Opinion Paper

Giuseppe Lippi*, Khosrow Adeli, Maurizio Ferrari, Andrea R. Horvath, David Koch, Sunil Sethi and Cheng-Bin Wang

Biosafety measures for preventing infection from COVID-19 in clinical laboratories: IFCC Taskforce Recommendations

https://doi.org/10.1515/cclm-2020-0633
Received May 1, 2020; accepted May 2, 2020

Abstract: Coronavirus disease 2019 (COVID-19) is the third coronavirus outbreak that has emerged in the past 20 years, after severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). One important aspect, highlighted by many global health organizations, is that this novel coronavirus outbreak may be especially hazardous to healthcare personnel, including laboratory professionals. Therefore, the aim of this document, prepared by the COVID-19 taskforce of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), is to provide a set of recommendations, adapted from official documents of international and national health agencies, on biosafety measures for routine clinical chemistry laboratories that operate at biosafety levels 1 (BSL-1; work with agents posing minimal threat to laboratory workers) and 2 (BSL-2; work with agents associated with human disease which pose moderate hazard). We believe that the interim measures proposed in this document for best practice will help minimazing the risk of developing COVID-19 while working in clinical laboratories.

Keywords: biosafety; coronavirus disease 2019; COVID-19; laboratory; SARS-COV-2.

***Corresponding author: Prof. Giuseppe Lippi,** IFCC Taskforce on COVID-19, International Federation of Clinical Chemistry and Laboratory Medicine, Milan, Italy; and Section of Clinical Biochemistry, Department of Neuroscience, Biomedicine and Movement, University Hospital of Verona, University of Verona, Piazzale L.A. Scuro, 10, 37134 Verona, Italy, Phone: +0039-045-8122970, Fax: +0039-045-8124308, E-mail: giuseppe.lippi@univr.it
Khosrow Adeli: IFCC Taskforce on COVID-19, International Federation of Clinical Chemistry and Laboratory Medicine, Milan, Italy; and Clinical Biochemistry, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada
Maurizio Ferrari: IFCC Taskforce on COVID-19, International Federation of Clinical Chemistry and Laboratory Medicine, Milan, Italy; and Vita-Salute San Raffaele University, Milan, Italy
Andrea R. Horvath: IFCC Taskforce on COVID-19, International Federation of Clinical Chemistry and Laboratory Medicine, Milan, Italy; and Department of Clinical Chemistry and Endocrinology, New South Wales Health Pathology, Prince of Wales Hospital, Sydney, Australia
David Koch: IFCC Taskforce on COVID-19, International Federation of Clinical Chemistry and Laboratory Medicine, Milan, Italy; and Department of Pathology and Laboratory Medicine, Emory University, and Director of Clinical Chemistry, Grady Memorial Hospital, Atlanta, GA, USA
Sunil Sethi: IFCC Taskforce on COVID-19, International Federation of Clinical Chemistry and Laboratory Medicine, Milan, Italy; and Department of Laboratory Medicine, National University Hospital, Singapore, Singapore
Cheng-Bin Wang: IFCC Taskforce on COVID-19, International Federation of Clinical Chemistry and Laboratory Medicine, Milan, Italy; and Department of Laboratory Medicine, Chinese PLA General Hospital, Beijing, China

Introduction

Coronavirus disease 2019 (COVID-19) is the third coronavirus outbreak that has emerged in the past 20 years, after severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) [1]. Unlike the previous two coronavirus epidemics, which could be almost confined to the territories of original emergence, COVID-19 has quickly spread all around the world, affecting over 3 million people and causing more than 200,000 deaths, such that it was finally declared a global pandemic by the World Health Organization (WHO) [2]. Although initial reports have delineated this new infectious disease as being less severe than SARS, recent epidemiologic data of the WHO attests that the worldwide death rate due to COVID-19 is progressively increasing, approximating that of SARS (i.e. 6.86% vs. 9.56%), especially in certain countries like Italy (13.53%) and Spain (11.07%) [3].

One important aspect, which has also been highlighted by many worldwide health organizations, is that this novel coronavirus outbreak may be especially hazardous to healthcare personnel [4]. A recent report of the Chinese Center for Disease Control and Prevention revealed that 3.8% of all COVID-19 patients were healthcare personnel (peaking to 63% during the initial outbreak in Wuhan), with nearly 15% of these experiencing a severe or critical form of disease [5]. More recent data from the Italian National Institute of Health revealed that the infection rate of healthcare workers among the total number of COVID-19 patients is as high as 10.7% [6]. These alarming figures call for guidance on adequate biosafety procedures to protect healthcare staff, including laboratory personnel, especially when infections and quarantines exacerbate the shortage of staff and impose additional burden on already overwhelmed healthcare services [7]. The purpose of this article, by the COVID-19 taskforce of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), is to provide a set of recommendations adapted from official documents of international and national health agencies and organizations, on biosafety measures to be used in routine clinical chemistry laboratories that operate at biosafety levels 1 (BSL-1; work with agents posing minimal threat to laboratory workers) and 2 (BSL-2; work with agents associated with human disease which pose moderate hazard) [8].

Characteristics of the virus

COVID-19 is caused by a virus belonging to the coronaviridae family, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses [9]. SARS-CoV-2 is a single-stranded RNA virus, with RNA genome size of approximately 30,000 bases and viral particle size comprised between 70 and 90 nm [10]. The virus has evolved by recombination from an ancestral bat virus, with which it shares between 73% and 100% gene identity [11, 12].

