounds to establish appropriate plans for the prevention and treatment of infectious diseases, 2) contribute to improving national health by controlling the spread of pathogens within the community, and 3) protect human resources engaged in autopsy-related work from the risk of infection. Several autopsy guidelines, including more recent ones focusing on COVID-19, have been adopted here.⁵⁻⁹ Most of them suggest that the principles of handling COVID-19 during autopsy are not different from that of the handling of other infectious diseases. This guideline does not present the current modus operandi, but

indicates the way in which we need to operate from now on, and which needs our continuous effort dedicated to forensics, as well as support from the related social systems.

II. OVERVIEW OF INFECTIOUS DISEASE AND ITS AUTOPSY

1. Background

1) *General classification*

The pathogen of infectious diseases includes various microorganisms, such as bacteria, viruses, fungi, parasites, and even prions. Among various routes of transmission, direct contact of blood or body fluids, and aerosol transfer via droplet or its nuclei are considered as important during the autopsy. Patients with active infection could have symptoms of acute, subacute, or chronic status, which is called clinical disease, or have no apparent symptoms, which is called subclinical or occult disease. Infection by some agents could be inactive for a certain period, which is called latent infection.

2) *Diagnostic clues during the autopsy*

The diagnosis of an infectious disease could be considered based on 1) medical history, from the statements of his or her acquaintances or formal medical records; 2) postmortem tests for the detection of microorganisms, such as serologic, genetic, or culture tests using blood, secretion, fluid, or tissue; 3) pathologic findings, using conventional and special stains; and 4) epidemiologic information about the deceased or his or her close contacts, such as the location of residence and workplace, occupation, travel history, and recent whereabouts.

3) *Regulations associated with the infectious diseases in Korea*

The Infectious Disease Control and Prevention Act of Korea designated some infectious diseases with epidemiologic importance as 'legal infectious diseases.' These diseases were classified into four classes according to their severity, infectiousness, and isolation level (**Appendix 1**). An emerging infectious disease with the possibility of severe symptoms or rapid transmission is considered an 'emerging infectious disease syndrome' in Class 1. COVID-19, caused by SARS-CoV-2, is an example of this temporary classification, which should be classified properly after the pathogenesis and clinical features are further revealed.

According to the act, a doctor who identified an infectious disease from a living patient or a dead body should report to the regional public health center. The director of the Korea Centers for Disease Control and Prevention (KCDC) may order an autopsy of the deceased who is suspected of having died from an infectious disease, to confirm the final diagnosis. The autopsy process should be conducted by a specialist in infectious disease, human anatomy, pathology, or forensic medicine, in a facility with an adequate level of biosafety.

4) *Risk group classification of the infectious agents*

The KCDC has suggested a revised classification of the risk groups of infectious agents (**Appendix 2**) in 2016, which is based on the classification for the biology laboratory published by the WHO in 2004.¹⁰ According to this classification, Risk Group 2 includes the pathogens that are unlikely to be a serious hazard, such as HBV and HCV, while Risk Group 3 includes the pathogens that usually cause serious diseases, such as *Mycobacterium tuberculosis*, SARS-CoV, and HIV. For both groups, effective treatment and preventative measures are available in general.

5) Biosafety level required for handling high-risk agents

The Infectious Disease Control and Prevention Act of Korea classifies the safety control measures of the facilities handling high-risk pathogens into four grades (**Appendix 3**), which correspond to the biosafety levels (BSLs or BLs) suggested by the WHO. They could be applied to all the pathogens identified so far. Registration with the KCDC is required for handling high-risk pathogens of Grade 1 and 2, while permission from the KCDC is required for those of Grade 3 or 4. The classification is as follows:

- Grade 1: facilities that handle high-risk pathogens that are unlikely to cause diseases to healthy adults.
- Grade 2: facilities that handle high-risk pathogens that can cause human diseases unlikely to be a serious hazard and for which effective treatment and preventive measures are available.
- Grade 3: facilities that handle high-risk pathogens that usually cause serious human diseases and for which effective treatment and preventive measures are available.
- Grade 4: facilities that handle high-risk pathogens that usually cause serious human diseases and for which effective treatment and preventive measures are not usually available.

In addition, the same act designates some infectious agents as 'high-risk pathogens' that require special attention from the nation and society, because of the potential of serious risk to public health if used for biological terrorism, or spread to the outside by accident (**Appendix 4**). Some agents in Risk Group 2, 3, and 4 recommended by the WHO and some causative agents of a recent outbreak, such as SARS-CoV and MERS-CoV, are included in this list. It is anticipated SARS-CoV-2 will be added here in the near future by revision of the act.

2. The purpose of the autopsy for infectious diseases

1) Identification of the causal relationship between death and infectious diseases

Autopsy plays a critical role in 1) determining the situation and specific causes of death, 2) excluding other causes of death when a patient dies during treatment or isolation for a confirmed infection, and 3) evaluating the medical relationships between infection and death if the infection is not a direct cause of death.

2) Provide medical and epidemiological information through a final diagnosis based on pathology

Autopsy is able to provide crucial information for 1) the establishment of an appropriate treatment plan based on the pathological mechanisms by confirming the clinical course, symptoms, histology, and prognosis, and 2) scientific evidence to control and prevent the spread of pathogens within the community, by identifying the path of transmission, and the prevalence of the target population.

3) Provide grounds for judgment on potential legal disputes

Since immediately after a particular death, the possibility of legal disputes related to the death are often unclear, and the bereaved family are often confused, the conducting of an autopsy should be decided under careful consideration of the circumstances surrounding the death. Potential legal disputes may be related to the validity and relevance of medical treatment or administrative actions, compensation claims against industrial accident insurance or commercial medical insurance, or professional negligence of a business owner. Most of the situations are already covered by the criteria for the decision of unnatural deaths suggested by the KSLM (**Appendix 5**), or the instructions for handling unnatural deaths declared by the Korean National Police Agency (**Appendix 6**).

3. Current issues regarding the autopsy for infectious diseases in Korea

1) Lack of medical history of the deceased

Most of the medical history provided before the autopsy by the police is limited to the statements of bereaved families or acquaintances, or concise data from the National Health Insurance Corporation. Obtaining the medical records of the deceased needs an additional effort of the police or the bereaved families. However, the medical information is mandatory in identifying the health status of the deceased, and preparing against the potential risk of infection. The incidence of tuberculosis among autopsy workers is known to be 100–200 times that of the general population,¹¹ while it has never been investigated in Korea. A small-group survey in Korea indicated that the prevalence of tuberculosis and hepatitis B among medical workers was suspected to be very high.¹² Because hepatitis C and AIDS are difficult to cure and have a poor prognosis, serologic tests are performed on all surgical patients to protect medical personnel. But currently in Korea, no particular tests are required to be conducted in the routine for a dead body before the autopsy.

2) A criminal justice-oriented death investigation system

The purpose of the medico-legal autopsy may be divided into a judicial one, to confirm criminal relevance, and an administrative one, to manage public issues related to infectious diseases, accidents, or disasters, while that of the clinical autopsy is usually focused on medical evaluation. In Korea, the legal basis for all forms of autopsy is prepared. For example, in the cases of infectious diseases that are not expected to be related to crime, the autopsy may be conducted by the Minister of Health and Welfare, the mayor, the governor, the Director of the KCDC, or the head of the quarantine office. But in practice, the autopsy is always requested by the police, which inevitably limits its purpose.

3) Regional and institutional deviation of autopsy facilities and equipment

Although autopsy rooms are installed at the National Forensic Service (NFS) and its local branches, and some medical schools having forensic or pathology departments, their BSLs are in different situations. For example, the headquarters of the NFS has a special autopsy room of BSL3, while some medical schools have only BSL1 rooms. In principle, if the deceased is known to be a tuberculosis patient, the autopsy should be conducted in the BSL3 autopsy room, because *Mycobacterium tuberculosis* belongs to Risk Group 3 with SARS-CoV and HIV.¹⁰ But this principle is hard to follow, due to the high prevalence of tuberculosis in Korea, and a lack of medical history, as mentioned above. Each institution is in charge of the management of personal protective equipment (PPE) required for the autopsy, without sharing a standardized protocol.

4) Insufficient health support for autopsy personnel

To assess the risk of infection caused by autopsy, the medical conditions of autopsy personnel should be checked periodically, especially after the autopsy of a high-risk person.⁵ Throughout the branches of the NFS and the universities, there are no principles for the list of target pathogens, the method and frequency of surveillance test, and the criteria for subjects who need such monitoring.

