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Infection control in the management of highly pathogenic infectious diseases: consensus of the European Network of Infectious Disease

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The European Network for Infectious Diseases (EUNID) is a network of clinicians, public health epidemiologists, microbiologists, infection control, and critical-care doctors from the European member states, who are experienced in the management of patients with highly infectious diseases. We aim to develop a consensus recommendation for infection control during clinical management and invasive procedures in such patients. After an extensive literature review, draft recommendations were amended jointly by 27 partners from 15 European countries. Recommendations include repetitive training of staff to ascertain infection control, systematic use of cough and respiratory etiquette at admission to the emergency department, fluid sampling in the isolation room, and analyses in biosafety level 3/4 laboratories, and preference for point-of-care bedside laboratory tests. Children should be cared for by paediatricians and intensive-care patients should be cared for by critical-care doctors in high-level isolation units (HLIU). Invasive procedures should be avoided if unnecessary or done in the HLIU, as should chest radiography, ultrasonography, and renal dialysis. Procedures that require transport of patients out of the HLIU should be done during designated sessions or hours in secure transport. Picture archiving and communication systems should be used. Post-mortem examination should be avoided; biopsy or blood collection is preferred.

Introduction

Over the past two decades, many new and re-emerging diseases have posed threats to public health and have provided new challenges for infectious disease researchers worldwide. Expansion of human populations has caused both a greater proximity to wildlife habitats, resulting in the emergence of new zoonoses, and a massive urbanisation process, which facilitates the rapid spread of communicable diseases in human beings. Travel across the world has become increasingly frequent, resulting in the ever-increasing risk of worldwide contagion spread. These emerging problems were highlighted during the severe acute respiratory syndrome (SARS) epidemic.¹ Imported highly infectious diseases (HID), such as Lassa fever and viral haemorrhagic fever, have been reported many times in the literature but have seldom been at the origin of an outbreak.^{2,3} Terrorist attacks with biological agents pose a substantial threat to the safety, health, and security of the citizens of every country.

As defined in the 2007 issue of the *Biosafety in Microbiological and Biomedical Laboratories* manual,⁴ “group 3 agents are pathogens that usually cause serious human or animal disease but do not ordinarily spread from one infected individual to another and effective treatment and preventive measures are available,” whereas “group 4 [agents] are pathogens that usually cause serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.” Several laboratory-associated infections with group 3 and 4 pathogenic agents have already been reported.^{5–20}

Although laboratories that handle group 3 and 4 agents should comply with biosafety regulations, laboratory leakage can happen at any time, for example, when working with a known agent or when attempting to isolate an unknown infectious agent, such as occurred with mimivirus.²¹ Experience shows that the recognition and isolation of a new infectious agent is often followed by a reported laboratory-acquired infection caused by the new isolate, as was reported for SARS.^{22,23} The infection of a single laboratory worker with a highly infectious agent could be the origin of an outbreak, particularly if the agent has the capability of human-to-human transmission (ie, SARS-associated coronavirus).²³ In some situations, such as a cough in so-called “super-spreader” patients with extremely drug-resistant tuberculosis, smallpox, or SARS-associated coronavirus, or exposure to infected blood of a patient with late-phase haemorrhagic fever, the inoculums to which health-care workers are exposed are likely to be equivalent to those received by a laboratory worker during specimen handling. The care of such patients should consequently be administered in a way to ensure the same level of protection and safety to health-care workers as to laboratory workers exposed to the same agent.

Methods

The European Network for Infectious Diseases (EUNID) comprises 30 national representatives and experts from 16 European member states and is funded by the European commission, within its Public Health and Risk Assessment Programme.²⁴ It was created to exchange information, share best practices, develop training, and improve the connection between national and regional

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infectious disease experts. This network of clinicians, public health epidemiologists, microbiologists, infection-control and critical-care clinicians, who are experienced in the management of HID, represent national or regional infectious diseases units designated to care for patients with HID. One of EUNID's agreed tasks was to develop a consensus statement on the design and operation of high-level isolation units (HLIU) in Europe.²⁵ An HID is transmissible from person to person, causes life-threatening illness, presents a serious hazard in health-care settings and the community, and therefore requires specific control measures.²⁵ An HLIU is defined as a health-care facility that is specifically designed to provide safe, secure, high-quality and appropriate care, with optimum infection containment, infection prevention, and control procedures for a single patient or a small number of patients who have, or who may have, an HID. These units have also been described as biocontainment units by US experts.²⁶ We define an isolation room as a single-bed room with negative pressure.