It is now acknowledged that the virus binds to angiotensin-converting enzyme 2 (ACE2), a transmembrane enzyme which plays a central role in the renin-angiotensin-aldosterone system (RAAS) [13, 14]. Recent evidence has been provided that ACE2 is widely expressed in human tissues and organs, especially in cells of the higher and lower respiratory tracts (especially alveolar epithelial cells), heart, kidney, esophagus, intestine, as well as in lymphocytes [15, 16]. Importantly, Xu et al. also reported that ACE2 is expressed on the mucosa of the oral cavity, especially in the epithelial cells of the tongue, thus providing an additional source of cells that can be vulnerable to infection by SARS-CoV-2 [16].

Route of transmission of SARS-CoV-2

SARS-CoV-2 is mostly transmissible by means of large respiratory droplets (i.e. ≥5 μm) rather than small aerosols, as well as from contaminated hands and surfaces. Aerosol transmission is also theoretically possible, as previously shown for the homologous SARS-CoV-1 [17], but may be limited to exceptional circumstances such as protracted exposure to elevated aerosol concentrations within closed spaces, as may happen within a COVID-19 patient room or within a closed and narrow laboratory environment [18]. According to the most recent evidence provided by the WHO and by the US Centers for Disease Control and Prevention (CDC) [3, 19], it is assumed that human-to-human SARS-CoV-2 transmission mainly occurs when large respiratory droplets are generated by SARS-CoV-2 patients, especially by coughing and/or sneezing, which then reach the nose, mouth or eyes of another person, or are inhaled. Large respiratory droplets are too heavy to be airborne, but they can still be deposited on many environmental surfaces, so that infection is transmitted by hands touching contaminated objects, materials and/or surfaces and then touching the eyes, nose or mouth [3, 19].

An interesting study published by Xie et al. has clearly shown that droplet propagation is highly dependent upon many factors, including the particle size, the speed of exhaled air, as well as the conditions of temperature and humidity [20]. Although most large respiratory droplets containing SARS-CoV-2 would fall to a surface within a distance of approximately 1 m (i.e. ~3 feet) during normal breathing, as they are conveyed by exhaled air at a speed of approximately 1 m/s, coughing or sneezing may considerably enhance propagation velocity (i.e. 10 m/s for coughing and 50 m/s for sneezing, respectively), as well as the corresponding propagation distance of these droplets (i.e. 2 m for coughing and 6 m for sneezing, respectively) (Figure 1). Importantly, the size of droplets generated by a conventional cough is highly variable, but nearly half of these virus-containing particles may be within the range of aerosol, thus remaining in the air for longer periods and potentially conveyed over distances greater than 1 m, thus promoting all national and international healthcare agencies to suggest at least 2 m (i.e. 6½ feet) social distancing [21, 22].

Therefore, this guidance paper addresses the following key questions and offers interim safety advice to clinical chemistry laboratory staff working at BSL1 and BSL2

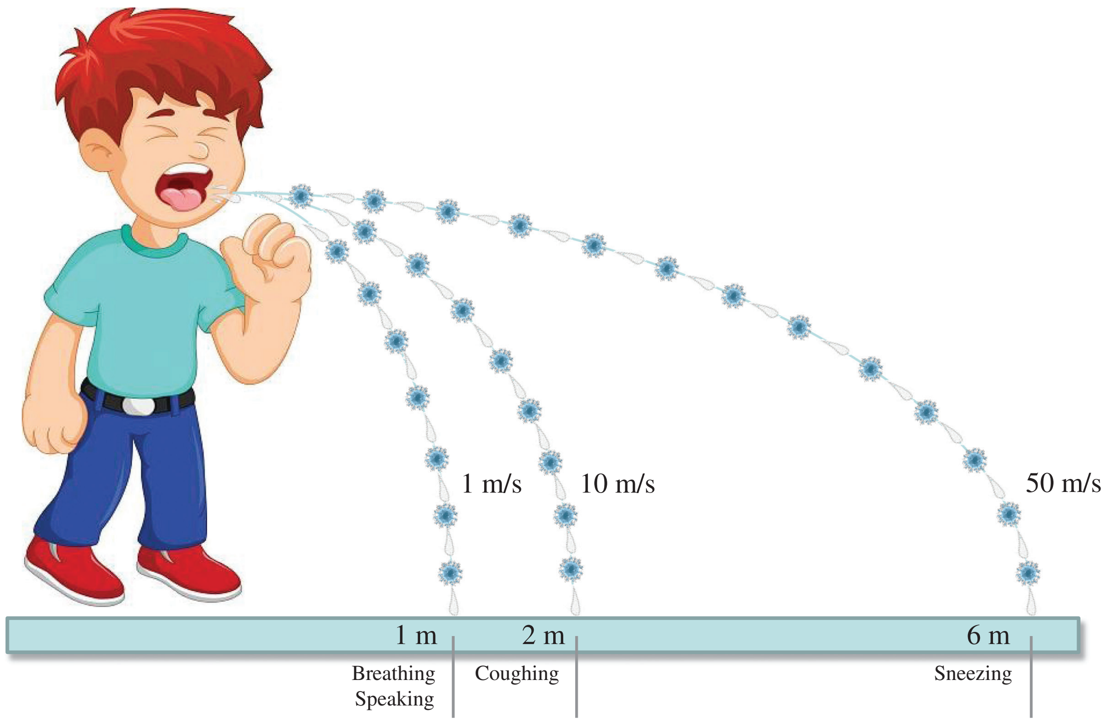

Figure 1: Potential air propagation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

laboratories (thus also including routine pediatric laboratories) during the COVID-19 pandemic.