5) Lack of safety considerations for other facilities and workers related to the autopsy

To conduct an autopsy, the sequence of procedures should be involved, of 1) transfer from the funeral home, 2) receive the body at the autopsy room, 3) check the identity of the body with the police or bereaved family, 4) perform the autopsy, 5) return the body to the funeral home, and 6) transfer the samples for postmortem test to other departments. The workers

who will be involved before and after the autopsy should be guided and trained in the use of PPE and hygiene control, because during the wrapping and transporting processes, there is a possibility of contagion from the deceased. Laboratory personnel dealing with samples taken from the body during the autopsy should be aware of the potential risk of infection in all autopsy samples, and receive the same level of health support as the autopsy personnel. In particular, all laboratories dealing with the initial sample that has not been chemically treated or biologically inactivated, must have BSL2 or higher level of facilities and appropriate PPE.¹⁰ Throughout the autopsy-related facilities in Korea, there is only a low level of safety considerations for these types of personnel who are not directly involved in the autopsy, and the level is insufficient to deal with a body or samples infected by a high-risk pathogen.

III. STANDARD AUTOPSY PROTOCOLS FOR INFECTIOUS DISEASES

1. Target subjects and principles

1) General principles

All bodies should be considered to be infected by unspecified microorganisms, until they are diagnosed as negative by a medically verified examination, using appropriate samples. The autopsy personnel have the right to be protected from infection by the body, for which the affiliated agencies should make appropriate efforts. Even if an infectious disease is newly diagnosed after the autopsy, the risk of infection to the autopsy personnel should be low level. A 'standard autopsy' for infectious diseases is defined as an autopsy conducted by an agreed procedure for this purpose, which should always be observed, regardless of the prevalence of the infectious disease. For confirmed cases, some conditions could be added for the optimal protection of the autopsy personnel. In contrast, if any of the facilities, personnel, equipment, or procedure did not meet the standard, an autopsy shall be considered as an 'ordinary autopsy'.

2) Risk classification

The risk of transmission during an autopsy could be assessed according to the infection status of the body (**Table 1**). To conduct an autopsy for a confirmed case, the biosafety levels of the facilities for autopsy and laboratory tests should be equivalent to or higher than that of the pathogen. During the prevalence of a certain infectious disease, all the unknown cases should be regarded at least as suspected cases. However, considering the realistic restrictions, if there were reasonable compensations, such as preliminary tests before the autopsy, adequate ventilation and disinfection of the facilities, or additional use of PPEs, the autopsy could be conducted by substandard protocols. Even for the negative cases that are allowed for the ordinary autopsy, a higher level of protection is recommended, because there is always the possibility of a false-negative.

Table 1. Case classification and their definitions

Cases	Definition	Protocol
Confirmed	A person whose disease has been confirmed by conducting a medically verified test with an appropriate sample for a specific pathogen, and maintained its infectivity until death	Standard autopsy for the confirmed
Suspected	A person who is not confirmed, but is suspected to have infectivity of a specific pathogen based on his or her history, symptoms, signs, and epidemiological relevance	Standard autopsy
Unknown	A person who is not confirmed, but has not been confirmed to be related to the infectious disease	Standard autopsy
Negative	A person who has been shown to be negative by a medically verified test with a premortem or postmortem sample	Ordinary autopsy

2. Preparations before autopsy

1) Consideration of preliminary test

Considering the prevalence and biological risks, a list of infectious pathogens should be selected, and periodically evaluated for surveillance. Preliminary tests for these pathogens are recommended. During the prevalence of high-risk pathogens (**Appendix 4**) or their equivalents, preliminary tests are mandatory for clinically suspected cases to determine the conduct and the coverage of the autopsy.⁴ The autopsy can be postponed until the results of the preliminary tests are available. Even for the cases in which the preliminary test was negative, if suspicious findings were found during the autopsy, it is recommended to repeat the test with the autopsy samples. The possibility of false-negatives should always be considered, because the results could be affected by the infection period, sampling methods, status of the samples or bodies, or the characteristics of the test itself.

2) Storage and transfer of the body

Place the body in a leak-proof transparent plastic bag with a thickness of 150 µm, and seal it. Do not use pins or clips that can damage the sealing conditions.¹³ Put the plastic bag into another opaque body bag, and wipe its outer surface with sodium hypochlorite diluted 1:4 (e.g., 5% sodium hypochlorite 100 mL + water 400 mL mix), and dry. Attach an identification tag to both the body and its bag, respectively, and make sure that they are not lost. Refrigerate the body at 4°C. At the beginning of the autopsy, disinfect the outer and inner surface of the body bag and the skin of the body with 70% alcohol or sodium hypochlorite diluted 1:99 (e.g., 5% sodium hypochlorite 5 mL + water 495 mL mix).

2. Management of the facilities and working environment

1) Facility standards

The biosafety standard of the autopsy-related facilities may correspond to the BSL in general, although a little modification is required to reflect the procedure and equipment of the autopsy. The concept of BSL is also adopted in the 'Standards for the installation and operation of facilities handling high-risk pathogens (Ministry of Health and Welfare Notice No. 2019-59)' (**Appendix 3**), which the Korean institutes should follow for handling microorganisms with potential biologic risk.

A BSL2 autopsy room is required for the ordinary autopsy, while a BSL3 or higher level is required for the standard autopsy, according to the risk group of the confirmed or suspected pathogen.¹⁰ In an autopsy room that does not meet the above criteria, at least 1) the air inside the autopsy room should not escape to other spaces in the building, 2) the route of exhaust should avoid other intake vent or public spaces, and 3) additional devices or PPEs should be utilized to compensate insufficiently met requirements. Considering the environment of the autopsy room and the prevalence status of the time, the preliminary test of all the requested bodies should be considered for certain pathogens, and be referred to the decision of the conduct and coverage of the autopsy.

2) Waste disposal

Waste generated in all processes related to the body correspond to medical waste. They should be immediately disposed of in a dedicated envelope or containerboard box. In particular, sharp tools, such as injection needles, suture needles, or scalpels, should be discarded in a dedicated plastic container. Waste are sealed, disinfected, and then refrigerated in a dedicated warehouse. They should be transported to a medical waste incinerator within 7 days, and disposed of within 2 days.

3) Disinfection

If a surface is contaminated, wipe it with sodium hypochlorite diluted 1:49 (e.g., 5% sodium hypochlorite 10 mL + water 490 mL mix), and leave it for 15–30 minutes, before wiping it again with water. If a metal surface is to be disinfected, wipe it with 70% alcohol (e.g. 100% alcohol 70 mL + water 30 mL mix). If a surface is visibly contaminated by blood and body fluids, wipe it with sodium hypochlorite diluted 1:4 (e.g., 5% sodium hypochlorite 100 mL + water 400 mL mix), and leave it for 10 minutes, before wiping it again with water. The sodium hypochlorite solution should be newly mixed each time. After disinfection is finished, thorough ventilation is required.

4) Laundry

Reusable surgical garments (e.g., gown, mask) made of cotton could be included in the alternative list of PPEs. The cotton contaminated with blood or body fluids should be washed with hot water at 70°C or higher. If unavailable, soak them in sodium hypochlorite diluted 1:49 (e.g., 5% sodium hypochlorite 100 mL + water 4,900 mL mix), and leave them for 30 minutes before washing. Handle as gently as possible, to avoid aerosols.

3. PPEs

1) General principles

Aiming to protect the whole body of the autopsy personnel, including respiratory tract, eyes, and hands, from the infection, PPE should be selected in consideration of the nature and the infection route of the pathogen, and the expected situation of possible exposure. PPE should in principle be disposable or single-use, but some items (e.g., powered air-purifying respirators (PAPR), goggles, face shields, surgical garments made of cotton, and boots or shoes) may be designed for reuse, which should be disinfected or sterilized according to the manufacturer's instructions. Keep hair from flowing down, and remove personal accessories, like watches, in advance. To prevent unnecessary contamination, each manual of the PPEs, including dressing and undressing orders, should be understood in advance, and properly applied. Once the PPEs are used, they shall be discarded or disinfected, being regarded as contaminated. Hand hygiene shall be carried out before and after dressing or undressing. Damaged or contaminated PPEs should be discarded, without being reused or stored again. Cross-check between the autopsy personnel is recommended of whether the PPEs are worn properly, or not.

2) Selection of PPEs

Table 2 lists the recommended PPEs and their alternatives. The components of PPEs can be adjusted to the extent that their purpose and function are guaranteed to be maintained. According to the expected risk of exposure to the pathogen through working, some parts of PPEs could be applied selectively, as marked in the column 'Transfer of bodies.'