Our task was to develop a consensus statement for infection control during clinical management and invasive procedures in HID patients admitted to an HLIU. To assess this task, an expert (PB) was co-opted and charged by EUNID to do an extensive review and draft

recommendations on infection control in the situations mentioned above. The draft recommendations were amended by the coordination team, and further refined jointly by the 27 partners from 15 European member states and the coordination team. The final consensus was reached and validated during two consecutive meetings in Rome in May and October, 2007. The draft manuscript was then shared within the network by e-mail and revised to incorporate comments and additional evidence provided by participants until a final version was reached.

Results

Situations in which a patient would need to be admitted in an HLIU

Among the several possible scenarios that may be considered, epidemics outside Europe of a yet unknown contagious agent or a known group 3 or 4 agent, such as SARS-associated coronavirus or viral haemorrhagic fever, are the most likely to occur. Alternatively, a laboratory worker may become sick after being exposed to a known agent in a registered biosafety level 3 or 4 laboratory while doing his or her duty, such as in the last SARS outbreak in China and Singapore.^{23,27} A third possible situation is intentional release of a bioterrorism agent. If an outbreak of a human-to-human transmissible disease begins in one country, the first case it likely to be missed. Thus,

Details		Risk group*	Human-to-human spread	EUNID recommendations†	
				Minimum	Optimum
Bacterial infections					
<i>Rickettsia</i> spp	<i>R. rickettsii</i> , <i>R. conorii</i> , <i>R. akari</i> , <i>R. australis</i> , <i>R. sibirica</i> , <i>R. japonicum</i> , <i>R. typhi</i> , <i>R. prowazekii</i> , <i>R. (Orientia) tsutsugamushi</i>	3	None	Standard	..
<i>Brucella</i> spp	..	3	None	Standard	..
<i>Francisella tularensis</i> type A	Tularaemia	3	None	Standard	..
<i>Mycobacterium bovis</i>	Not BCG	3	None	Standard	..
<i>Coxiella burnetii</i>	Q fever	3	Yes ³¹⁻³³	Standard	Droplet; personal protective equipment required during delivery ³³
<i>Yersinia pestis</i>	Pulmonary plague	3	Yes ³⁴	Droplet	..
<i>Burkholderia pseudomallei</i>	Melioidosis	2/3	Unusual ³⁵	Droplet	..
Mycobacterial infections					
Multidrug-resistant <i>Mycobacterium tuberculosis</i>	..	3	Yes	Airborne ³⁶	..
Extensively drug-resistant <i>M. tuberculosis</i>	..	4 (clinical issues ^{37‡})	Yes	Airborne ³⁶	High-level isolation units
Fungal infections					
<i>Histoplasma capsulatum</i>	..	3	None	Standard	..
*As defined by the Centers for Disease Control and Prevention, WHO, and the European Community Directive. ³⁸ †Note that most of the guidelines are based on a very small number of clinical cases and that level of evidence and grading are not necessarily accurate. Standard precautions include hand hygiene, use of personal protective equipment, prevention of needle stick, environment cleaning, and the appropriate handling of waste. Droplet precautions are standard precautions and the use of a single room, surgical masks for health-care workers when working within 1–2 m of the patient, and a surgical mask on the patient if transport is necessary. Airborne precautions are standard precautions and a single monitored negative-pressure room, closed door, special high-filtration particulate respirators (N95 or FFP2 mask) for health-care workers, and movement of the patient, wearing a surgical mask, only when essential. ‡Extensively drug-resistant <i>M. tuberculosis</i> classified as group 4 because mortality exceeded 30%.					
Table 1: European Network of Infectious Disease (EUNID) recommendations for care of patients with known bacterial and fungal infections					

other implementations, such as routine respiratory and hand hygiene in health-care settings, health-care personnel surveillance, and prompt reporting of such patients to national public-health authorities are mandatory.²⁸

The decision to care for patients in an HLIU is based on the capability of the agent to have human-to-human transmission, its transmission rate, and the availability of primary or secondary prophylaxis, such as vaccines or effective antimicrobial therapy. Although the role of