1) How can the generic biosafety measures be implemented in clinical chemistry laboratories during the COVID-19 pandemic?

2) What personal hygiene and personal protective equipment (PPE) should be used in clinical chemistry laboratories during the COVID-19 pandemic?

3) How should laboratory staff handle routine patient specimens during the COVID-19 pandemic?

4) How should staff decontaminate laboratory equipment and surfaces during the COVID-19 pandemic?

The following recommendations are based on limited and often weak evidence of mostly observational studies or extrapolations from what has been learned during earlier epidemics caused by the SARS and MERS coronaviruses. This biosafety advice reflects the consensus of this IFCC Task Force after a rapid review of relevant documents of various international organizations and the available literature. The list of these representative documents, focused on handling, and processing of blood, urine, feces and respiratory specimens at BSL-1 and BSL-2 laboratories during COVID-19 outbreak is shown in Table 1.

Due to the rapidly evolving pandemic and the emergence of new data and information day-by-day, the advice given in this document may change over time.

How can the generic biosafety measures be implemented in clinical chemistry laboratories during the COVID-19 pandemic?

Due to the nature of transmission, most countries advocate and enforce “social distancing” measures to maintain the conventionally “safe” 2-m distance between individuals Although social distancing within healthcare settings has only been recommended by the WHO, the widespread efficiency of this strategy has now been universally acknowledged for purposes of outbreak containment [29, 30].

The possibility of SARS-CoV-2 transmission by asymptomatic or mildly symptomatic individuals is another matter of concern. Although definitive numbers are not available, recently published studies showed that the proportion of asymptomatic individuals may be as high as 50%–75% [31]. This observation is especially important if one considers that the viral load in upper respiratory specimens of SARS-CoV-2-infected patients who are asymptomatic or only mildly symptomatic can be similar to that of symptomatic COVID-19 patients [32, 33]. Therefore, a potentially infected (asymptomatic) laboratory professional may infect many other colleagues if adequate protective measures are not routinely used.

Table 1: General biosafety indications or recommendations for coronavirus disease 2019 (COVID-19) in clinical laboratories with biosafety levels 1 (BSL-1) and 2 (BSL-2).

Protective measure	WHO/ECDC [23, 24]	CDC [25]	PHE [26]	ABSA [27]	FAHZU [28]
Maintain social distance	Yes (1 m)	N/A	N/A	N/A	N/A
Perform hand hygiene	Frequently	Frequently	Frequently	N/A	Frequently
Avoiding touching eyes, nose and mouth	Yes	Yes	N/A	N/A	N/A
Use of respirators	Surgical mask	N95 respirator (surgical mask when N95 unavailable)	No[a]	Surgical mask	Yes N95 respirator (surgical mask when N95 unavailable)
Wearing gloves	Yes, disposable	Yes, disposable	Yes, disposable	Yes, disposable	Yes, disposable
Wearing laboratory coats/ Gowns	Based on contamination risk[b]	Based on contamination risk[b]	Based on contamination risk[b]	Lab coat	Based on contamination risk[b]
Eye protection	When risk of splash	Yes	Yes	Yes	Yes
Wearing disposable surgical cap	N/A	N/A	N/A	N/A	Yes
Use of automated instruments and analyzers	N/A	Preferable	Preferable	Preferable	N/A
Centrifugation with safety cups and/or sealed rotors	Yes	Yes	Preferable to minimize aerosol	N/A	N/A
Working surfaces decontamination	Yes[c]	Yes[d]	Yes	Yes	Yes[e]

[a]Processing respiratory tract, urine, fecal or tissue samples under safety cabinet or when there is risk of aerosol, is recommended; [b]Laboratory coats in general; nonsterile, disposable gown when managing highly infectious materials, such as respiratory specimens. [c]Full list of WHO-suggested decontaminants available here: https://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/. [d]Full list of CDC-suggested decontaminants available here: https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2. [e]Full list of FAHZU-suggested decontaminants available here: https://iau-aiu.net/Zhejiang-University-Handbook-of-COVID-19-Prevention-and-Treatment. The Therapeutic Goods Administration (TGA): Appropriate use of disinfectants: Information for consumers, health professionals and healthcare facilities. 27 March 2020; https://www.tga.gov.au/appropriate-use-disinfectants-information-consumers-health-professionals-and-healthcare-facilities. ABSA, American Biological Safety Association International; CDC, US Centers for Disease Control and Prevention; ECDC, European Centre for Disease Prevention and Control; FAHZU, First Affiliated Hospital, Zhejiang University School of Medicine; N/A, non-available information; PHE, Public Health England; WHO, World Health Organization.

Recommendations

1a. Laboratories should adopt social distancing measures within the workplace as much as possible and feasible.

This goal can be achieved by splitting personnel into two (or more) teams and rostering staff in such a way that each team has no contact with members of the other team. Workstations in the laboratory can be spaced out; staff authorizing/validating results or doing more administrative tasks (e.g. quality assessment review) can be removed from the laboratory space and do their work in an office space or remotely. Operationally within hospitals and laboratories, team segregation and social distancing is to be enforced. This step will allow lower potential for cross-infection between the teams, but at the same time allows execution of their duties independently. Staggered meal and break times with avoidance of group gathering is to be advised.

During this period, education and training should continue, and it is recommended that this be conducted via remote video conferencing services. Traditional face-to-face meetings and educational sessions are to be canceled until the threat has passed.