3) Dressing and undressing orders

The dressing order of PPE should be as follows:

Hand hygiene → Inner gloves → Lower part of full-body suit → Boots or shoes →
Mask → Goggles or face shield → Upper part of the full-body suit or surgical gown
and cap → Outer gloves

Table 2. Recommended components of PPEs, and their alternatives

Part	Recommended items	Alternative items	Requirements	Transfer of bodies	Autopsy or Lab works	Cleaning or laundry
Respiratory	Disposable mask (KF94/N95 or higher)	PAPR with HEPA filters	Blocks aerosol inflow Easy to breath	0	0	0
Eyes	Goggles	Face shield	Complete covering of the periocular area Anti-frosting and scratching glasses	-	0	0
Body	Full-body protective suit ^a	Surgical gown Surgical gown with plastic apron	Includes at least one layer of waterproof function	0 -	- 0	- 0
Head	Surgical cap	-	Complete covering of the hairs and ears	-	0	0
Hands	Double surgical gloves interposed with cut-proof steel mesh layer	Double surgical gloves interposed with other cut-proof layer ^b	Covers wrists overlapping the end of the suit or gown	0	0	0
Feet	Long rubber boots	Rubber shoes or shoe covers	Anti-slipping bottoms Avoids exposure of any part of lower body	0	0	0

PPE = personal protective equipment, PAPR = powered air-purifying respirators, HEPA = high-efficiency particulate air.

^aIf a full-body suit is not available, surgical cap and long boots can be used to minimize exposed parts. Also, if the suit or gown is not made of waterproof material, the waterproof function of the PPEs can be supplemented with a plastic apron or arm covers; ^bAlthough they are not truly cut-proof, work gloves made of cotton may interrupt the movement of blades.

The undressing order of PPE should be as follows:

Outer gloves → Disinfection of inner gloves → Full-body suit or surgical gown and cap → Boots or shoes → Disinfection of inner gloves again → Goggles or face shield → Mask → Inner gloves → Hand hygiene

It is recommended to disinfect inner gloves at each step, as during the undressing they may become contaminated. If PPEs are found to be damaged, these cases should be considered as exposure to the pathogen, followed by proper management for the personnel.

4. Autopsy procedures

1) General principles

All the processes should be supervised by an experienced forensic pathologist. The number of people who participate in the autopsy should be minimized. However, it is recommended that at least two people be present in the autopsy room, in case of an emergency.⁸ To prevent cutting injuries, the dissection of each body part should be conducted by only one person at a time. A person who is not directly participating in the autopsy, such as the bereaved family member or police, is restricted from entering the autopsy room. During the prevalence of certain infectious diseases or the autopsy for confirmed cases, the access of trainees, such as medical students or residents, is also restricted. If necessary, observation through a window or a monitor is recommended, in a completely separate space from the autopsy room.

2) The main points of autopsy procedures

All the autopsy personnel should be cautious with sharp objects, such as scalpels, knives, needles, or bone sections, which can cause cutting injuries. Damaged or contaminated PPEs should be immediately discarded, and replaced with new ones. In the case of exposure to infection source, disinfect the exposed area immediately in a proper way; and if there is medical evidence, start prophylactic treatment.

If the body is suspected to have an airborne disease, the following should be operated with special caution, to prevent aerosols: 1) cutting bone with electronic saws, for which replacement

by manual saws or additional use of vacuum inhalers is recommended, 2) opening the containers or centrifugation of samples, 3) body movement during transportation or postural adjustment during autopsy, which may cause spout of oral and nasal contents, 4) incision of the bronchus or lung parenchyma, which may expose the secretion inside, and 5) washing the body with a showerhead, which may spray its body fluids or adhesives together.

3) *Test to confirm the infection*

For the suspected cases or the unknown/negative cases with suspicious findings in the autopsy, a medically verified test at the time for each pathogen or disease should be requested, with appropriate samples. In these cases, the autopsy personnel and facilities should be managed as if they participated in the autopsy for confirmed cases, until the test result is assured to be negative.

4) *Handling and transport of the autopsy-derived samples*

The initial sample, which is not chemically treated nor biologically inactivated, should be handled within the biosafety cabinet installed in the BSL2 laboratory by experienced personnel wearing the PPEs equivalent to that used in the autopsy room. Meanwhile, after chemical treatment or biologic inactivation, the samples can be handled on an ordinary bench. Purified DNA or protein can be handled in the BSL1 laboratory, but the use of a biosafety cabinet or its equivalent is recommended.

To transport the autopsy samples, they should be prepared in the following order: 1) put the samples into the primary container, and seal it, 2) disinfect the outer surface of the primary container with 70% alcohol, and label it with an identification tag, 3) wrap the primary container with an absorbent (e.g., paper towel), 4) put the primary container into the secondary container, and seal it, 5) put the secondary container into the tertiary container and seal it, and then label it with a tag. The personnel who pack or open the containers should wear the PPEs equivalent to that used in the autopsy room or laboratory. Any work that requires contact with the containers, for example, simple transportation in sealed status, requires at least the wearing of gloves.

5. Human resource management

1) *General principles*

The affiliated agency should recognize the major infection history of all personnel who participate in autopsy or handle postmortem samples, and take necessary measures to prevent infections. If the standard autopsy was conducted without any damage of PPEs, the risk of infection is generally low. However, if the biologic nature of the pathogen or the epidemiology and pathophysiology of the disease are not fully identified, all the participants should be alert during the expected incubation period, even though they are not obviously exposed, with self-monitoring of the symptoms and the minimizing of face-to-face contacts. All the personnel who have accessed the autopsy room should be recorded: not only the direct participants in the autopsy, but also assistants for the maintenance of the facilities.

2) *Preparations before autopsy*

Considering the prevalence and biological risk, a list of infectious pathogens should be selected, and periodically evaluated for surveillance. If there is clinical evidence, prophylaxis, like vaccination, is recommended. In particular, each participant in the autopsy of confirmed cases should check whether he or she is already infected with the pathogen or not, so that if he or she is infected during the autopsy, the infection source could be traced.

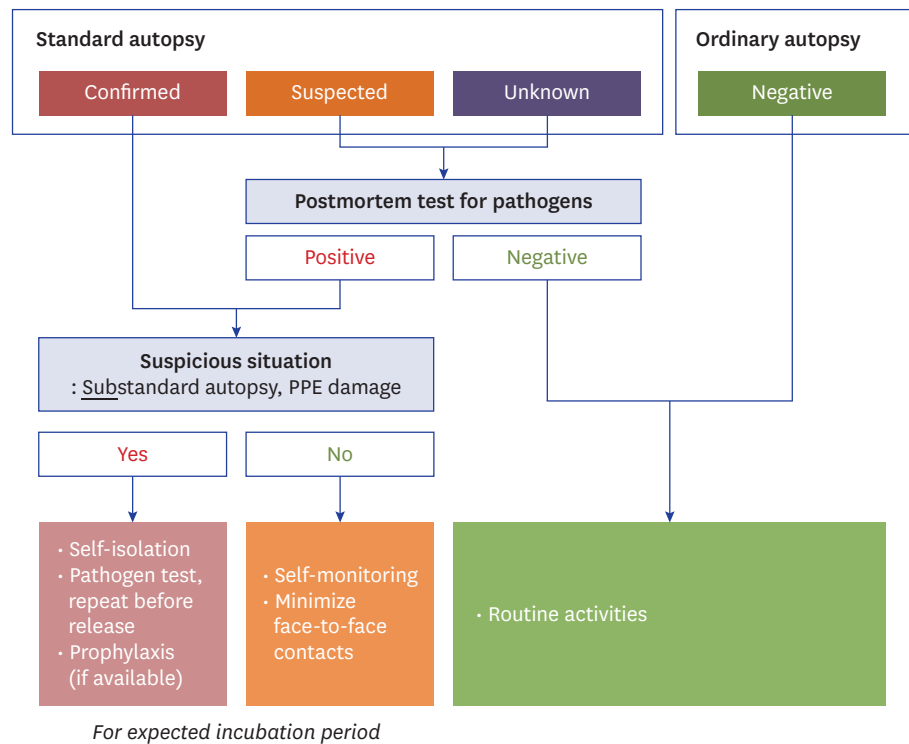


Fig. 1. Flow chart of the actions required to protect autopsy personnel after an autopsy, according to the infection status of the body, postmortem test for pathogens and its result, and the presence of suspicious situation for exposure. PPE = personal protective equipment.

3) *Actions for the suspicious exposure*

Fig. 1 summarizes the actions needed for the autopsy personnel and his or her affiliated agency after the autopsy, according to the infection status of the body, postmortem test for pathogens and its result, and the presence of suspicious situation for exposure.