	Details	Risk group*	Human-to-human spread	EUNID recommendations†	
				Minimum	Optimum
Flaviviruses					
Japanese encephalitis virus	Mosquito borne	3‡	None	Standard	..
West Nile virus	Mosquito borne	3	Yes, by blood transfusion	Standard	..
Central European tick-borne flaviviruses	Absettarov, Hanzalova, Hypr, and Kumlinge viruses	3	None	Standard	..
Yellow fever virus	Mosquito borne	3‡	None	Standard	..
Kyasanur Forest disease virus and Omsk haemorrhagic fever virus	Tick borne	4	Unknown	HLIU	..
Russian spring-summer encephalitis	Tick borne	4	Unknown	HLIU	..
Arenaviruses					
Lymphocytic choriomeningitis virus	Rodent borne	3	None	Standard	..
Junin virus	Argentine haemorrhagic fever	4 (3‡)	Unknown	HLIU	..
Lassa fever virus	..	4	Yes ³⁹	HLIU ⁴⁰	..
Guanarito virus	Venezuelan haemorrhagic fever	4	Yes ³⁹	HLIU ⁴⁰	..
Machupo virus	Bolivian haemorrhagic fever	4	Yes ³⁹	HLIU ⁴⁰	..
Sabiá virus	Brazilian haemorrhagic fever	4	Unknown	HLIU ⁴⁰	..
Phleboviruses					
Rift Valley fever virus	Mosquito borne	3	None	Standard	..
Togoviruses					
Venezuelan equine encephalomyelitis	Mosquito borne	3	None	Standard	..
Chikungunya virus	Mosquito borne	3	Yes, one suspected hospital-acquired infection by contact ⁴¹	Standard	..
Bunyaviruses					
Hantaan viruses	Haemorrhagic fever with renal syndrome, and other Puumala, Seoul, and Sin nombre viruses	3	Yes ^{34,42}	Droplet	Airborne
Congo-Crimean haemorrhagic fever virus	..	4	Yes ³⁹	HLIU ⁴⁰	..
Paramyxoviruses					
Hendra and Hendra-like virus	Equine morbillivirus encephalitis	3	Unknown	Airborne	HLIU
Rhabdoviruses					
Vesicular stomatitis virus	..	3	Highly contagious by contact	Airborne	HLIU
Filoviruses					
Ebola virus	..	4	Yes ³⁹	HLIU ⁴⁰	..
Marburg virus	..	4	Yes ³⁹	HLIU ⁴⁰	..
Other viruses					
SARS-associated coronavirus	..	3	Yes	HLIU ^{43,44}	..
Prepandemic influenza virus	..	3	Yes	HLIU for the first human-to-human transmission cases, then refer to the national plan ^{43,44}	..
Small pox and other pox viruses	..	4 (2 for vaccine‡)	Yes ³⁹	HLIU ⁴⁰	..
Herpesvirus simiae (B)	..	3 or 4	Yes ^{34,45}	HLIU	..
Giant viruses					
Mimivirus	Hospital-acquired pneumonia ²¹	3§	Unknown	Standard	Droplet

HLIU=High-level isolation unit. SARS=severe acute respiratory syndrome. *As defined by the Centers for Disease Control and Prevention, WHO, and the European Community Directive.³⁸ †Note that most of the guidelines are based on a very small number of clinical cases and that level of evidence and grading are not necessarily accurate. ‡In vaccinated personnel. §Not an official classification, but we recommend this level because laboratory-acquired pneumonia has previously occurred.

Table 2: European Network of Infectious Disease (EUNID) recommendations for care of patients with known viral infections

Panel 1: European Network for Infectious Disease (EUNID)²⁵ recommendations for infection control while managing patients with a highly infectious disease (HID)

Situations in which a patient would need to be admitted to an HLIU

- Patients with an unknown human-to-human transmittable or a potentially transmittable epidemic febrile illness that is native or imported from abroad
- Patients with a known infectious disease caused by a group 3 or 4 agent*

At admission of patients with HID to an emergency department

- Systematically apply standard precautions and cough and respiratory etiquette
- Set up at least one single room with a dedicated route and direct access, or an isolation room as recommended by EUNID for a referral hospital,† if HLIU cannot be used for ruling out HID diagnoses
- Offer special training to the emergency department team
- Retain close relationships with the HLIU team of the referral hospital

Sampling of patients with HID for laboratory analysis

- Sampling should be done in the isolation room of the emergency department or in the HLIU
- If possible, use point-of-care bedside laboratory tests
- If not, possibly do all analyses in a biosafety level 3/4 laboratory
- Once inactivated (via formalin), samples can be tested in a routine laboratory
- No consensus recommendation can be provided on the use of a routine auto-analyser‡

Admission and management of paediatric patients with HID in an HLIU

- For infection-control reasons, all children suspected to be infected with an HID should be admitted to an HLIU
- Family participation should be minimised
- The HLIU responsible manager should make all efforts to be prepared and be able to provide nursing care compatible with children's requirements