1b. The potential exposure and health status of the laboratory personnel is monitored daily.

This aim can also be achieved by interviewing staff at the beginning of their shift (e.g. were they traveling to other regions in the last 14 days; were they in contact with a known COVID-19 case; do they have flu-like symptoms, etc.), and then recording the information within an attestation form. Simple temperature taking, e.g. once daily, facilitates early identification of acute respiratory infection symptoms. Should a laboratory staff be infected with COVID-19, quarantine measures would need to be initiated for all close contacts in the team. Business continuity and contingency plans with other departments and laboratories should be established in case a significant number of team members fall ill or are required to be quarantined.

What personal hygiene and personal protective equipment (PPE) should be used in clinical chemistry laboratories during the COVID-19 pandemic?

With respect to sample transportation, it is recommended that all conventional laboratory specimens (blood, urine, respiratory, feces and so forth) be tightly capped and transported to the laboratory in biohazard zip-locked bags, within a leakproof cryobox with a clearly visible biohazard label. Unlike previous warnings, the CDC now allows transportation of all laboratory samples via pneumatic tube systems, with the exception of respiratory specimens, which shall be instead manually delivered [34]. Transportation of infectious samples to a secondary laboratory should otherwise be managed in compliance with the WHO and international air transport association (IATA) guidelines [35].

During the COVID-19 pandemic, all specimens collected for *in vitro* diagnostic testing should be considered potentially infectious with SARS-CoV-2. Therefore, laboratory professionals must adhere rigorously to standard precautions to minimize the risk of exposure to the virus. Frequent hand hygiene and avoidance of touching the eyes, nose and mouth are universally recommended measures that laboratory staff should also adhere to. Notably, regarding hand contamination, instant hand wiping with a wet towel soaked in water containing 1.00% soap powder, 0.05% active chlorine or 0.25% active chlorine from sodium hypochlorite has also been proven effective to remove over 90% of the virus [36]. Kratzel et al. have investigated two alcohol-based WHO hand sanitizer formulations for their virucidal effects. They found that ethanol and 2-propanol were efficient in inactivating the virus in 30 s at a minimal final concentration of at least 30% [37].

In terms of PPE, laboratory staff should follow standard laboratory practice, i.e. wear masks, wear disposable gloves, use eye protection devices and wear a lab coat or gown. Recommendations for the type of laboratory coats and/or gowns depend on the type of activity. Conventional laboratory coats can be used when managing usual biological materials, where the threat of direct contagion is reasonably lower (i.e. blood, urine, cerebrospinal fluid and so forth). Nonsterile, disposable gowns shall be worn when managing highly infectious materials, such as respiratory specimens (e.g. sputum, nasal or throat swab, pleural fluid). No clear evidence has emerged on the efficacy of a disposable surgical cap to prevent SARS-CoV-2 infection, and this recommendation is only provided by the First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU).

Wearing facial masks in a routine laboratory where there is no direct patient contact has been a debated issue. The logic here is that this is perceived more as an enhanced social distancing measure rather than for concern of direct patient contact or infectious samples, also considering that the prevalence of asymptomatic people can be very high, even over 70% as attested by highly focused studies [38]. The efficacy of face and respirator masks to reduce viral transmission was mostly studied in *in vitro* experiments using nonbiological particles. In an experimental simulation, van der Sande et al. evaluated the filtering capability of a standard surgical mask (aimed at preventing contagion with microorganisms conveyed by large-particle droplets, splashes, sprays or splatter) and FFP2 (i.e. the European equivalent of N95) masks, concerning the efficacy of stopping droplets between 0.2 and 1 µm in size, thus corresponding to "aerosols" [39]. The overall retention of particles expelled inside the mask (i.e. outward protection) was nearly identical for surgical and FFP2 masks, which are conventionally known to block at least 95% of small (i.e. 0.3 µm) particles [40]. As expected, however, the barrier of toward inward protection was considerably higher for FFP2 than for surgical masks. In another study, Li et al. compared the physical properties of N95 respirators and surgical masks [41], and concluded that although the former devices would provide higher *in-vivo* filtration efficiency (i.e. up to 97%), surgical masks also exhibited adequate water repellent and antibacterial activities. More recently, Ma et al. showed that N95 and medical masks are capable of stopping 99.98% and 97.14% of the virus in aerosols, respectively [36]. It can hence be concluded that surgical masks are valuable for preventing virus propagation from infected individuals, whilst their efficacy toward preventing droplet-driven infection of those wearing the mask is lower than that of N95 masks. Nevertheless, the widespread use of relatively inexpensive surgical masks is regarded as a valuable public health intervention that helps intercept transmission of the virus in the general population, as recently show by Leung et al. [42, 43], and by Feng et al. [44], but shall also be regarded as a valuable visible reminder of an otherwise invisible yet widely prevalent virus, thus reminding people about the importance of adopting social distancing and other infection-control measures [45].

Regarding facemasks, the majority of the official documents that we have analyzed (Table 1), along with many international experts [46], recommend that laboratory professionals should wear preferably an N95 mask while engaged in all types of aerosol-generating procedures related to non-centrifuged samples (i.e. manually opening specimen tubes, pipetting, vortexing, aliquoting, shaking, centrifuging, extracting) carried out on samples potentially contaminated with SARS-CoV-2. For enhanced safety reasons, this equipment may also be used when BSL1 or BSL2 cabinets are used, even if the cabinet provides protection and shield. Due to global shortage of facial masks during the COVID-19 pandemic, this recommendation must be weighed against the local availability of this PPE [47, 48]. Health authorities shall optimize the distribution of face masks, prioritizing vulnerable populations, but also protecting frontline healthcare workers and support services, such as clinical laboratories without which the diagnosis, prognostication and therapeutic monitoring of COVID-19 would be impossible [49]. According to the CDC, the face masks shall always be used, re-used and/or cleaned as indicated by the manufacturer, in order to preserve their protective function [50]. In particular, the FDA strongly advises against recycling surgical masks after being removed, as these devices are not intended to be used more than once [51].