In the case of personnel who participated in the autopsy of a body confirmed to be infected but the standard protocol was followed, there is no possibility of exposure, so only self-monitoring of the symptoms and the minimizing of face-to-face contacts during the expected incubation period are required. However, if the autopsy procedures failed to meet the standard protocol, or the PPEs were damaged, infection should be suspected. In this case, self-isolation during the expected incubation period, and if available, prophylaxis, is required. The relevant personnel should be tested for the pathogen at the time point when related symptoms are shown, or the isolation period is nearly ended. If a test was requested after the autopsy, but the results are pending, the same actions are required in the interim.

If the autopsy procedures failed to meet the standard protocol, or the PPEs were damaged, the forensic pathologist in charge of the autopsy may consider adjusting the participant members, or discontinuing and delaying the autopsy schedule, to protect the autopsy personnel.

If a test for certain infection was requested after the autopsy, the process and the result should be shared with all the personnel who had, or would have, contact with the body, including the police, the bereaved family, the person who has discovered, reported, inspected, or transported the body, and the funeral staff. They are required to minimize face-to-face contacts, until the test result is confirmed.

6. Special considerations for COVID-19

1) Overview

COVID-19 is a respiratory syndrome caused by the infection of SARS-CoV-2, which belongs to the coronavirus family. Currently, in Korea, COVID-19 is regarded as an 'emerging infectious disease syndrome,' which is included in Class 1 legal infectious disease (**Appendix 1**), and SARS-CoV-2 is considered a high-risk pathogen, which needs 'urgent management' (**Appendix 4**). It is known to be transmitted through aerosols, droplets, or direct contact, while the viruses have also been found in tears and feces.^{14,15} The incubation period is up to 14 days, and symptoms were expressed within 12.5 days after exposure in 95% of the infected. According to the studies published so far, the survival period of SARS-CoV-2 is 3 hours in aerosols, 4 hours on copper surfaces, 24 hours on cardboard surfaces, and 2–3 days on plastic or iron surfaces, which indicate that SARS-CoV-2 can survive for a considerable period outside of the host.¹⁶

2) Clinical and pathologic findings

SARS-CoV-2 patients show diverse symptoms, ranging from asymptomatic to severe respiratory failure. Major symptoms are fever, fatigue, dry cough, muscle ache, and shortness of breath; and a few cases included sputum, headache, hemoptysis, and diarrhea. Recently, the CDC of the United States and the KCDC added ageusia and anosmia as major symptoms of COVID-19.

The patients are frequently diagnosed with viral pneumonia, regardless of the actual severity of their symptoms. As of yet, there is no specific therapeutic agent or vaccine. Severe patients suffer from respiratory failure, septic shock, and multiple organ failure. The median time to respiratory failure was 8.0 days from symptom onset, while that to mechanical ventilation was 10.5 days.

According to a few reports of autopsy or histopathology test, microscopic findings included diffuse alveolar damage, fibromucinous exudates, inflammatory infiltration in the interstitium or intra-alveolar area, viral cytopathic-like change, and thrombogenic vasculopathy.¹⁷⁻²¹

3) Indication for the diagnostic tests

A diagnostic test for SARS-Cov-2 could be considered based on 1) medical history or symptoms, which are mainly fever or respiratory symptoms, and also include headache, abdominal pain, and fatigue, 2) epidemiologic connection, such as temporal, spatial, or geographical relationships with an epidemic region or confirmed patient, and 3) gross pathologic findings of the lungs, such as consolidation, thick exudates, excessive mucus, or other findings suggestive of acute or severe pneumonia, regardless of the clinical symptoms.

4) Facilities and procedures of the autopsy

The autopsy of confirmed and suspected cases should be conducted at BSL3 or equivalent facilities. For unknown cases, the autopsy could be conducted under BSL3 facilities, but there should be reasonable compensations, such as preliminary tests before the autopsy, adequate ventilation and disinfection of the facilities, or additional use of PPEs. The management of autopsy related facilities follows the standard autopsy protocol as mentioned above. Even though the generation of droplets or aerosols from bodies is unlikely, it is recommended to minimize direct contact with the bodies or postmortem samples, and prevent damage of PPEs.²²

5) Sample handling

In the case of samples for virus test, attach the swabs for sample collection to the upper

airway (pharynx, larynx) and the lower airway (lung) for a few seconds, so that the secretions or exudates could be absorbed sufficiently. Put the swabs into the transport medium immediately, and seal the caps. Other samples for postmortem tests should be regarded as ordinary cases only after they are confirmed to have an adequate level of biological risk, including the possibility of aerosol generation.²³ Toxicology samples, such as blood and gastric contents, should be disinfected by mixture with 100% alcohol for 3 (sample):7 (alcohol) ratios, and left for more than an hour. This method can be applied to various postmortem samples, except for alcohol concentration test.²⁴

For pathologic study, the respiratory system, including proximal and distal trachea, pulmonary hilum, main and segmental bronchi, pulmonary parenchyma, and other organs, such as the heart, the liver, kidney, spleen, and intestines, could be sampled, according to the purpose of the study. Fix them with 10% formalin for 2–3 days.²⁵

6) Actions after the autopsy

(1) The autopsy for confirmed cases

The management of facilities, environment, and human resources follows the standard autopsy protocol suggested above. The initial samples should be sent to the BSL3 laboratory.

If there is a risk of infection due to damage of PPEs, skin exposure, aerosol-prone manipulation, or cutting injuries, the relevant autopsy personnel and his or her contacts should be provided with proper medical treatment, including disinfection and virus test. Also, for 2 weeks from the exposed time point, which is the expected incubation period of COVID-19, they should be isolated and excluded from the work, even though the initial test result is negative. The affiliated agency should monitor his or her symptoms.

(2) The autopsy for suspected or unknown cases

If a virus test for the body is carried out during the autopsy, the participated autopsy personnel should minimize face-to-face contact, until the results are notified.

If the result of the virus test is positive, a postmortem test, such as toxicology (except for alcohol), biochemical, or genetic test should be requested, after the disinfection of the samples by mixing with 100% alcohol for 3 (sample):7 (alcohol) ratios.²⁴ Then the samples should be transported according to the standard protocol above. The management of the facilities, environments, and human resources generally follows the standard protocol above, while the disinfection process of the autopsy room and related facilities should refer to the KCDC guideline. If an infection is suspected, for example, due to a substandard autopsy procedure or damaged PPEs, the autopsy personnel and their contacts should be provided with proper medical treatment, including disinfection and virus test, with isolation and monitoring for 2 weeks, as mentioned above in section 6)-(1). When the body is confirmed to be negative for the virus test, the isolation and monitoring could be discontinued.

IV. SUGGESTION FOR THE DEATH INVESTIGATION SYSTEM IN KOREA

Since the autopsy personnel are under constant risk of infection, there should be consistent effort for the implementation of the standard autopsy guidelines. First of all, expecting the periodic spread of infectious diseases in the future, the preparation of adequate level of PPEs

and BSL of the autopsy related facilities, and the establishment of a health monitoring and surveillance system are required.

To compensate for the problems of the current death investigation system, which is focused on the judicial purpose, in the short term, the range of unnatural death considered as the subject of judicial autopsy should be expanded as wide as possible, in consultation with the police and the prosecution. In the long term, the autopsy request ordered by the directors of the Ministry of Health and Welfare or the KCDC should be encouraged with systemic supports. Also, the Ministry of Health and Welfare or the KCDC should be in charge of the management of biosafety requirements in the autopsy facilities and the arrangement of the qualified human resources and financial support, so that this guideline could be satisfactorily implemented.

Forensic medicine has developed and gradually improved over a long period, despite all the difficulties such as unfavorable environment and systemic constraints. However, in the upcoming post-COVID-19 era, there should be more integrated and organized provision, especially against the risk of infectious diseases. Health authorities and forensic pathologists should work together to improve the autopsy environment and the death investigation system, so that a better national health system can be established in the near future.