Intensive-care practice in patients with HID

- If possible, perform intensive-care therapy in the HLIU in collaboration with the infectious disease team; the HLIU should be pre-equipped for critical care
- If a patient with HID is cared for in the intensive-care unit, the unit should be subjected to negative pressure
- Manual ventilation duration during resuscitation procedures should be reduced to a minimum
- Use NPPV instead of facial mask aerosol therapy when possible and intubation/mechanical ventilation instead of NPPV when safely achievable with maximum precautions
- Endotracheal intubation should be done with rapid sequence induction by the most skilled person available, who should wear personal protective equipment
- Meticulous infection-control measures must be followed in case of ventilated patients with HID, particularly during suctioning, tracheotomy, and bronchoscopy with or without bronchoalveolar lavage

HLIU=High-level isolation unit; NPPV=non-invasive positive pressure ventilation. *As summarised in tables 1 and 2. †A hospital to which the patients with HID are usually referred to either by national authority directives or by their own expertise and reference. ‡This remains a matter of debate in our group.

super-spreaders was highlighted during transmission in the SARS outbreak, the respective parts of nosocomial transmission versus super-spreader events are still under debate.²⁹ A strict correspondence between the risk-group classification of an infectious agent for laboratory practices and the classification for the human disease that it causes cannot overlap.^{4,30} EUNID recommendations

for the hospital care of patients with a known infection caused by group 3 or 4 agents are summarised in tables 1 and 2. EUNID recommendations for infection control in the management of patients with HID are shown in panel 1.

Admission of patients with HID to emergency departments

Emergency departments of general hospitals are the primary units where interaction with an unknown HID is most likely, and because many such units were not prepared for this kind of medical situation, they paid a heavy price during the SARS outbreak.^{46–49} Even now, most of our hospitals are still not prepared to face these kinds of situations.⁵⁰ Until a suitable network of care for such patients, with communication between health-care workers prior to referral, becomes effective in each country, patients suspected of being infected with a highly contagious agent are more likely to be referred to the emergency department of a general hospital by their general practitioner. As a consequence, the emergency department of any hospital should be prepared for such events, and both training and structural features should be implemented.²⁸

Based on studies of SARS transmission, measures designed to control respiratory droplets and secretions, along with hand hygiene, would seem to offer significant protection to other patients and health-care workers who have close contact with source patients.^{51,52} Given the challenge of recognising early HID cases, and considering the potential for the spread of respiratory infections in health-care settings, the US Centers for Disease Control and Prevention (CDC) recommended a broader strategy to prevent health-care-associated transmission of respiratory illnesses in response to SARS.⁵³ In addition to standard precautions, the CDC suggest that an efficient measure to reduce the risk of infection transmission needs to be systematically implemented by health-care workers. The CDC described the new standard approach to manage patients with febrile respiratory illness as “respiratory hygiene” or “cough etiquette”.⁵⁴ Patients with cough and fever should be encouraged to report symptoms at admission and should be encouraged or asked to wear a surgical mask and wash their hands after contact with respiratory secretions. These patients should be separated from other patients in the waiting area, and should be examined and assessed as soon as possible by the emergency staff in a single room.⁵⁴ Signs should be displayed in the waiting areas to promote these measures and to educate patients and health-care workers, and emergency staff should comply with droplet precautions.

However, because the modes of infectious agent transmission are often underestimated, as was recently reported for influenza and SARS,⁵⁵ and because tuberculosis cannot be identified without biological testing, EUNID recommends that droplet precaution should be upgraded to airborne precaution each time

that involvement of one of these agents is suspected. Consequently, chest radiography should be done separately from other patients, a systematic examination of sputum for acid-fast bacteria should be prescribed when pneumonia is diagnosed (to rule out tuberculosis), and the patient should remain in isolation until the threat of tuberculosis is eliminated.⁵⁶

Patients with suspected HID should be placed directly in an emergency department isolation room (EDIR), if available. During admission, such patients should avoid any contact with other patients and unprotected health-care workers, and therefore direct access to the EDIR from outside the unit is required.⁵⁷ EDIRs should comply as much as possible with the design and operational management recommendations made by EUNID for HLIU.²⁵ Whereas general respiratory hygiene rules and cough etiquette should apply to every emergency department of every general hospital, isolation rooms could be available in referral hospitals only. A patient with a possible or confirmed HID, if not admitted directly to an HLIU, should be transferred from the EDIR to the HLIU in a secure manner, by use of a safe isolation transportation system,⁵⁸ or at least by staff wearing personal protective equipment and using a clear and secure route. Although these general recommendations may be difficult to apply in the usual understaffed, overworked, and busy environments, implementation of these measures is important. These recommendations would also help prevent the transmission of many other important pathogens that are spread by the droplet route, such as influenza and *Mycoplasma pneumoniae*.⁵³

