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Prevention of Infection and Disruption of the Pathogen Transfer Chain in Elective Surgery.

Emanuele Chisari MD, Chad A. Krueger MD, C. Lowry Barnes MD, Stefaan Van Omsen MD, William Walter MD, Javad Parvizi MD FRCS

1 Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, PA, US
2 Department of Orthopaedic Surgery, University of Arkansas for Medical Sciences, Little Rock, AR, US
3 Royal North Shore Hospital, Sydney, Australia

*Correspondence should be addressed to:
Javad Parvizi MD
125 S 9th Street, Suite 1000, Philadelphia, PA, US
Prevention of Infection and Disruption of the Pathogen Transfer Chain in Elective Surgery

Emanuele Chisari MD¹, Chad A. Krueger MD¹, C. Lowry Barnes MD², Stefaan Van Omsen MD³, William Walter MD³ Javad Parvizi MD FRCS¹*

¹Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, PA, US
²Department of Orthopaedic Surgery, University of Arkansas for Medical Sciences, Little Rock, AR, US
³Royal North Shore Hospital, Sydney, Australia.

*Correspondence should be addressed to:
Javad Parvizi MD
125 S 9th Street, Suite 1000, Philadelphia, PA, US
Introduction

The date was September 28th, 1918. 200,000 Philadelphia and Pennsylvania citizens united to celebrate the end of World War I. It was the day of the Liberty Loan Parade, a government initiative to promote the new bonds being issued to pay for war-associated cost. Most of the city’s population joyfully attended the event. Three days later, 635 of attendees of the event fell ill to what was assumed to be common flu. By six months, over 16,000 of the event participants had died, and a half million more were infected in Pennsylvania. [1–3] Such was the power and impact of the ‘Spanish Flu’ (H1N1) which remains one of the worst pandemics in our history. Based on some estimations, it killed over 50 million people around the globe [1]. Ironically, and within the context of current pandemic 102 years later, some lessons are being re-learnt.

While the outbreak of COVID-19, caused by SARS-CoV-2, does not appear to be on the same scale as the pandemic of 1918, it does share some of the same signatures of the “Spanish-flu” and, for that matter, some more recent pandemics. All of these pandemics were caused by a virus originating from an animal source and spreading amongst humans by droplets and/or contact with bodily fluids. [4]. The SARS-Cov-1 epidemic during 2002-2004, which started in China, was also caused by a coronavirus and killed 774 people with a 9% fatality rate [5]. In 2009, the H1N1 pandemic spread across the globe and killed over 18,000 people in the United States alone [6,7]. Then, in 2012, another fatal coronavirus, known as Middle East Respiratory Syndrome (MERS), hit the Arabic peninsula[8]. All of these outbreaks were similar to what we face today but occurred on a much smaller scale. The major difference between the current pandemic, caused by SARS-CoV-2, and those before it is that the current virus appears to be highly contagious. In fact, COVID-19 has already caused ten-times as many cases as SARS in a quarter of the time [9]. The SARS-CoV-2 virus can also infect some people without causing many, or any, symptoms and is capable of surviving on surfaces for a relatively long period of time. The aforementioned qualities of SARS-CoV-2 makes the current COVID-19 pandemic a truly challenging one to manage. Especially
when considering that we live in an increasingly connected world that appears ideally suited for the rapid spread of diseases across countries and continents.