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Appendix 1. Classification of legal infectious diseases designated by the Infectious Disease Control and Prevention Act of Korea

Class	Class 1 (17 species)	Class 2 (20 species)	Class 3 (26 species)	Class 4 (23 species)
Definition	Infectious diseases that require <u>negative pressure isolation</u> and immediate reporting of diagnosis or outbreak, due to the high risk of bioterrorism or mass infection, and high mortality rate	Infectious diseases that need to be reported and isolated within 24 hr in the case of outbreak or epidemic, due to high infectivity	Infectious diseases that need to be reported within 24 hours in the case of outbreak or epidemic, and monitored continuously	Infectious diseases other than Classes 1-3, that require sample monitoring to identify an outbreak
Species	<p>A. Ebola virus disease</p> <p>B. Marburg fever</p> <p>C. Lassa fever</p> <p>D. Crimean-Congo haemorrhagic fever</p> <p>E. South American haemorrhagic fever</p> <p>F. Rift valley fever</p> <p>G. Variola (smallpox)</p> <p>H. Pest</p> <p>I. Anthrax</p> <p>J. Botulism</p> <p>K. Tularemia</p> <p>L. <u>Emerging infectious disease syndrome</u></p> <p>M. <u>Severe acute respiratory syndrome (SARS)</u></p> <p>N. <u>Middle east respiratory syndrome (MERS)</u></p> <p>O. Animal influenza infection in human</p> <p>P. Novel influenza (H1N1) infection</p> <p>Q. Diphtheria</p>	<p>A. <u>Tuberculosis</u></p> <p>B. Varicella (chickenpox)</p> <p>C. Rubella (measles)</p> <p>D. Cholera</p> <p>E. Typhoid</p> <p>F. Paratyphoid</p> <p>G. Shigellosis, bacillary dysentery</p> <p>H. Colon bacillus infection with enterorrhagia</p> <p>I. Viral hepatitis A</p> <p>J. Pertussis</p> <p>K. Mumps</p> <p>L. Rubella</p> <p>M. Polio</p> <p>N. Meningococcal meningitis</p> <p>O. Haemophilus influenzae type B</p> <p>P. Pneumococcosis</p> <p>Q. Hansen's disease (Leprosy)</p> <p>R. Scarlet fever</p> <p>S. Vancomycin Resistant Staphylococcus Aureus infection</p> <p>T. Carbapenem-resistant Enterobacteriaceae infection</p>	<p>A. Tetanus</p> <p>B. <u>Viral hepatitis B</u></p> <p>C. Japanese encephalitis</p> <p>D. <u>Viral hepatitis C</u></p> <p>E. Malaria</p> <p>F. Legionellosis</p> <p>G. Vibrio vulnificus sepsis</p> <p>H. Epidemic typhus</p> <p>I. Murine typhus</p> <p>J. Scrub typhus</p> <p>K. Leptospirosis</p> <p>L. Brucellosis</p> <p>M. Rabies</p> <p>N. Hemorrhagic fever with renal syndrome</p> <p>O. <u>Acquired immunodeficiency syndrome</u></p> <p>P. Creutzfeldt-Jakob disease and variant Creutzfeldt-Jakob disease</p> <p>Q. Yellow fever</p> <p>R. Dengue fever</p> <p>S. Q fever</p> <p>T. West Nile fever</p> <p>U. Lyme disease</p> <p>V. Tick-borne encephalitis</p> <p>W. Melioidosis</p> <p>X. Chikungunya fever</p> <p>Y. Severe fever with thrombocytopenia syndrome</p> <p>Z. Zika virus infection</p>	<p>A. Influenza</p> <p>B. Syphilis</p> <p>C. Ascariasis</p> <p>D. Trichuriasis</p> <p>E. Enterobiasis</p> <p>F. Clonorchiasis</p> <p>G. Paragonimiasis</p> <p>H. Intestinal trematodas</p> <p>I. Hand-foot-and-mouth disease</p> <p>J. Gonorrhoea</p> <p>K. Chlamydial infection</p> <p>L. Chancroid</p> <p>M. Genital herpes</p> <p>N. Condyloma acuminata</p> <p>O. Vancomycin-Resistant Enterococci infection</p> <p>P. Methicillin-Resistant Staphylococcus aureus infection</p> <p>Q. Multidrug-resistant Pseudomonas aeruginosa infection</p> <p>R. Multidrug-resistant Acinetobacter baumannii infection</p> <p>S. Various intestinal infections</p> <p>T. Acute respiratory infections</p> <p>U. Foreign parasite infections</p> <p>V. Enterovirus infections</p> <p>W. Human papilloma virus infection</p>
Monitoring		Total cases	Total cases	Sampled cases
Report time	Without delay		Within 24 hr	Within 7 days
Report subjects		Diagnosis, death, and the result of pathogen test		Diagnosis and death
Report route	From medical doctor, dentist, oriental medical doctor, head of medical institute, commander of military unit, head of local laboratory to head of public health clinic by letter	Advance notice by words or by telephone		

Appendix 2. Classification of Pathogen Risk Groups suggested by the Korea Centers for Disease Control and Prevention and the National Institute of Health⁷⁾

1. Risk Group 1

The pathogens not included in Risk Group 2-4. Exclude the species of which the pathogenicity against human is not known yet.

2. Risk Group 2

Bacteria	Viruses	Fungi	Parasites
▶ <i>Acinetobacter baumannii</i>	▶ Adenoviridae	▶ <i>Acremonium</i> spp.	▶ <i>Ancylostoma</i>
▶ <i>Actinobacillus</i>	Human adenovirus	▶ <i>Aspergillus</i> spp.	<i>A. ceylanicum</i>
▶ <i>Actinomyces</i>	▶ Arenaviridae	▶ <i>Arthroderma</i> (<i>Trichophyton</i>)	<i>A. duodenale</i>
<i>A. bovis</i>	Junin virus candid #1 vaccine strain	<i>A. simii</i> (some strains)	▶ <i>Ascaris</i>
<i>A. israelii</i>	Lymphocytic choriomeningitis virus (non-neurotropic strains)	▶ <i>Blastomyces</i> (<i>Ajellomyces</i>)	<i>A. lumbricoides</i>
<i>A. naeslundii</i>	Tacaribe virus complex	<i>B. dermatitidis</i>	<i>A. suum</i>
<i>A. pyogenes</i>	▶ Bunyaviridae	▶ <i>Candida</i> spp.	▶ <i>Babesia</i>
▶ <i>Aeromonas</i>	Bunyamwera virus	▶ <i>Cladosporium bantianum</i>	<i>B. bovis</i>
<i>A. hydrophila</i>	Puumala virus	▶ <i>Cladosporium</i> (<i>Xylohypha</i>) <i>trichoides</i>	<i>B. divergens</i>
<i>A. punctata</i>	Seoul virus	▶ <i>Cryptococcus</i>	<i>B. microti</i>
▶ <i>Amycolata autotrophica</i>	Rift Valley fever virus vaccine strain MP-12	<i>C. neoformans</i> var	▶ <i>Brugia</i>
▶ <i>Archanobacterium haemolyticum</i>	Others excluded from Group 3 and 4	<i>C. gattii</i>	<i>B. malayi</i>
▶ <i>Arizona hinshawii</i>	▶ Caliciviridae	<i>C. neoformans</i>	<i>B. timori</i>
▶ <i>Bacillus cereus</i>	Norovirus Sapovirus	▶ <i>Dactylaria</i> (<i>Ochroconis</i>) <i>gallopava</i>	▶ <i>Clonorchis sinensis</i>
▶ <i>Bartonella henselae</i>	▶ Coronaviridae	▶ <i>Emmonsia</i>	▶ <i>Cryptosporidium parvum</i>
▶ <i>Bartonella quintana</i>	Coronavirus	<i>E. parva</i>	▶ <i>Cysticercus cellulosae</i>
▶ <i>Bartonella vinsonii</i>	▶ Flaviviridae	<i>E. parva</i> var	▶ <i>Echinococcus</i>
▶ <i>Bordetella</i>	Dengue virus serotypes 1, 2, 3, and 4	<i>E. crescens</i>	<i>E. granulosus</i>
<i>B. pertussis</i>	Japanese encephalitis virus	▶ <i>Epidermophyton</i> spp.	<i>E. multilocularis</i>
<i>B. parapertussis</i>	Yellow fever virus vaccine strain 17D	▶ <i>Exophiala</i> (<i>Wangiella</i>) <i>dermatitidis</i>	<i>E. vogeli</i>
▶ <i>Borrelia</i>	Hepatitis C virus	▶ <i>Fonsecaea</i>	▶ <i>Echinostoma Hortense</i>
<i>B. recurrentis</i>	Others excluded from Group 3 and 4	<i>F. pedrosol</i>	▶ <i>Entamoeba</i>
<i>B. burgdorferi</i>	▶ Hepadnaviridae	<i>F. compacta</i>	<i>E. coli</i>
▶ <i>Burkholderia</i> (Except <i>B. mallei</i> , <i>B. pseudomallei</i>)	Hepatitis B virus	▶ <i>Fusarium</i>	<i>E. gingivalis</i>
▶ <i>Calymmatobacterium granulomatis</i>	Hepatitis D virus	<i>F. moniliforme</i>	<i>E. hartmanni</i>
▶ <i>Campylobacter</i>	▶ Herpesviridae	<i>F. solani</i>	<i>E. histolytica</i>
<i>C. coli</i>	Epstein Barr virus	▶ <i>Madurella</i>	▶ <i>Enterobius vermicularis</i>
<i>C. fetus</i>	Human cytomegalovirus	<i>M. grisea</i>	▶ <i>Fasciola</i>
<i>C. jejuni</i>	Herpes simplex virus 1 and 2	<i>M. mycetomati</i>	<i>F. hepatica</i>
▶ <i>Chlamydia</i>	Human herpesvirus types 3, 4, 5, 6, and 7	▶ <i>Microsporium</i> spp.	<i>F. gigantica</i>
<i>C. psittaci</i>	Varicella zoster virus	▶ <i>Neotestudina rosatii</i>	▶ <i>Giardia lamblia</i>
<i>C. trachomatis</i>	▶ Orthomyxoviridae	▶ <i>Paecilomyces</i> spp.	▶ <i>Gymnophalloides seoi</i>
<i>C. pneumoniae</i>	All types including Influenza viruses types A, B, and C	▶ <i>Paracoccidioides brasiliensis</i>	▶ <i>Heterophyes nocens</i>
▶ <i>Clostridium</i>	▶ Papovaviridae	▶ <i>Penicillium marneffeii</i>	▶ <i>Hymenolepis</i>
<i>C. botulinum</i>	Human papilloma viruses all types	▶ <i>Pneumocystis carinii</i>	<i>H. diminuta</i>
<i>C. chauvoei</i>	▶ Paramyxoviridae	▶ <i>Sporothrix schenckii</i>	<i>H. nana</i>
<i>C. difficile</i>	Human parainfluenza viruses types 1, 2, 3, and 4	▶ <i>Trichophyton</i> spp.	▶ <i>Iodoamoeba butschlii</i>
<i>C. haemolyticum</i>	Human respiratory syncytial virus		▶ <i>Isospora</i>
<i>C. histolyticum</i>	Measles virus		<i>I. belli</i>
<i>C. novyi</i>	Mumps virus		<i>I. hominis</i>
<i>C. perfringens</i>	Newcastle disease virus		▶ <i>Leishmania</i>
<i>C. septicum</i>			<i>L. aethiopica</i>
<i>C. tetani</i>			<i>L. braziliensis</i>