Although surgical masks are not an ideal surrogate of N95 respirator masks, their usage in clinical laboratories is encouraged, especially in areas of workflow where samples are handled manually and where more protection is required against splashes and the possible inhalation of sprays and aerosols. The Centre for Evidence-Based Medicine of Oxford University has recently concluded that although no randomized trial has yet been published during the COVID-19 outbreak, standard surgical facemasks may be as effective as N95 devices for preventing infection of healthcare workers in outbreaks of viral respiratory illnesses [52]. Either type of face mask will also be effective to prevent inter-human contagion in the possible adverse circumstance that one laboratory operator has been infected by SARS-CoV-2 and may hence transmit the virus to the rest of the personnel [39]. In particular, Leung and colleagues recently showed that surgical face masks were shown to significantly reduce the detection of respiratory viruses in droplets, and aerosols [42]. In light of increasing evidence toward the efficacy of this type of masking, the WHO has reversed its initial recommendation and now supports government initiatives that require or encourage the public wearing of masks. The CDC has also encouraged general masking, highlighting the importance of masking for all healthcare workers whether patient facing or not.

Regarding the laboratory environment, aerosols can be generated during normal laboratory activities such as centrifuging, pipetting or pouring liquids, shaking or vortexing tubes, stirring, filling a syringe, removing supernatant, resuspending pellets, sonicating, homogenizing, blending, grinding and other cell disruption processes, cage cleaning, extracting organic material, sample spill over, heating inoculating loops, or using a blender. These procedures can all be an additional source of transmission, while managing samples potentially containing high loads of vital SARS-CoV-2 particles such as upper and lower respiratory specimens, sputum, bronchoalveolar lavage, blood and feces [22, 53]. In an experimental study by van Doremalen et al. [54], SARS-CoV-2 was found to be viable for about 3 h in aerosols during experimental conditions, thus emphasizing further the importance of adequate personal protection of laboratory staff.

Recommendations

> *2a. Laboratory professionals must adhere rigorously to universally recommended standard precautions* (i.e. frequent hand washing for at least 40 s with soap and water, or hand sanitizer when there is no access to handwashing, and to avoid touching the face) *to minimize the risk of exposure to the virus.*
>
> *2b. Laboratory professionals must wear standard laboratory PPE (i.e. masks and gloves, laboratory coat or gown, and eye protection) at all times.*
>
> *2c. Laboratory professionals should wear preferably an N95 mask while engaged in aerosol-generating procedures on all non-centrifuged samples potentially containing vital SARS-CoV-2 particles.*

How should laboratory staff handle routine patient specimens during the COVID-19 pandemic?

Most international organizations agree that automated instruments and analyzers with closed preanalytical robotics for decapping and recapping of tubes should be used as much as possible. When manual laboratory techniques are used for processing specimens and there is a risk of generating aerosols, samples with safety caps should be centrifuged in sealed rotors with a lid on. Consider the min/max filling volume of vessels. Do not exceed the vessel speed limit. Use plastic vessels instead of glass, which are more likely to break or leak. Alternatively, open and load/unload the rotor in a biosafety cabinet. If a tube breaks or leaks, wait for 30 min before opening the centrifuge or aerosol-tight lid or cap to let the aerosols settle. Further manual processing such as opening tubes, jars, pipetting, aliquoting, diluting, vortexing and extracting specimens should be handled in a BSL 2 cabinet to avoid contamination during performance of aerosol-producing activities in samples potentially containing SARS-CoV-2 particles.

Recommendations

3a. For routine testing of blood, urine and body fluids, laboratories should use automated instruments and analyzers with closed preanalytical robotics, where possible.

3b. When manually handling non-respiratory specimens, aerosol-generating non-centrifuged sample processing steps should be carried out in a BSL2 cabinet, wearing the recommended PPE.

3c. The specimens should be sealed immediately after testing. High-risk specimens should be promptly disinfected or autoclaved.

3d. If there are no accidents, wait for more than 10 min for further processing after centrifugation stops. When the specimen suspected of COVID-19 is centrifuged, the operator must not leave the centrifuge. If an accident is suspected, or in some way the centrifugation is abnormal, stop the centrifugation. After replacing the biosafety level 3 protection equipment, stop centrifugation for more than 30 min, carefully open the lid, and spray and sterilize with 75% ethanol or other disinfectants. Take out the centrifuge rotor with blood collection tubes and then put them in the biosafety cabinet to treat.

How should staff decontaminate laboratory equipment and surfaces during the COVID-19 pandemic?

Regarding surface contact transmission, van Doremalen et al. recently showed that the stability of SARS-CoV-2 is similar to that of SARS-CoV-1 under experimental conditions [54]. Therefore, SARS-CoV-2 was found to be stable, though exhibiting exponential decay of virus titer, for up to 72 h on plastic, 48 h on stainless steel and 4 h on copper.