The medical community has been mindful of infection origination and pathogen transfer for centuries. As surgeons, we meticulously exercise the necessary steps to decrease the possibility of pathogen transfer and are acutely aware of the consequences of infection affecting our patients. Societies also have considerable knowledge regarding the importance of “breaking the chain of pathogen transfer”. In the middle of 19th century, Ignac Semmelweis, known as the Saviour of Mothers, [10] recognized the personal chain of pathogen transfer and mandated hand-washing to disrupt this process. Quarantines have an even more remote history, dating back to 14th century[11]. In an effort to protect the coastal cities from diseases arriving on incoming boats, passengers were placed in isolation for a period of time and monitored for the presence of disease before being allowed to interact with the local community. All of the measures implemented to address the COVID-19 pandemic, which have been in practice in the medical and surgical community for centuries, are intended to break the chain of pathogen transfer. There is no doubt that this pandemic shall also pass and we will return to our “normal” lives. Many, however, believe that the new normalcy will have different features than what was present prior to COVID-19. Our profession will also witness changes in everyday routines that will be necessary to overcome the issues with the current pandemic and diminish the scale and gravity of future epidemic/pandemics. As we prepare to emerge from this pandemic and contemplate resuming our practices, we are faced with the ever-pertinent question of what changes will we need to implement in our daily routines. This article is written, with reliance on available evidence from the past and the current events, to provide some guidance on strategies that may need to be implemented to disrupt the chain of pathogen transfer. These strategies may also translate to a reduction in the rate of surgical site infections in the future.

Resuming Elective Arthroplasty
There will come a day, hopefully in not so distant of a future, when the current pandemic subsides and elective surgical procedures are resumed. The decision of when to re-start elective procedures will be a complicated one being affected by societal, political, geographic, economic and health related factors. Once such normalcy resumes, we have to entertain the major question of what changes we will need to introduce in our practices to prevent the spread of SARS-CoV-2 from infected hosts to others. We will also need to be cognizant of the potential for re-infection with the virus and the emergence of a second wave.

While any discussion regarding a SARS-CoV-2 ‘reinfection’ remains theoretical, a few recent articles have raised this possibility [12,13]. If such a phenomenon is indeed possible, three distinct explanations exist. First, patients who contract the disease do not develop lasting immunity against the virus and are just as vulnerable as those without a prior infection in contracting the disease. Second, there are issues with the accuracy of the test, with false positives and false negatives existing. So, it is possible that some of these presumed reinfections are a result of the re-test being a false negative result which was incorrectly interpreted as the individual being declared as “cured”. Finally, it is plausible, and indeed scientifically proven [14–17], that viruses undergo marked genetic mutations, even during an active pandemic. Hence those infected with the virus develop partial immunity and are still vulnerable for infection with the ‘new’ mutated version of the virus [14–17]. We are familiar with the concept of partial immunity as it relates to the flu-vaccine, as it affords only 60-70% immunity against the disease in any given year [18]. Based on scientific data, the genetic footprint of the initial SARS-CoV-2 affecting individuals in Wuhan is different than the RNA sequence of the virus affecting people in other countries [19]. The virus has certainly undergone mutation. In fact, these mutations likely explain why some epidemics come to an abrupt end as the continued viral alterations may revoke the virulence of the pathogen.

So, without an effective vaccine against the virus, and without an absolute test for detection of the disease, we need to assume that every patient under our care, and for that matter healthcare personnel around us in the hospitals, are potential carriers of the virus and capable of spreading the infection. The
latter does not imply that we should not insist on large scale testing of every individual who comes out of social isolation and enters the society. The medical profession is aware of the importance of “screening” patients for a condition or a disease. Identifying carriers of a pathogen is critical step in disruption of the chain of transfer.

Disrupting the chain of pathogen transfer

Infection, either viral, bacterial or fungal, can be transferred from one individual to another through air (droplets), direct contact with skin or bodily fluids or contact with a surface harboring the pathogens. Here, we summarize the importance of good practices that are known to be effective in disrupting the chain of pathogen transfer. We are aware that there remains many unknowns regarding COVID-19 and excited that the scientific discoveries and innovations arising from the current pandemic will serve the society in general, and healthcare profession in particular, for years to come.

Patient screening.

To determine the risk of a patient being infected with SARS-COV-2, all patients scheduled for elective surgery should be screened for symptoms and exposure. Symptoms of infection include fever, sore throat, cough, and anosmia are common with a COVID-19 infection. Patients should also be asked if they have been exposed to anyone with known COVID-19 infection or anyone with symptoms of COVID-19 to determine the risk. Furthermore, the rate of infection in the community will be important as well as a patient’s history of travel from a region with known high rates of COVID-19 infection.