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2. (Continued) Risk Group 2

Bacteria	Viruses	Fungi	Parasites
<ul style="list-style-type: none"> ▶ <i>Corynebacterium</i> <i>C. bovis</i> <i>C. jeikeium</i> <i>C. diphtheriae</i> <i>C. pseudotuberculosis</i> <i>C. renale</i> <i>C. ulcerans</i> ▶ <i>Dermatophilus congolensis</i> ▶ <i>Edwardsiella tarda</i> ▶ <i>Erysipelothrix rhusiopathiae</i> ▶ <i>Escherichia coli</i> ▶ <i>Fusobacterium necrophorum</i> ▶ <i>Fusiformis necrophorus</i> ▶ <i>Haemophilus</i> <i>H. ducreyi</i> <i>H. influenza</i> ▶ <i>Helicobacter pylori</i> ▶ <i>Klebsiella</i> ▶ <i>Legionella</i> ▶ <i>Leptospira interrogans</i> ▶ <i>Listeria monocytogenes</i> ▶ <i>Moraxella</i> ▶ <i>Mycobacterium</i> <i>M. avium complex</i> <i>M. asiaticum</i> <i>M. bovis</i> (BCG strain) <i>M. chelonae</i> <i>M. fortuitum</i> <i>M. kansasii</i> <i>M. leprae</i> <i>M. malmoense</i> <i>M. marinum</i> <i>M. paratuberculosis</i> <i>M. scrofulaceum</i> <i>M. simiae</i> <i>M. szulgai</i> <i>M. ulcerans</i> <i>M. xenopi</i> ▶ <i>Mycoplasma</i> ▶ <i>Neisseria</i> <i>N. gonorrhoeae</i> <i>N. meningitidis</i> ▶ <i>Nocardia</i> <i>N. asteroides</i> <i>N. brasiliensis</i> <i>N. farinica</i> <i>N. otitidiscaviarum</i> <i>N. transvalensis</i> 	<ul style="list-style-type: none"> ▶ Parvoviridae Human parvovirus (B19) ▶ Piconaviridae Hepatitis A virus Human echoviruses Human coxsackieviruses types A and B Human rhinoviruses Polioviruses all types ▶ Poxviridae All types including Monkeypox virus, Alastrim, Smallpox, Whitepox ▶ Reoviridae All type including Coltivirus, Human Rotavirus, Orbivirus ▶ Rhabdoviridae Rabies virus Vesicular stomatitis virus adapted to the laboratory including VSV-Indiana, San Juan, Glasgow Rubella virus ▶ Togaviridae Chikungunya virus 131/25 vaccine strain Eastern equine encephalomyelitis viruses O'nyong-nyong virus Ross river virus Bebaru virus Sindbis virus Venezuelan equine encephalomyelitis vaccine strain TC-83 Western equine encephalomyelitis viruses ▶ Unclassified Hepatitis E virus 		<ul style="list-style-type: none"> <i>L. donovani</i> <i>L. major</i> <i>L. Mexicana</i> <i>L. peruviana</i> <i>L. tropica</i> ▶ <i>Loa loa</i> ▶ <i>Metagonimus yokogawai</i> ▶ <i>Microsporidium</i> ▶ <i>Naegleria fowleri</i> ▶ <i>Neator americanus</i> ▶ <i>Onchocerca volvulus</i> ▶ <i>Paragonimus westermani</i> ▶ <i>Plasmodium</i> <i>P. cynomolgi</i> <i>P. falciparum</i> <i>P. malariae</i> <i>P. ovale</i> <i>P. vivax</i> ▶ <i>Pygidiopsis summa</i> ▶ <i>Sarcocystis</i> <i>S. lindemanni</i> <i>S. suihominis</i> ▶ <i>Schistosoma</i> <i>S. haematobium</i> <i>S. intercalatum</i> <i>S. japonicum</i> <i>S. mansoni</i> <i>S. mekongi</i> ▶ <i>Strongyloides stercoralis</i> ▶ <i>Taenia</i> <i>T. solium</i> <i>T. saginata</i> <i>T. asiatica</i> ▶ <i>Toxocara canis</i> ▶ <i>Toxoplasma gondii</i> ▶ <i>Trichinella spiralis</i> ▶ <i>Trichomonas</i> <i>T. hominis</i> <i>T. tenax</i> <i>T. vaginalis</i> ▶ <i>Trypanosoma</i> <i>T. brucei</i> <i>T. cruzi</i> <i>T. gambiense</i> <i>T. rangeli</i> <i>T. rhodesiense</i> ▶ <i>Wuchereria bancrofti</i>

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2. (Continued) Risk Group 2

Bacteria	Viruses	Fungi	Parasites
<ul style="list-style-type: none"> ▸ <i>Pasteurella</i> <ul style="list-style-type: none"> <i>P. haemolytica</i> <i>P. multocida</i> (Except <i>P. multocida</i> type b) <i>P. pneumotropica</i> ▸ <i>Plesiomonas shigelloides</i> ▸ <i>Pseudomonas aeruginosa</i> ▸ <i>Rhodococcus</i> <ul style="list-style-type: none"> <i>R. equi</i> ▸ <i>Salmonella</i> ▸ <i>Shigella</i> <ul style="list-style-type: none"> <i>S. dysenteriae</i> <i>S. boydii</i> <i>S. flexneri</i> <i>S. sonnei</i> ▸ <i>Staphylococcus aureus</i> ▸ <i>Streptobacillus moniliformis</i> ▸ <i>Streptococcus</i> <ul style="list-style-type: none"> <i>S. agalactia</i> <i>S. pneumoniae</i> <i>S. pyogenes</i> ▸ <i>Treponema</i> <ul style="list-style-type: none"> <i>T. carateum</i> <i>T. pallidum</i> <i>T. pertenue</i> ▸ <i>Vibrio</i> <ul style="list-style-type: none"> <i>V. cholerae</i> <i>V. parahaemolyticus</i> <i>V. vulnificus</i> ▸ <i>Yersinia</i> <ul style="list-style-type: none"> <i>Y. enterocolitica</i> <i>Y. pseudotuberculosis</i> 			