Chin et al. investigated the stability of SARS-CoV-2 at different temperatures and pH values, on different surfaces, and in the presence of various disinfectants. They found that the virus is highly stable at 4 °C after 2 weeks, but can be deactivated after 5 min at 70 °C. The virus tolerates a broad range of pH (from 3 to 10) at room temperature. This study showed no infectious virus on print paper after 3 h, on wood and cloths after 2 days, on glass and banknotes after 4 days, and on stainless steel and plastic after 7 days. Interestingly, detectable level of infectious virus was found on the outer layer of a surgical mask on day 7 [55].

A review by Kampf et al. on endemic human coronaviruses found that the virus can remain infectious on metal, wood, paper, glass and plastic up to 4–9 days, depending on the size of the viral inocula. Higher temperatures of 30 °C or 40 °C reduced the persistence of pathogenic coronaviruses, and persistence of the virus on different surfaces was longer with higher viral load and at higher relative humidity [56].

This evidence highlights the need for appropriate decontamination of laboratory surfaces for preventing unwarranted contact transmission of the virus. Besides, interesting evidence has recently been provided by Ong et al. [57], who failed to find contamination by SARS-CoV-2 of PPE under environmental conditions (i.e. persistence in airborne infection isolation rooms with 12 air exchanges per hour).

COVID-19 is an enveloped virus. The outer layer of enveloped viruses is relatively easily damaged by most environmental disinfectants. In a study by Chin et al., 5-min incubation of a virus culture with various disinfectants, including 1:50 household bleach, 60%–70% ethanol, up to 7.5% povidone-iodine, over 0.05% chloroxylenol or chlorhexidine and 0.2%–0.4% benzalkonium chloride, has killed the virus [55]. A recent review of 22 studies by Kampf et al. investigates the virucidal effects of various disinfectants at various concentrations in virus suspension and surface carrier tests [56]. The effective concentrations of disinfectants vary depending on what virus strain, contact time and viral load was used in the studies (for details, refer to tables II and III of this publication). Findings for the biocidal effects of 62%–71% ethanol and up to 7.5% povidone-iodine agree with data published by Chin et al. However, the review by Kampf et al. suggests that surface disinfection with 0.1% sodium hypochlorite or a dilution of 1:50 of standard bleach significantly reduces the infectivity of human coronaviruses on surfaces within 1 min exposure time. The evidence on the effective concentration of benzalkonium chloride is conflicting. Within 10 min, a concentration of 0.2% revealed no efficacy against coronaviruses whereas a concentration of 0.05% was quite effective in another study. In Australia and New Zealand, the Therapeutic Goods

Table 2: Recommendations for preventing contagion from coronavirus disease 2019 (COVID-19) in clinical laboratories with biosafety levels 1 (BSL-1) and 2 (BSL-2).

- Adhere rigorously to standard precautions to minimize the risk of virus exposure
- Laboratory staff shall maintain (whenever possible and feasible) ~2 m (i.e. ~6½ feet) interpersonal distance while operating within the laboratory
- Perform hand hygiene frequently
- Avoid touching eyes, nose and mouth
- Use N95 respirators or surgical masks when N95 respirators are lacking
- Wear disposable gloves
- Use eye protection devices
- Wear conventional laboratory coats for managing conventional biological materials (blood, urine, feces, etc.).
- Wear nonsterile, disposable gown when managing highly infectious materials (such as respiratory specimens)
- Prefer automated instruments and analyzers
- Use safety cups and/or sealed rotors during centrifugation
- Carry out accurate decontamination of working surfaces

Administration (TGA) has recently approved a surface disinfectant, containing 0.42% benzalkonium chloride, as effective against SARS-CoV-2. Testing of this agent's efficacy was carried out on a surrogate murine hepatitis virus using a surface carrier method [58].

Most studies published so far on coronaviruses other than SARS-CoV-2 indicate that standard disinfection processes and agents containing ≥70% alcohol, or freshly diluted household bleach (including products containing sodium hypochlorite) are suitable for use in medical laboratories for surface disinfection.

Decontamination of work benches, instruments and frequently touched surfaces in the laboratory (e.g. door handles, refrigerators/freezers, phones, touchscreens, keyboards, mouse, etc.) should be disinfected more frequently, perhaps every 3 h. Unfortunately, a definitive recommendation cannot be made at this point in time and the frequency shall hence be decided on local basis, according to the volume of work (a specific list of disinfectants is available from references in Table 2).

Recommendations

4a. Laboratory staff should decontaminate working surfaces with standard disinfectants approved for SARS-CoV-2 infections. The frequency shall be decided on local basis according to the volume of work, but shall not be basically less frequent than every 3 h.

4b. If a sample positive for SARS-CoV-2 is suspected of being leaked or contaminates the biosafety cabinet and bench and causes limited pollution: use a disinfectant with an effective chlorine content of 5500 mg/L for disinfection for more than 30 min; the disinfectant must be prepared immediately and used within 24 h. If positive specimens cause laboratory contamination: keep the laboratory space closed to prevent access by unauthorized personnel and to prevent the spread of pollutants. Cover the contaminated area with a towel containing 5500 mg/L of effective chlorine disinfectant and disinfect for more than 30 min. Peracetic acid (2 g/m^3) or other disinfectants (3% H_2O_2, 100 mg/L chlorine dioxide, etc.) can be used to fumigate the laboratory overnight or disinfectant aerosol can be sprayed for 1–2 h [59].

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Research funding: None declared.
Employment or leadership: None declared.
Honorarium: None declared.
Competing interests: Authors state no conflict of interest.