Routine screening of nasopharyngeal swabs or throat swabs by PCR (polymerase chain reaction) to detect viral genetic material is subject to false positive and false negative results, and is therefore not indicated in low-risk patients. Serological tests for IgG and IgM are not currently widely available but may become useful tools to determine the patient’s status. There is limited data on their accuracy and they are not
regulated in the same manner as more standard antibody tests at this time so enthusiasm for these tests need to be tempered. All of these tests will undergo further refinements as we continue to expand our knowledge regarding immunity to COVID-19. We believe that questions regarding who should be screened and what screening should be in place is a pertinent one. Most, if not all, institutions will need to have access to a rapid turnaround test for COVID-19. A point of care test is currently available and should be utilized for emergency cases. Industry has also been able to develop special swabs that can be used to detect the presence of SARS-CoV-2 in the oral cavity, eliminating the need for more invasive nasopharyngeal swabs for testing.

Prevention of transfer through direct contact

Direct contact with an infected host is also a major pathway for the spread of pathogens. Thus, wearing protective gloves and gowns by all in the OR should be routine. Furthermore, scrub changes should be frequent throughout the day. Again, without a widespread screening mechanism in place for COVID-19, it is impossible for us to determine who is ‘safe.’ Another mechanism to glean information about the status of a patient would be the use of an antibody testing to identify those who had contracted the disease and developed immunity.

Prevention of spread in the air

Aerosolized particles have proven to be a mechanism of spread of SARS-CoV-2[20]. Aerosolization of virus particles usually does not occur with breathing or talking but some procedures in the operating room may cause aerosolization of virus particles. Droplets are expelled during talking and breathing but these usually do not become aerosolized and land on surfaces within a few minutes. Patients undergoing elective arthroplasty should be supplied with a simple surgical mask that will prevent the spread of droplets carrying the virus. Personal protection equipment (PPE) should be available to all the healthcare
workers and should focus on masks that are able to filter any pathogen, while allowing for enough
comfort to be worn for a substantial length of time. We, as surgeons, and healthcare workers in general,
should also be fitted with such masks.

It is fortunate that the majority of arthroplasties are performed under regional anesthesia. Intubation
of patient can cause aerosolization of a large number of particles in the upper airways and particular
caution should be taken with this procedure when there is a risk that the patient may be carrying
SARS-COV-2. Anesthesia teams dealing with patients who require general anesthesia and airway
management should be fitted with secure personal protection equipment (PPE). As orthopaedic surgeons,
we use power tools (drills, saws, etc.) that releases aerosolized material [21] containing blood, bone and
fat tissue. The amount of virus particles in these tissues is not known but these instruments could
potentially aerosolize virus particles in the operating room. In patients who are positive for the virus,
when surgery cannot be delayed, the power settings should be as low as possible, and suction devices
should be carefully handled to remove any aerosol formation [22]. This may include suction fitted to
electrocautery devices or sterile towels dropped over cutting surfaces to potentially decrease the amount
of aerosolized.

In cases of known SARS-CoV-2 positive patients, surgeons and other healthcare workers should also
have ventilation systems that are able to filter and capture SARS-CoV-2, as well as other bacteria and
fungi. These systems can be used outside of the operating area but should be present in every operating
room. Given that coronaviruses are approximately 0.125 mm (125 um) in diameter [23] high-efficiency
particulate air (HEPA) filters might be one possible solution. [24] Thus, filtration of the operating room
with devices that intake the air and remove the micro-organisms may be preferable to the positive
pressure laminar flow settings. Negative pressure operating rooms will reduce the risk of virus particles
being forced out of the room into the corridors.

The current surgical helmets (by Stryker and Zimmer-Biomet, for example) are not protective against
spread of virus, as learnt during the 2012 SARS epidemic. They are designed to protect the user against
splash back and can actually pull and condense sub-micron particles within the hood system [25]. All
reusable material should also be sanitized or sterilized at the conclusion of each procedure. Tests on the proper length of use for each mask and eventual reusing, should be performed to provide evidence-based guidelines to medical staff. Many questions remains: How long we should wear the mask?; How often should we change the masks?; Can the masks be sterilized and safely reused? And many others still remain unanswered. Further data is needed in order to provide evidence-based recommendations on these issues.