3. Risk Group 3

Bacteria	Viruses	Fungi
<ul style="list-style-type: none"> ▸ <i>Bacillus anthracis</i> ▸ <i>Bartonella bacilliformis</i> ▸ <i>Brucella</i> <ul style="list-style-type: none"> <i>B. abortus</i> <i>B. canis</i> <i>B. melitensis</i> <i>B. ovis</i> <i>B. suis</i> ▸ <i>Burkholderia mallei</i> ▸ <i>Burkholderia pseudomallei</i> ▸ <i>Coxiella burnetii</i> ▸ <i>Francisella tularensis</i> ▸ <i>Mycobacterium</i> <ul style="list-style-type: none"> <i>M. africanum</i> <i>M. bovis</i> (excluding BCG strain) <i>M. tuberculosis</i> ▸ <i>Orientia tsutsugamushi</i> ▸ <i>Pasteurella multocida</i> type B ▸ <i>Rickettsia</i> <ul style="list-style-type: none"> <i>R. akari</i> <i>R. australis</i> <i>R. canada</i> <i>R. conorii</i> <i>R. japonica</i> <i>R. montana</i> <i>R. parkeri</i> <i>R. prowazekii</i> <i>R. rhipicephali</i> <i>R. rickettsii</i> <i>R. siberica</i> ▸ <i>Rickettsia typhi</i> ▸ <i>Yersinia pestis</i> 	<ul style="list-style-type: none"> ▸ <i>Arenaviridae</i> <ul style="list-style-type: none"> Lymphocytic choriomeningitis virus (neurotropic strain) Mopeia virus ▸ <i>Bunyaviridae</i> <ul style="list-style-type: none"> Estero Real virus Shokwe virus Fort Sherman virus Akabane virus Germiston virus Kairi virus Oropouche virus Rift Valley fever virus Thiafora virus Dugbe virus Nairobi sheep disease virus Hantaan virus Sin nombre virus ▸ <i>Coronaviridae</i> <ul style="list-style-type: none"> SARS-CoV ▸ <i>Flaviviridae</i> <ul style="list-style-type: none"> Cacipacore virus Gadgets Gully virus Israel turkey meningitis virus Kedougou virus Koutango virus Louping ill virus Meaban virus Murray Valley encephalitis virus Negishi virus Powassan virus Rocio virus Sal Vieja virus San Perlita virus Saumarez Reef virus Sepik naranjal virus Spondweni virus St. Louis encephalitis virus Tick-borne encephalitis virus Wesselsbron virus West Nile virus Yaounde virus Yellow fever virus ▸ <i>Orthomyxoviridae</i> <ul style="list-style-type: none"> Avian influenza virus affecting human ▸ <i>Poxviridae</i> <ul style="list-style-type: none"> Monkeypox virus ▸ Prions <ul style="list-style-type: none"> Transmissible spongiform encephalopathies (TSEs) agent (Creutzfeldt-Jacob disease and kuru, Bovine spongiform encephalopathy and other related animal TSEs) ▸ <i>Retroviridae</i> <ul style="list-style-type: none"> Human immunodeficiency virus types 1 and 2 Human T cell lymphotropic virus types 1 and 2 Simian immunodeficiency virus ▸ <i>Rhabdoviridae</i> <ul style="list-style-type: none"> Vesicular stomatitis virus Rabies virus (wild strain) ▸ <i>Togaviridae</i> <ul style="list-style-type: none"> Semliki Forest virus Venezuelan equine encephalomyelitis virus 	<ul style="list-style-type: none"> ▸ <i>Blastomyces (Ajellomyces)</i> <ul style="list-style-type: none"> <i>B. dermatitidis</i> ▸ <i>Coccidioides immitis</i> ▸ <i>Histoplasma</i> <ul style="list-style-type: none"> <i>H. capsulatum</i> var. <i>H. capsulatum</i> <i>H. capsulatum</i> var. <i>H. capsulatum</i> <i>H. duboisii</i>

4. Risk Group 4

Viruses	
▸ Arenaviridae	Central European encephalitis virus
Guanarito virus	Hanzalova virus
Junin virus	Hypr virus
Lassa virus	Kumlinge virus
Machupo virus	Kyasanur Forest disease virus
Sabia virus	Russian spring-summer encephalitis viruses
South American haemorrhagic fever virus	▸ Herpesviridae
▸ Bunyaviridae	Herpesvirus simiae (Herpesvirus B or Monkey B virus Cercopithecine herpesvirus [CHV-1], B virus)
Crimean-Congo hemorrhagic fever virus	▸ Paramyxoviridae
▸ Filoviridae	Equine morbillivirus (Hendra virus)
Ebola virus	Hendra-like virus
Marburg virus	Nipah virus
▸ Flaviviridae	▸ Poxviridae Variola virus
Omsk hemorrhagic fever virus	▸ Other unknown viruses cause hemorrhagic fever

Appendix 3. Standards for the installation and management of high-risk pathogen handling facilities by Enforcement Decree of the Infectious Disease Control and Prevention Act of Korea

1. Installation

Terms of compliance		Safety control grades			
		1	2	3	4
Location and Approach	Isolate the laboratory from the general area	R	M	M	M
	Install a locking system in the main entrance (use card key, fingerprints, security alarm, etc.)	R	M	M	M
Approach	Install a locker for personal clothes or experimental garments before the entrance of the laboratory	R	R	M	M
	Make an anteroom before the entrance of the laboratory	-	R	M	M
	Arrange an area for delivering materials and equipment	-	R	M	M
	Install a double-door entry (manual operation is possible)	-	-	M	M
	Install an airlock entry	-	-	R	M
	Place the air conditioning room near the isolated area	-	-	R	M
	Set the isolated facility by separation of a building dedicated to the experiment surrounded by concrete walls (earthquake-proof design for grade 4 facilities)	-	-	R	M
	Prepare a space for maintenance work	-	-	M	M
	Use materials capable of chemical disinfection and fumigation for inside finishing of the isolated area	-	R	M	M
Sections	Use sealing-guaranteed materials, such as concrete, for the wall structure of the isolated area	-	-	M	M
	Use a non-hardening sealant for sealing the joints of the isolated area	-	-	M	M
	Apply HEPA filter to the inflow vacuum pump line	-	-	M	M
	Design the inside wall to withstand a pressure of 1.25 times the default without distortion or damage	-	-	-	M
Ventilation	Maintain negative pressure always, and avoid recirculation in the isolated area	-	-	M	M
	Maintain the difference between the maximum negative pressured area and the outside of over -24.5Pa (allow ±30% of variation)	-	-	M	M
	Ventilate more than 10 times per hour (more than 20 times per hour in grade 4 facilities)	-	-	M	M
	Correlate the exhaust and supply systems	-	-	M	M
	Apply HEPA filter to the exhaust duct	-	-	R	M
	Apply HEPA filter to the supply duct (double HEPA filter for grade 4 facilities)	-	-	M	M
	Install a spare exhaust filter box	-	-	R	M
	Apply backdraft damper to the exhaust and supply ducts	-	-	M	M
	Apply airtight damper in the front-end of the exhaust HEPA filter (bubble-tight or its equivalent type of damper for grade 4 facilities)	-	-	M	M
	Make the front-end duct and the filter box of the exhaust HEPA filter tolerate pressure over 1,000 Pa 30 minutes with less than 10 % of leakage for grade 3, and pressure over 2,500 Pa with less than 1 % of leakage for grade 4	-	-	M	M
	User protection	Install hand sterilizers and eye washers in the experimental area or the laboratory (exclude eye washer in the grade 4 facilities in which full suits are used)	-	R	M
Install an emergency shower facility in the isolated area (except the grade 4 facilities, in which full suits are used)		-	-	M	M
Install a shower facility for chemical materials for undressing contaminated experimental garments		-	-	-	M
Equipment	Wear positive pressured full suits and PAPRs (except the grade 4 facilities, in which a biosafety cabinet is used)	-	-	-	M
	Install autoclaves (pass-through door type autoclave for the grade 3 and 4 facilities)	M	M	M	M
	Install biosafety cabinets	-	M	M	M
Waste	Install leakage-proof centrifuges for aerosols	-	R	M	M
	Prepare for the elimination of the biologic activity of waste by autoclave, chemical treatment, etc.	M	M	M	M
	Prepare for the elimination of the biologic activity of wastewater by autoclave, chemical treatment, etc. (autoclave for the grade 4 facilities)	M	M	M	M
	Install the wastewater tank to tolerate a pressure of 1.5 times maximum pressure for autoclave or a hydraulic pressure of 70 kPa for chemical treatment, for 10 minutes	-	-	M	M
Others	Exhaust through HEPA filter (double HEPA filter for grade 4 facilities)	-	R	M	M
	Install communication devices connected to the outside, and monitoring device for the inside	R	R	M	M
	Apply backdraft damper to the exhaust ducts	-	R	M	M
	Install a nozzle for detox and test in the HEPA filter box	-	-	M	M
	Install an observable internal pressure measuring instrument and alarm device	-	-	M	M
	Prepare for blackout by installing a spare power supply unit for air conditioning and essential facilities	-	-	M	M

R = recommended, M = mandatory, HEPA = high-efficiency particulate air, PAPR = powered air purifying respirators.