Sampling HID patients for laboratory analysis

Clinicians should remember that the most likely cause of fever in a tropical traveller is malaria, which is far more common than a new or emerging HID. Consequently, EUNID first advocates that everything possible should be done to rule out the most frequent differential diagnoses without delay. To reduce the risk of transmission to health-care workers, samples from patients should be taken in the EDIR or HLIU, depending on availability. Severely ill patients may necessitate frequent blood sampling and intravenous line placement for reliable antimicrobial or antiviral drug administration. To reduce exposure due to accidental needle-stick incidents, we recommend the use of a routinely secured arterial line and central venous line access by an HID-trained physician, thus allowing safe serial blood sampling and drug administration without further needle-based procedures.

If possible, all routine diagnostic tests should be processed in a biosafety level 3 or 4 laboratory that is located close to the HLIU or on the same campus to avoid unnecessary transportation of contaminated samples.^{4,25,59} Once inactivated, the sample can be processed in a routine clinical laboratory with PCR or blood film analysis. Under certain handling precautions, the use of

a certified autoanalyser in routine tests has been suggested as being safe. However, some experts believe that samples that are likely to be highly contagious, such as blood contaminated by Ebola virus, cannot be handled safely in a routine laboratory. The development of a point-of-care test, such as for arterial blood gas, blood electrolyte, or haemoglobin content, and more recently for microbiology (ie, malaria), or for early diagnosis of lower respiratory-tract infections, offers an alternative to routine tests because they can be done at patients' bedsides.⁶⁰

Caring for paediatric patients with HID in an HLIU

Hospital-acquired infections can cause major problems in paediatric wards, and compliance with isolation procedures needs to be ensured.^{61,62} During the SARS epidemic, infection-control measures overshadowed family-centred nursing practices in the management of paediatric patients,⁶³ and created inevitable conflict.⁶⁴ To effectively control infection, family participation should be minimised, and all children with suspected HID should be admitted to the HLIU. Consequently, everything should be organised in the HLIU to provide nursing care that respects the privacy of the parents and children.

Intensive care units and patients with HID

The risk of being infected with SARS-associated coronavirus was reported to be about 13-times higher among physicians and nurses who performed or assisted in endotracheal intubations in intensive care units (ICUs) than in those who did not.⁶⁵ Nurses who became ill were often exposed to SARS-associated coronavirus within 48 h of a patient's admission, during which time the patient usually deteriorated with symptoms, increasing the spread of droplets or aerosols (eg, dyspnoea, cough, etc).^{66,67} Patients admitted to the ICU are usually severely ill, and are likely to have a high viral load and to be at a point of maximum infectiousness.⁶⁸

Non-invasive positive pressure ventilation (NPPV) is a mode of ventilation assistance used in early acute respiratory failure and acute respiratory distress syndrome. NPPV reduces the intubation rate and is effective in the treatment of SARS-related acute respiratory failure without posing infection risks to health-care workers.⁶⁹⁻⁷² In this setting, intubation has been avoided in up to two-thirds of cases in some studies.^{73,74} If aerosolisation and airborne transmission are discounted, respiratory secretions or fluids, or both, are the main route of SARS transmission, ultimately leading to an overwhelming risk of infection via intubation. However, this mode of transmission does not occur with other airborne pathogens, most notably avian influenza, which can aerosolise or disperse up to 0.5 m around a patient undergoing NPPV.⁷⁵ The main problem with dispersion through NPPV is not the exhalation portion of the respiratory circuit but the inevitable mask

leaks. Consequently, intubation or mechanical ventilation should be preferred to NPPV if safely achievable to control droplet aerosolisation and dispersion. Consequently, endotracheal intubation should be done by the most skilled person available. In addition, that person should wear personal protective

equipment, including eye protection, and use rapid sequence induction.⁴³

ICU rooms should be subjected to negative pressure and a minimum of 15 air changes per hour.^{76,77} Some researchers advocate the use of a powered air-purifying respirator, particularly during high-risk manipulations such as endotracheal intubation, because it offers supplementary protection with a better fit to the health-care worker's face.^{78,79} However, its use is a matter of debate because the risk of dysfunction seems important, which may increase the risk of exposure. Problems in cleaning, disinfection, and storage of the respirator may also increase the risk of exposure.