References

1. Lippi G, Sanchis-Gomar F, Henry BM. Coronavirus disease 2019 (COVID-19): the portrait of a perfect storm. Ann Transl Med 2020;8. doi: https://doi.org/10.21037/atm.2020.03.157.
2. Mahase E. Covid-19: WHO declares pandemic because of “alarming levels” of spread, severity, and inaction. Br Med J 2020;368:m1036.
3. World Health Organization. Coronavirus disease (COVID-2019) situation reports. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports. Last accessed: April 29, 2020.
4. Bowdle A, Munoz-Price LS. Preventing infection of patients and healthcare workers should be the new normal in the era of novel coronavirus epidemics. Anesthesiology 2020. doi: https://doi.org/10.1097/ALN.0000000000003295. [Epub ahead of print].
5. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. J Am Med Assoc 2020. doi: https://doi.org/10.1001/jama.2020.2648. [Epub ahead of print].
6. Italian National Institute of Health – Istituto Superiore di Sanità. Daily infographic on COVID-19. https://www.epicentro.iss.it/coronavirus/. Available at: https://www.iss.it/. Last accessed: April 29, 2020.
7. Ranney ML, Griffeth V, Jha AK. Critical supply shortages – the need for ventilators and personal protective equipment during the Covid-19 pandemic. N Engl J Med 2020;382:e141.
8. Centers for Disease Control and Prevention and National Institutes of Health. Biosafety in Microbiological and Biomedical Laboratories, 5th edition. Centers for Disease Control and Prevention and National Institutes of Health, Bethesda, USA. Last update, February 2007.
9. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 2020;5:536–44.

10. Kim JM, Chung YS, Jo HJ, Lee NJ, Kim MS, Woo SH, et al. Identification of coronavirus isolated from a patient in Korea with COVID-19. Osong Public Health Res Perspect 2020;11:3–7.
11. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. Nat Med 2020;26:450–2.
12. Ceraolo C, Giorgi FM. Genomic variance of the 2019-nCoV coronavirus. J Med Virol 2020;92:522–8.
13. Xia H, Lazartigues E. Angiotensin-converting enzyme 2: central regulator for cardiovascular function. Curr Hypertens Rep 2010;12:170–5.
14. Sanchis-Gomar F, Lavie CJ, Perez-Quilis C, Henry BM, Lippi G. Angiotensin-converting enzyme 2 and anti-hypertensives (angiotensin receptor blockers and angiotensin converting enzyme inhibitors) in coronavirus disease 2019 (COVID-19). Mayo Clin Proc 2020;95. doi: https://doi.org/10.1016/j.mayocp.2020.03.026.
15. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med 2020. doi: https://doi.org/10.1007/s11684-020-0754-0. [Epub ahead of print].
16. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12:8.
17. Yu IT, Li Y, Wong TW, Tam W, Chan AT, Lee JH, et al. Evidence of airborne transmission of the severe acute respiratory syndrome virus. N Engl J Med 2004;350:1731–9.
18. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19) [Updated 2020 Mar 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/.
19. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19) – How Coronavirus Spreads. Available at: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html. Last accessed: April 1, 2020.
20. Xie X, Li Y, Chwang AT, Ho PL, Seto WH. How far droplets can move in indoor environments–revisiting the Wells evaporation-falling curve. Indoor Air 2007;17:211–25.
21. Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: emission of respirable pathogens. J Occup Environ Hyg 2005;2:143–54.
22. Santarpia JL, Rivera DN, Herrera V, Morwitzer MJ, Creager H, Santarpia GW, et al. Transmission potential of SARS-CoV-2 in viral shedding observed at the University of Nebraska Medical Center. MedRxiv 2020.03.23.20039446; doi: https://doi.org/10.1101/2020.03.23.20039446.
23. World Health organization. Rational use of personal protective equipment for Coronavirus disease 2019 (COVID-19) – Interim guidance 27 February 2020.
24. European Centre for Disease Prevention and Control. Infection prevention and control for COVID-19 in healthcare settings. March 2020.
25. Centers for Disease Control and Prevention. Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19).
26. Public Health England (PHE). COVID-19: safe handling and processing for samples in laboratories. Updated 28 March 2020.
27. American Biological Safety Association International (ABSA). Considerations for Handling Potential SARS-CoV-2 Samples.
28. First Affiliated Hospital, Zhejiang University School of Medicine (FAHZU). Handbook of COVID-19 Prevention and Treatment.
29. Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Glob Health 2020;8:e488–96.
30. Prem K, Liu Y, Russell TW, Kucharski AJ, Eggo RM, Davies N, et al. The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. Lancet Public Health 2020. doi: https://doi.org/10.1016/S2468-2667(20)30073-6. [Epub ahead of print].
31. Day M. Covid-19: identifying and isolating asymptomatic people helped eliminate virus in Italian village. Br Med J 2020;368:m1165.
32. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral load in upper respiratory specimens of infected patients. N Engl J Med 2020;382:1177–9.
33. Woelfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Mueller MA, et al. Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. medRxiv 2020.03.05.20030502; doi: https://doi.org/10.1101/2020.03.05.20030502.
34. Centers for Disease Control and Prevention. 04/06/2020: Lab advisory: guidance for use of pneumatic tube systems for transport of respiratory specimens from suspected or confirmed COVID-19 patients. Available at: https://www.cdc.gov/csels/dls/locs/2020/transport_recommendations_for_covid-19_specimens.html. Last accessed: April 29, 2020.
35. World Health Organization. Guidance on regulations for the transport of infectious substances 2019–2020. Geneva: World Health Organization, 2019 (WHO/WHE/CPI/2019.20).
36. Ma QX, Shan H, Zhang HL, Li GM, Yang RM, Chen JM. Potential utilities of mask-wearing and instant hand hygiene for fighting SARS-CoV-2. J Med Virol 2020. doi: https://doi.org/10.1002/jmv.25805. [Epub ahead of print].
37. Kratzel A, Todt D, Vkovski P, Steiner S, Gultom ML, Nhu Thao TT, et al. Efficient inactivation of SARS-CoV-2 by WHO-recommended hand rub formulations and alcohols. BioRxiv 2020.03.10.986711. doi: https://doi.org/10.1101/2020.03.10.986711.
38. Baggett TP, Keyes H, Sporn N, Gaeta JM. Prevalence of SARS-CoV-2 Infection in Residents of a Large Homeless Shelter in Boston. J Am Med Assoc 2020. doi: https://doi.org/10.1001/jama.2020.6887. [Epub ahead of print].
39. van der Sande M, Teunis P, Sabel R. Professional and homemade face masks reduce exposure to respiratory infections among the general population. PLoS One 2008;3:e2618.
40. US Food and Drug Administration. N95 Respirators. Available at: https://www.fda.gov/medical-devices/personal-protective-equipment-infection-control/n95-respirators-and-surgical-masks-face-masks. Last accessed: April 1, 2020.
41. Li Y, Wong T, Chung J, Guo YP, Hu JY, Guan YT, et al. In vivo protective performance of N95 respirator and surgical facemask. Am J Ind Med 2006;49:1056–65.
42. Leung NH, Chu DK, Shiu EY, Chan K-H, McDevitt JJ, Hau BJ, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. Nat Med 2020. https://doi.org/10.1038/s41591-020-0843-2.
43. Leung CC, Lam TH, Cheng KK. Mass masking in the COVID-19 epidemic: people need guidance. Lancet 2020;395:945.