Autopsy Guideline for Infectious Diseases

2. Management

Terms of compliance		Safety control grades				
		1	2	3	4	
Entrance	Keep the entrance closed with allowing only authorized person access	R	M	M	M	
	Record all entries in the control ledger, and store them	-	R	M	M	
	Prepare and use PPEs	R	M	M	M	
	Attach a biosafety sign on the entrance door, including the name of handling pathogens, safety control grades, and the name and contact details of the manager of the facilities	M	M	M	M	
Activities	Perform the experiment only in the designated area, and wash hands after finishing the experiment or leaving the room	M	M	M	M	
	Put on the experimental garments in the experimental area, and take them off before moving to the general area	R	M	M	M	
	Use mechanical pipettes for experiments	M	M	M	M	
	Minimize the generation of aerosols during the experiment	R	M	M	M	
	Do not eat or store food, smoke, or makeup in the experimental area	M	M	M	M	
	Do not bring in anything not related to the experiment, such as plants, animals, clothes, etc.	R	M	M	M	
	When transporting infectious materials, use a robust air-tight container	R	M	M	M	
	Prepare and operate a manual against the introduction of outside organisms, such as insects or rodents	M	M	M	M	
	After finishing the experiment, disinfect the bench (or when contamination occurs during the experiment, immediately)	M	M	M	M	
	Decontaminate by shower when leaving the experimental area	-	-	R	M	
	Prepare a manual for sharp materials, such as needles	M	M	M	M	
	Biosafety	Attach "Biohazard" sign on the devices used for handling or storing high-risk pathogens, such as biosafety cabinet, centrifuge, refrigerator, deep-freezer, etc., and the entrance doors of these areas	M	M	M	M
		Organize a committee for biosafety	R	M	M	M
Appoint an exclusive supervisor for high-risk pathogens, and a chief manager for biosafety		M	M	M	M	
Appoint a manager for biosafety		R	R	M	M	
Educate the personnel about biosafety		M	M	M	M	
Record and store information about the management and operation of high-risk pathogens		M	M	M	M	
Record, report, and store information about the infection events that occur in the facilities		M	M	M	M	
Prepare and apply the standard operating procedure for biosafety		R	M	M	M	
Prepare and apply the regulations and protocols for biosafety (including facility operation for grade 3 and 4 facilities)		R	M	M	M	
When opening infectious materials, use a biosafety cabinet or its equivalent for physical airtightness		-	M	M	M	
Collect and store the baseline serum of the handler of high-risk pathogens (if needed, collect the serum periodically, and do regular checkups)		-	M	M	M	
Vaccinate against the handling pathogens, if available		-	R	M	M	
Prepare an emergency response system including emergency instructions (including medical management for grade 3 and 4 facilities)		M	M	M	M	
Waste	Before disposal, temporarily store the waste in a separated area or container	M	M	M	M	
	Eliminate the biologic activity of the waste	M	M	M	M	
	Prepare regulations for the disposal of experimental waste	M	M	M	M	

R = recommended, M = mandatory, PPE = personal protective equipment.

Appendix 4. High-risk Pathogens designated by Enforcement Regulation of the Infectious Disease Control and Prevention Act of Korea**1. Bacteria and fungi**

- A. *Yersinia pestis*
- B. *Bacillus anthracis* (excluding *Bacillus anthracis* Sterne)
- C. *Brucella melitensis*, *Brucella suis*
- D. *Burkholderia mallei*
- E. *Burkholderia pseudomallei*
- F. *Clostridium botulinum*
- G. *Shigella dysenteriae* type 1
- H. *Chlamydia psittaci*
- I. *Coxiella burnetii*
- J. *Francisella tularensis*
- K. *Rickettsia prowazekii*
- L. *Rickettsia rickettsii*
- M. *Coccidioides immitis*, *Coccidioides posadasii*
- N. *Vibrio cholerae* O1-O139

2. Viruses and prions

- A. Cercopithecine herpesvirus 1, herpes B virus
- B. Crimean-Congo haemorrhagic fever virus
- C. Eastern equine encephalitis virus
- D. Ebola virus
- E. Hendra virus
- F. Lassa virus
- G. Marburg virus
- H. Monkeypox virus
- I. Nipah virus
- J. Rift Valley fever virus
- K. South American haemorrhagic fever; Flexal, Guanarito, Junin, Machupo, Sabia
- L. Yellow fever virus
- M. Western equine encephalitis virus
- N. Tick-borne encephalitis complex virus; Central European tick-borne encephalitis virus, Far Eastern tick-borne encephalitis virus, Siberian tick-borne encephalitis virus, Kyasanur Forest disease virus, Omsk haemorrhagic fever virus
- O. Variola virus
- P. Variola minor virus, Alastrim
- Q. Venezuelan equine encephalitis virus
- R. SARS-CoV
- S. Avian influenza virus H5N1, H7N7, H7N9 (excluding the strains approved by WHO as the subject for vaccination)
- T. High-risk influenza virus containing one or more of 8 pathogenic genes of 1918 influenza virus (H1N1)
- U. Transmission of spongiform encephalopathy agent; Bovine spongiform encephalopathy prion, variant Creutzfeldt-Jakob disease prion
- V. MERS-CoV

3. Other pathogens designated by the Minister of Health and Welfare for urgent management because they are expected to be harmful to public health if released to the community

Appendix 5. The Criteria for the Decision of Unnatural Deaths suggested by the KSLM, 2018.

1. Death suspicious, or confirmed to be related to a crime
2. Death from all types of accident
3. Suicide, or death suspected as suicide
4. Decomposed or unidentified body
5. Body found in the water, or related to fire
6. Death in the course of judicial execution, such as arrest, interrogation, detention, etc.
7. Death at the accommodation for health, welfare, and nursing, etc. (except medical institutions)
8. Unexpected death of over 15-year-old who has seemed to be healthy
9. Death of under 15-year-old not related to medical treatment
10. Death suspected as acute poisoning
11. Death by unknown cause that occurred in a medical institution

Appendix 6. Instructions for Handling Unnatural Deaths declared by the Korean National Police Agency, 2019.

Article 2 (Definitions)

1. The term “unnatural death” means a death falling under any of the following whose cause is unclear:
 - A. Death suspicious, or confirmed to be related to a crime
 - B. Accidental death due to natural disaster, traffic accident, safety accident, industrial accident, fire, drowning, etc.
 - C. Suicide, or Death suspected as suicide
 - D. Death in the course of judicial execution, such as arrest, interrogation, detention, etc.
 - E. Death at the accommodation for health, welfare, and nursing
 - F. Death suspected as acute poisoning by drug, pesticide, alcohol, gas, etc.
 - G. Other death with unknown cause
2. The term “unnatural death case” means a case in which one or more bodies that correspond to, or are suspected of unnatural death, are found.

Article 22 (Autopsy)

1. The director of an unnatural death case shall apply for a warrant for an autopsy in any of the following cases (referred to as a “priority control case”), unless there are special circumstances:
 - A. Death suspected to be by murder
 - B. Unidentified body, despite the investigation of belongings, fingerprints, etc. at the scene
 - C. Death that is expected to draw social attention, such as collective death, child abuse, etc.
 - D. Severely decomposed body, so hard to identify injuries or cause of death
2. The director of an unnatural death case shall consider a warrant for an autopsy in any of the following cases (referred to as a “autopsy-considered case”), to confirm the relation to a crime:
 - A. Unexpected death of infant or child
 - B. Death in the course of judicial execution, such as arrest, interrogation, detention, etc.
 - C. Death suspected as acute poisoning by drug, pesticide, alcohol, gas, etc.
 - D. Death suspected to be drowning or falling, for which eyewitness or CCTV footage is unavailable
 - E. Body that is carbonized or skeletonized
 - F. Death for which the bereaved family harbors suspicions about the cause
 - G. Death by traffic accident suspicious for the relationship to other crime
 - H. Death of a person with excessive death benefit, compared to his or her property
 - I. Death with disagreement about the cause between the inspection doctor, the investigators, or the director of the case
 - J. Other death for which autopsy is required to confirm its cause or circumstance