Endotracheal intubation is not the only high-risk procedure in ICU patients; cardiopulmonary resuscitation was also reported to be a very high-risk procedure during the SARS epidemic.⁸⁰ Patients with other HIDs, such as viral haemorrhagic fever, should also be treated in an ICU. Although the main route of transmission of viral haemorrhagic fever is contact with body fluids, airborne transmission has been suggested with the Reston and Zaire strains of Ebola virus in monkeys.⁸¹ In an outbreak of Ebola in a Johannesburg hospital, no subsequent cases of the disease occurred despite the staff being involved in numerous hazardous procedures.⁸² Despite the fact that this hospital opted for high-level barrier nursing, which entailed the isolation of the patient in a cubicle and the use of protective clothing plus high-efficiency particulate air-filtered respirators to minimise exposure to aerosols, universal blood and body-fluid precautions may have been sufficient for protection.⁸²

Special procedures

The management of invasive diagnostic or therapeutic procedures in a patient with HID is a challenge. However, there were few reports on hospital-acquired HIDs during invasive procedures before the SARS era. In fact, until now, HID outbreaks had only occurred in countries or at times when such techniques were not available, and the recent SARS epidemic has revealed the risks in such situations.⁸³ Of note, available evidence on risk factors is weak and somewhat indirect, according to the commonly accepted hierarchy of evidence. Much work needs to be done to separate the essential risk factors from the superfluous ones. High-risk aerosol-generating procedures were well summarised in the last WHO interim guidelines.⁴³ Panel 2 shows the EUNID recommendations for infection control in the management of patients with HID during these special procedures.

Bronchoscopy

Although diagnostic bronchoscopy or flexible lung endoscopy is not necessary in some scenarios (ie, an ongoing outbreak of a known disease), some situations need such invasive procedures to rule out differential diagnoses or to collect samples for laboratory

Panel 2: European Network for Infectious Disease (EUNID)²⁵ recommendations for infection control during special procedures in patients with a highly infectious disease (HID)

Bronchoscopy

- Avoid all unnecessary procedures
- Comply with established guidelines for prevention of respiratory infection during such procedures
- Perform the bronchoscopy in the HLIU at the bedside, avoiding moving the patient unnecessarily; if not possible, perform these procedures in an air-controlled environment

Gastrointestinal endoscopy

- Avoid in HID patients, unless absolutely necessary
- Adherence to current guidelines for the reprocessing of endoscopes is recommended to prevent transmission of group 3/4 agents via both potentially contaminated gastrointestinal endoscopes and bronchoscopes
- Perform endoscopy in the HLIU at the bedside, avoiding unnecessary moving of the patient; if not possible, perform these procedures in an air-controlled environment

Imaging (chest radiography, ultrasonography, CT, and MRI)

- The examination should be kept as short as possible to answer the clinical questions
- For HLIU-admitted patients, bedside radiography should be provided to avoid transport of patients; radiographic equipment should then be kept in the HLIU
- Radiographs should be interpreted only by a designated radiologist who is aware of infection-control procedures, and by use of a picture-archiving and communication system, if available⁸⁴
- For ultrasound scanning, a sonographic scanner should be designated as a portable radiograph to be used only for HID patients
- For CT or MRI, we strongly recommend that the department appoints a staff member to monitor and ensure that all department staff fully comply with the infection-control measures according to the guidelines
- Designated sessions or hours, either out of office hours or at the end of a session, should be assigned for such patients

Renal dialysis

- Treat HID patients who require dialysis at their bedside with either peritoneal dialysis or haemodialysis
- Designate dedicated haemodialysis machines
- Decontaminate dialysate as infectious waste

Post-mortem examination

- Risks and benefits must be carefully considered
- Limited autopsy or post-mortem collection of blood and percutaneous biopsy are preferred
- The biosafety precautions recommended for clinicians and laboratory staff working with infected patients and specimens must also be followed during post-mortem examination
- Perform the autopsy only if necessary and in a biosafety level 3/4 isolation room, which can serve as the HLIU

HLIU=High-level isolation unit.

investigation. SARS transmission has been reported or suggested after the intubation of patients,⁸⁴ and use of a nebuliser by health-care workers in patients with SARS resulted in a major outbreak of the disease.⁸⁵ In a retrospective study among critical-care nurses in Toronto,⁸⁶ the probability of a SARS infection was 6% in nurses who assisted during intubation, suctioning, and manipulating the oxygen mask. In the same study, wearing a mask, especially an N95 mask, was deemed protective.⁸⁶ A high-flow-rate oxygen mask may also result in health-care worker infection,⁸³ and we have thus suggested that NPPV is preferred to facial mask aerosol therapy if available.