Decontamination of Surfaces

Every pathogen is capable of surviving on inanimate surfaces for a period of time [26]. We have come to understand that SARS-CoV-2 is a robust virus capable of surviving on the surfaces of metal and plastic for up to a few days and is not easily removed by standard air filtration systems [20,27,28]. Thus, another approach to disrupt the chain of pathogen transfer needs to concentrate on the decontamination and sanitization of inanimate and skin surfaces. One agent that has been demonstrated to be viricidal, including activity against coronaviruses, is dilute povidone iodine [29–31]. Dilute povidone iodine was tested against SARS, MERS and Ebola and found to have absolute efficacy. Other agents with potential activity against viruses, as well as bacterial and fungal pathogens, includes hypochlorite and high-concentration alcohol. Thus, it is crucial that all reusable material in the OR, that includes helmets, lead aprons, tourniquets, X-ray machines, navigation consoles, keyboards, screens and robots be sanitized and decontaminated routinely. The current sterilization systems in the hospitals for instruments and trays are effective in eliminating viruses and may not need to be altered. We may, however, need to implement a practice that requires these instruments to be placed in a bath of antiseptic solution during the procedure to prevent potential contamination. We must also be aware that there is a wide variation in the terminal cleaning of the operating rooms across the globe. Effective infection prevention and viricidal protocols need to be implemented in every operating room and arguably in every patient room after discharge.
Conclusion

The current pandemic has taken us into uncharted territories. The economic and health impact of this pandemic may be irreversible and will be felt for years to come. While we mourn the loss of lives to this pandemic, society needs to prepare for the eventual lift of social isolation and attempt to return to normalcy. As our knowledge of this pathogen expands and we continue to work towards an effective vaccine and potential treatments for SARS-CoV-2, further strategies for the disruption of the chain of pathogen transfer needs to be implemented. We have attempted to highlight some of the changes that arthroplasty surgeons will need to instigate now and when elective arthroplasties are resumed (Table 1). While SARS-CoV-2 may be a novel pathogen, the actions needed to protect ourselves and our patients against the pathogen are not. The medical community and, more specifically, orthopedic surgeons have been acutely aware of the devastating impact of infections for centuries. We, as a medical community, have always been in the forefront of developing infection prevention protocols and implementing evidence-based strategies to combat these pathogens. Our fight against the COVID-19 will be no different. The ultimate changes that we implement as a result of this pandemic stand to serve our patients and the society well for years to come and help us all safely return to caring for our patients.
References

[1] Johnson NPAS, Mueller J. Updating the accounts: global mortality of the 1918-1920 “Spanish” influenza pandemic. Bull Hist Med 2002;76:105–15. doi:10.1353/bhm.2002.0022.

[2] 1918 Pandemic (H1N1 virus) | Pandemic Influenza (Flu) | CDC n.d. https://www.cdc.gov/flu/pandemic-resources/1918-pandemic-h1n1.html (accessed April 10, 2020).

[3] Starr I. Influenza in 1918: Recollections of the epidemic in Philadelphia. Ann Intern Med 2006;145:138–40. doi:10.7326/0003-4819-145-2-200607180-00132.

[4] Gates B. The next epidemic - Lessons from Ebola. N Engl J Med 2015;372:1381–4. doi:10.1056/NEJMp1502918.

[5] World Health Organization. WHO | Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003 2015.

[6] Dawood FS, Jain S, Finelli L, Shaw MW, Lindstrom S, Garten RJ, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med 2009;360:2605–15. doi:10.1056/NEJMoa0903810.

[7] Bautista E, Chotpitayasunondh T, Gao Z, Harper SA, Shaw M, Uyeki TM, et al. Clinical aspects of pandemic 2009 influenza a (H1N1) virus infection. N Engl J Med 2010;362:1708. doi:10.1056/NEJMra1000449.