44. Feng S, Shen C, Xia N, Song W, Fan M, Cowling BJ. Rational use of face masks in the COVID-19 pandemic. Lancet Respir Med 2020. doi: https://doi.org/10.1016/S2213-2600(20)30134-X. [Epub ahead of print].
45. Klompas M, Morris CA, Sinclair J, Pearson M, Shenoy ES. Universal masking in hospitals in the COVID-19 era. N Engl J Med 2020. doi: https://doi.org/10.1056/NEJMp2006372. [Epub ahead of print].
46. Radonovich LJ Jr, Simberkoff MS, Bessesen MT, Brown AC, Cummings DA, Gaydos CA, et al. N95 respirators vs medical masks for preventing influenza among health care personnel: a randomized clinical trial. J Am Med Assoc 2019;322:824–33.
47. Livingston E, Desai A, Berkwits M. Sourcing personal protective equipment during the COVID-19 pandemic. J Am Med Assoc 2020. doi: https://doi.org/10.1001/jama.2020.5317. [Epub ahead of print].
48. Iacobucci G. Covid-19: Lack of PPE in care homes is risking spread of virus, leaders warn. Br Med J 2020;368:m1280.
49. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin Chem Lab Med 2020. doi: https://doi.org/10.1515/cclm-2020-0240. [Epub ahead of print].
50. Centers for Disease Control and Prevention. Recommended Guidance for Extended Use and Limited Reuse of N95 Filtering Facepiece Respirators in Healthcare Settings. Available at: https://www.cdc.gov/niosh/topics/hcwcontrols/recommendedguidanceextuse.html. Last accessed: April 14, 2020.
51. Food and Drug Administration. N95 Respirators and Surgical Masks (Face Masks). Available at: https://www.fda.gov/medical-devices/personal-protective-equipment-infection-control/n95-respirators-and-surgical-masks-face-masks. Last accessed: April 14, 2020.
52. Centre for Evidence-Based Medicine. What is the efficacy of standard face masks compared to respirator masks in preventing COVID-type respiratory illnesses in primary care staff? Available at: https://www.cebm.net/covid-19/what-is-the-efficacy-of-standard-face-masks-compared-to-respirator-masks-in-preventing-covid-type-respiratory-illnesses-in-primary-care-staff/. Last accessed: April 1, 2020.
53. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in different types of clinical specimens. J Am Med Assoc 2020. doi: https://doi.org/10.1001/jama.2020.3786. [Epub ahead of print].
54. van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. N Engl J Med 2020;382:1564–7.
55. Chin AW, Chu JT, Perera MR, Hui KP, Yen H-L, Chan MC, et al. Stability of SARS-CoV-2 in different environmental conditions. Lancet Microbe 2020. Published online April 2. https://doi.org/10.1016/S2666-5247(20)30003-3.
56. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect 2020;104:246–51.
57. Ong SW, Tan YK, Sutjipto S, Chia PY, Young BE1, Gum M, et al. Absence of contamination of personal protective equipment (PPE) by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Infect Control Hosp Epidemiol 2020:1–6. doi: https://doi.org/10.1017/ice.2020.91. [Epub ahead of print].
58. The Therapeutic Goods Administration (TGA). Appropriate use of disinfectants: Information for consumers, health professionals and healthcare facilities. Available at: https://www.tga.gov.au/appropriate-use-disinfectants-information-consumers-health-professionals-and-healthcare-facilities. Last accessed: 27 March 2020.
59. Wang C, Wang H, et al. Expert Consensus on biosafety for 2019 novel coronavirus pneumonia in clinical laboratory. Chinese J Lab Med 2020;43:203–8.