Bronchoscopy has also been suggested to increase SARS-associated coronavirus transmission in health-care workers.⁷¹ The aerosolisation of lung pathogens during flexible endoscopy and hospital-acquired infections during these procedures are both well documented and have led to standard guidelines for flexible endoscopy.⁸⁷ Similar transmissions would probably occur with other respiratory agents, such as avian influenza and hantavirus pulmonary syndrome. Bronchoscopy, airway suctioning, and other procedure that may induce coughing and expose health-care workers to potentially infected aerosolised respiratory droplets pose an increased risk of transmission of those agents. In most hospitals, rooms dedicated for bronchoscopy are under negative pressure, but these rooms are not necessarily air filtered.⁸⁸

Gastrointestinal endoscopy

In addition to airborne transmission, SARS-associated coronavirus may also be transmitted by direct contact with infected respiratory secretions and other body fluids, similar to viral haemorrhagic fever viruses.^{49,89–91} Contact with contaminated environmental surfaces and inanimate objects is suspected to have resulted in the transmission of SARS, as suggested by reports that some health-care workers became infected even though they had no direct contact with SARS-infected patients.^{47,89,92–94} Data also suggest that SARS-associated coronavirus and orthopoxvirus can survive on hard surfaces such as plastic and stainless steel for several hours, if not days.^{40,47,94} Moreover, many group 3 and 4 viruses, including SARS-associated coronavirus, have been identified in human faeces.^{47,90,93,94} Although there is no published report of transmission of SARS to health-care workers and other patients during gastrointestinal endoscopy, the potential for such transmission exists.⁹⁵

Radioimaging: CT and MRI, chest radiography, and ultrasonography

Most of our knowledge on managing infection control in radiology departments comes from experience of tuberculosis and SARS. Radiology technicians have a relative risk for a positive tuberculin skin test of 1.7 compared with other health-care workers, and those working for less than 1 year have a lower risk of infection,

indicating that radiology technicians are more exposed to tuberculosis during their practice.⁹⁶ At the Prince of Wales Hospital in Hong Kong in March, 2003, at least 50 health-care workers, including radiographers, were infected by SARS.⁹⁷ Because imaging plays an important part in the diagnosis and management of HID, the role of the radiology department is to provide an immediate and efficient radiological service for patients with suspected or confirmed HIDs. Chest radiography is mandatory in such a situation.

To minimise the risk of cross-infection, transportation of patients with HID should be as limited as possible. For ambulatory patients with suspected HIDs, a satellite radiography centre should be set up with portable radiography equipment in the vicinity of the EDIR dedicated to HID patients in order to confirm or to reject the diagnosis.⁹⁸ For patients in the HLIU, bedside radiography should be provided to avoid transportation of patients.^{97,99} To avoid transmission of fomites, the radiograph film should be handled with care and should only be interpreted by a designated radiologist who is aware of infection control. The film-processing area, where cassettes are brought back to the department after bedside radiography in the HLIU, should be considered as high risk, unless the cassettes were processed in the HLIU by following a protocol of double bag sealing, and should be disinfected.^{98,99} Images should be interpreted through a picture-archiving and communication system, if available.^{84,97,100}

For ultrasound scanning, a sonographic scanner should be designated as a portable radiograph that is only used for HID patients. One machine should be dedicated for a specific area such as the HLIU. The examination should be kept as short as possible to answer the clinical questions. The transducer should be covered with disposable covers that are discarded between patients.

The value of a CT scan in assessing the diagnosis of HIDs, such as SARS, has been established, and a CT scan is sometimes mandatory for a patient's assessment.¹⁰¹ Because this examination can be done only in the radiology department, stringent infection-control measures need to be followed, and the examination should be done only if absolutely necessary for the patient's recovery.

We strongly recommend that the radiology department appoint a staff member to monitor and ensure that all staff fully comply with the infection-control measures according to the guidelines. Designated sessions or hours, either outside office hours or at the end of a session, should be assigned for such patients. Patients should be transported in a special isolation carrier or in a defined way to avoid any contact with other patients or unprotected personnel.^{58,100} The department should be divided into low-risk and high-risk areas. After a CT scan, the gantry table and floor should be cleaned, and any bed linen should be changed. Film cassettes should be decontaminated properly before film processing. In all

Search strategy and selection criteria

The literature review was done by use of Medline and the Web of Science with the following key words: "SARS [all]", "laboratory-acquired infection", "laboratory-associated infection", "imported [each agent's name]", and "[each group 3 and 4 agent's name]". More than 1400 references were obtained. Selection criteria within the topics were the impact factor and half-life of the journal, followed by journal availability. The topics selected were as follows: patient's criteria for admission to the HLIU, admission to the emergency department, safe sampling for laboratory investigation, isolation of suspected HID patient in HLIU, intensive-care management of HID patients, HID in paediatric patients, practice of invasive procedures such as bronchoscopy and gastroscopy, radio imaging, renal dialysis, and post-mortem examination of HID patients. Only English-language articles were reviewed. Websites such as WHO, CDC, and other scientific and international research society's guidelines were also used.

cases, radiology technicians, radiologists, and other radiology personnel should comply with universal precautions, including the wearing of a mask, cap, gown, and gloves during direct contact with patients.