[8] About Middle East Respiratory Syndrome (MERS) | CDC n.d. https://www.cdc.gov/coronavirus/mers/about/index.html (accessed April 10, 2020).

[9] Gates B. Responding to Covid-19 — A Once-in-a-Century Pandemic? N Engl J Med 2020. doi:10.1056/nejmp2003762.

[10] Dunn PM. Ignac Semmelweis (1818-1865) of Budapest and the prevention of puerperal fever. Arch Dis Child Fetal Neonatal Ed 2005;90:F345. doi:10.1136/adc.2004.062901.

[11] Gensini GF, Yacoub MH, Conti AA. The concept of quarantine in history: From plague to SARS. J Infect 2004;49:257–61. doi:10.1016/j.jinf.2004.03.002.
[12] Chen D, Xu W, Lei Z, Huang Z, Liu J, Gao Z, et al. Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report. Int J Infect Dis 2020;93:297–9. doi:10.1016/j.ijid.2020.03.003.

[13] Zhang J, Yan K, Ye H, Lin J, Zheng J, Cai T. SARS-CoV-2 turned positive in a discharged patient with COVID-19 arouses concern regarding the present standard for discharge. Int J Infect Dis 2020;0. doi:10.1016/j.ijid.2020.03.007.

[14] Benvenuto D, Giovanetti M, Ciccozzi A, Spoto S, Angeletti S, Ciccozzi M. The 2019-new coronavirus epidemic: Evidence for virus evolution. J Med Virol 2020;92:455–9. doi:10.1002/jmv.25688.

[15] Ortega JT, Serrano ML, Pujol FH, Rangel HR. Role of changes in SARS-CoV-2 spike protein in the interaction with the human ACE2 receptor: An in silico analysis. EXCLI J 2020;19:410–7. doi:10.17179/excli2020-1167.

[16] Wang C, Liu Z, Chen Z, Huang X, Xu M, He T, et al. The establishment of reference sequence for SARS-CoV-2 and variation analysis. J Med Virol 2020. doi:10.1002/jmv.25762.

[17] Stefanelli P, Faggioni G, Lo Presti A, Fiore S, Marchi A, Benedetti E, et al. Whole genome and phylogenetic analysis of two SARS-CoV-2 strains isolated in Italy in January and February 2020: additional clues on multiple introductions and further circulation in Europe. Eurosurveillance 2020;25. doi:10.2807/1560-7917.es.2020.25.13.2000305.

[18] Zhang X, Zhao Y, Neumann AU. Partial immunity and vaccination for influenza. J Comput Biol 2010;17:1689–96. doi:10.1089/cmb.2009.0003.

[19] Forster P, Forster L, Renfrew C, Forster M. Phylogenetic network analysis of SARS-CoV-2 genomes. Proc Natl Acad Sci 2020;202004999. doi:10.1073/pnas.2004999117.

[20] 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. doi:10.1056/nejmc2004973.

[21] Yeh HC, Jones RK, Muggenburg BA, Turner RS, Lundgren DL, Smith JP. Characterization of aerosols produced during surgical procedures in hospitals. Aerosol Sci Technol 1995;22:151–61.
Zheng MH, Boni L, Facs MD, Fingerhut A. Minimally invasive surgery and the novel coronavirus outbreak: lessons learned in China and Italy. n.d.

Fehr AR, Perlman S. Coronaviruses: An overview of their replication and pathogenesis. Coronaviruses Methods Protoc., Springer New York; 2015, p. 1–23. doi:10.1007/978-1-4939-2438-7_1.

Martsolf GR, Barrett ML, Weiss AJ, Kandrack R, Washington R, Steiner CA, et al. Impact of race/ethnicity and socioeconomic status on risk-adjusted hospital readmission rates following hip and knee arthroplasty. J Bone Jt Surg - Am Vol 2016;98:1385–91. doi:10.2106/JBJS.15.00884.

Derrick JL, Gomersall CD. Surgical Helmets and SARS Infection. Emerg Infect Dis 2004;10:277–9. doi:10.3201/eid1002.030764.

Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC Infect Dis 2006;6:130. doi:10.1186/1471-2334-6-130.

Tsai Y-H, Wan G-H, Wu Y-K, Tsao K-C. Airborne Severe Acute Respiratory Syndrome Coronavirus Concentrations in a Negative-Pressure Isolation Room. Infect Control Hosp Epidemiol 2006;27:523–5. doi:10.1086/504357.

Booth TF, Kournikakis B, Bastien N, Ho J, Kobasa D, Stadnyk L, et al. Detection of Airborne Severe Acute Respiratory Syndrome (SARS) Coronavirus and Environmental Contamination in SARS Outbreak Units. J Infect Dis 2005;191:1472–7. doi:10.1086/429634.

Eggers M, Eickmann M, Kowalski K, Zorn J, Reimer K. Povidone-iodine hand wash and hand rub products demonstrated excellent in vitro virucidal efficacy against Ebola virus and modified vaccinia virus Ankara, the new European test virus for enveloped viruses. BMC Infect Dis 2015;15:375. doi:10.1186/s12879-015-1111-9.

Kariwa H, Fuji N, Takashima I. Inactivation of SARS coronavirus by means of povidone-iodine, physical conditions and chemical reagents. Dermatology, vol. 212, 2006, p. 119–23. doi:10.1159/000089211.
Eggers M, Eickmann M, Zorn J. Rapid and Effective Virucidal Activity of Povidone-Iodine Products Against Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Modified Vaccinia Virus Ankara (MVA). Infect Dis Ther 2015;4:491–501. doi:10.1007/s40121-015-0091-9.
| SURGICAL STEP               | SUGGESTED ACTION                                                                                                                                 |
|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| WAITING ROOM               | These should not be used. Family members can be called when the surgery is complete and should not enter or wait within the hospital unnecessarily. |
| CHECK-IN                   | A form of ‘mobile’ check-in would be preferable where the patient can call the desk and, when the staff is ready, be escorted directly to their pre-operative holding area room and provided a mask. Patients would ideally not stop at a ‘front desk.’ |
| PRE-OPERATIVE HOLDING AREA | Registration would ideally take place here before each patient prepared for surgery. All beds should be adequately spaced. If curtains separate beds, they should be cleaned after each patient. |
| OPERATING ROOMS            | Each operating room would ideally have its own air-handling system to minimize air-based contamination and consider using high-efficiency particulate air (HEPA) filters. Minimize the number of people in the room. Minimize non-sterile equipment such as X-ray machines, navigation consoles and robots as virus may last up to 72 hours on these surfaces. |
| ANESTHESIA                | Spinal anesthesia should be used preferentially over general anesthesia to decrease aerosolized particles from each patient within the operating room. |
| SURGICAL HOODS/HELMETS     | Surgical helmets/hoods should be modified for increased protection against viruses for those wearing these systems. Alternatively, operating room personnel can eschew the helmets/hoods and use a N-95 mask and face shield in their place. |
| FORCED-AIR WARMING SYSTEM  | These devices should be used with caution as they may increase the distribution of aerosolized particles during the case. Blankets may be more effective at decreasing particulate generation and distribution. |
| SCRUBS                     | Scrubs should be changed frequently, potentially after each patient. Each room should be cleaned between cases with solutions such as dilute povidone-iodine and alcohol that are effective against viruses and other pathogens. |
| ROOM TURNOVER              | All beds should be adequately spaced. If curtains separate beds, they should be cleaned after each patient. Patients who are not going home on the same day should be brought to their hospital room expeditiously. |
| POST-ANESTHESIA CARE UNIT  | If patients can be safely discharged on the same day as their surgery, they should be sent home. Protocols should be in place to facilitate this process and patients and their families should be educated of this policy prior to undergoing their total joint arthroplasty. |
| ‘ROUNDS’                   | Telemedicine should be used to ‘round’ on the patients post-operatively to limit direct contact. |

Table 1: Common steps for the surgical procedure and recommendations for decreasing the potential viral load for each step.