Renal dialysis

The main reported dialysis-associated infection is viral hepatitis. As a consequence, guidelines have been edited to prevent nosocomial transmission of this agent to personnel and patients.¹⁰² When the guidelines were followed in a European study,¹⁰³ no reported hospital-acquired cases of hantavirus haemorrhagic fever with renal syndrome were reported, despite 30–50% of patients being in need of haemodialysis.

Most of our knowledge in the management of HID with renal failure has been acquired from SARS outbreaks. By comparison with other patients, the care of patients undergoing renal dialysis poses several additional infection-control issues in the disposal of spent dialysate (both haemodialysis and peritoneal dialysis) and in the prevention of cross-contamination within the dialysis unit.¹⁰⁴ During the SARS episode, patients receiving dialysis were kept in the SARS isolation ward with the other patients with SARS. All patients with peritoneal dialysis were treated with intermittent peritoneal dialysis during their hospital stay. The dialysis exchange was done by the ward staff, who wore full protective gear, as recommended by WHO, including waterproof disposable gowns, caps, gloves, face shields, and N95 face masks.¹⁰⁴ The spent peritoneal dialysis effluent was decontaminated with a 2% sodium hypochlorite solution.

Haemodialysis was also done by the ward staff, who wore full protective gear, in a room especially equipped for SARS patients in the isolation ward.¹⁰⁴ Dedicated haemodialysis machines were used with an ordinary tap

water supply that passed through a filter without reverse osmosis or any other water treatment. Spent dialysate was decontaminated as described above, and all of the blood tubing was discarded as infectious waste. Because they were potentially contaminated, unspent dialysate concentrate and the sodium bicarbonate cartridge were also discarded as infectious waste. The dialysis machine was disinfected after each haemodialysis session with a sodium hypochlorite solution according to the manufacturer's instructions. Particular attention should be paid to the infection control of dialysate effluents and decontamination of the machines.

Post-mortem examination

Although autopsies have been done safely on patients with HID in some circumstances, without prior knowledge of diagnoses such as Ebola haemorrhagic fever, HID agents are transmissible at autopsy, which raises concerns about the protection of pathologists and autopsy personnel.¹⁰⁵ Tuberculosis was the first autopsy-transmitted disease to be reported in the literature,¹⁰⁶ and transmission is also thought possible with multidrug-resistant or extremely drug-resistant tuberculosis. Aerosol production during autopsy, particularly from ruptured organs, had been recognised early in this situation and has led to some precautions.¹⁰⁷

During the first reported episode of hantavirus pulmonary syndrome, the first five suspected patients were autopsied with standard precautions only, even though the agent was isolated and classified as a group 3 agent.¹⁰⁸ Fortunately, no transmission to autopsy personnel occurred. During the SARS episode, many autopsies were done, and although there was no case of transmission, several investigators have raised concerns over biosafety in autopsy rooms.^{105,108,109} Recent guidelines have been published to prevent infection during autopsy.¹¹⁰ Before an autopsy is done on a patient suspected to have died from an HID, the possible risks and benefits must be carefully considered.⁵⁸ Limited autopsy or post-mortem collection of blood and percutaneous liver biopsy material may be appropriate. Several pathologists suggest that safety measures applied to laboratory workers should also be applied during and after autopsy. Furthermore, patients who have died from an unknown HID or from a known group 3 or 4 agent should be autopsied only if necessary and in a biosafety level 3 or 4 isolation room.^{58,108,109}

Conclusions

The literature on HIDs, particularly SARS, indicates that there is a need for hospitals to be prepared for these events and that HLIUs urgently need to be built in European member state hospitals. Research and development of universal, bedside, reproducible, and transferable diagnostic tools are mandatory. Prompt reporting to the authorities is needed so that a rapid response can be organised. These measures should be accompanied by harmonised recommendations for the

safe care of these unusual patients. The recommendations reported here by our group will hopefully help establish consensual protocols. Networking for the standardisation of procedures and the management of these patients is mandatory.

Conflicts of interest

We declare that we have no conflicts of interest.

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