

Considerations for the containment of COVID-19 in cadavers: ensuring the continuance of human dissection for the education of healthcare professionals

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SUMMARY

Human cadavers may present risks to staff and students in anatomy, particularly when new infectious diseases, such as COVID-19, arise. The processing of human tissues in relation to infectious diseases, particularly the fixatives used, was reviewed to try to formulate knowledge to safeguard staff and students working in anatomy laboratories. Advice from virologists indicates that the SARS-CoV-2 virus is unlikely to remain in cadavers that are adequately fixed, particularly if the cadavers are left undisturbed for a prolonged period. However, bodies that are known to be COVID-19-positive should not be accepted into donor programs. It is also recommended that staff and students who come into contact with cadavers should be vaccinated against the virus. In the light of these precautions, teachers and students can retain confidence in being able to continue their education using human cadaveric material.

Key words: COVID-19 – Body donation programs – Anatomy education – Dissection

COMMENTARY

The SARS-CoV-2 virus appeared in Wuhan, China in late 2019 and spread rapidly across the globe. By March 2020, the World Health Organisation (WHO) had designated the global health emergency as a pandemic owing to the virulence of the virus and the spread of infection. The pandemic has caused disruption of global economies and interference with the operation of organizations and institutions (Bianchi et al., 2020, Brassett et al., 2020), particularly health sciences institutions.

The coronavirus was named severe acute respiratory distress syndrome 2 (SARS-CoV-2) (Lai et al., 2020), with the disease being termed COVID-19 (Gosney et al., 2020). The virus is classified as a “risk group 3” human pathogen (PHA, 2020). Transmission of COVID-19 (SARS-CoV-2) is by droplets and fomites (WHO, 2020). While faeces in some instances have tested positive for SARS-CoV-2, faecal material does not appear to be infectious at this time (AST, 2020).

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Submitted: March 12, 2021. Accepted: March 30, 2021

Although it was at first postulated that COVID-19 could not be spread through exposure to a COVID-19-positive dead body (WHO, 2020), evidence exists to the contrary (Sriwijitalai and Wiwanitkit, 2020). However, in a fast changing research field such as this, it has subsequently been reported from an in-depth analysis among pathologists that, if adequate personal protective equipment (PPE) is worn, there is little risk of transmission of COVID-19 at autopsy (Davis and Williamson, 2020). Postmortem swabs have detected the virus for up to 13 days after death (RCP, 2020a). Further data are required to authenticate the handling of COVID-positive bodies as current guidelines on safety provide differing evidence (Dijkhuizen et al., 2020; Yaacoub et al., 2020). It is of major importance that staff and students in anatomy laboratories are protected from possible infection by this, and other, viruses. The advent of a new virus such as SARS-CoV-2 presents challenges for anatomists in dealing with dissection and anatomy laboratory sessions, and finding the appropriate procedures to render the body “safe” for dissection is crucial.

Although the use of human cadaveric material for the teaching, learning and assessment of anatomy has over time been hotly debated (e.g Dyer and Thorndike, 2000; Gregory and Cole, 2002; McLachlan et al., 2004; Peterson and Regan de Bere, 2006; Papa and Veccarezza 2013; McMenamin et al., 2018; Memon 2018; Moxham and Pias, 2017), there is considerable evidence that anatomists, students and laypersons regard human dissection as necessary for the training of healthcare professionals (Patel and Moxham, 2006; Moxham and Plaisant 2007; Kerby et al., 2011; Moxham et al., 2016), not just for the acquisition of anatomical knowledge but also for the development of professional skills and attitudes (Lempp, 2005; Moxham and Moxham, 2007; Pearson and Hoagland 2010; Kerby et al., 2011; Palmer et al, 2021). However, with the advent of the COVID-19 pandemic, teaching has used a virtual platform, laboratory work has been prohibited and has led some anatomists to suggest that virtual cadavers will replace real cadavers (Singal et al., 2020; Iwanga et al., 2021; Nakloo et al., 2021). Recent evidence that the advent of the

coronavirus has affected institutions and caused discontinuance of face-to-face teaching comes from the reports in 2020 of Bianchi et al., Evans et al., Longhurst et al., Pather et al., and Iwanaga et al. Although these measures have led to much ingenuity for teaching, the negative consequences relate to loss of staff-student face-to face teaching, loss of experiential and practical teaching and loss of acquisition of team and professional skills. In addition, high workloads are causing additional stress for staff. An overreliance on electronic methodologies in a computer-dominated age has become apparent at a time when patient-doctor relationships should be re-evaluated as patients might require a more personal relationship. In our view, blended learning, including the use of cadaver-based laboratory tuition alongside computer-assisted technologies, offers the best of all worlds for the education of the emergent healthcare professional. In consequence, it is crucial that the risks of using cadavers that might be infected by SARS-CoV-2 be evaluated.

Working in an anatomy laboratory has always had some challenges in relation to infectious diseases. Historically, as sterile techniques were not applied in the early days of dissection and bodies were not fixed, students and staff were often infected by the transfer of diseases from the cadaver (Kaufman, 2005; Shoja et al., 2013). As a result of the introduction of appropriate precautions, few deaths of anatomists and students are now known to occur (Shoja et al., 2013). A variety of pathogens may be present in an unembalmed dead body. For example, *Mycobacterium tuberculosis* is said to have been transmitted to an embalmer, possibly during the process of embalming a cadaver (Sterling et al., 2000). Pathogens which may be present include, *Mycobacterium tuberculosis*, HIV, hepatitis B and C, prions and corona viruses (Roth et al., 1992; De Craemer, 1994; Healing et al., 1995; Kappel et al., 1996; Catteneo et al., 1999).

Institutions around the world have fostered body donor programs (Garment et al., 2007; McHanwell et al., 2008; Cornwall and Stringer, 2009; Reiderer et al., 2012; Hutchinson et al., 2020) in order to safeguard dissection of the human body (Hildebrandt, 2010; Rokade and Gaikawad, 2012;

Cornwall, 2014; Kramer and Hutchinson, 2014). The advent of the novel coronavirus affected institutions and caused discontinuance of the acceptance of bodies for dissection into donor programs (see Brassett et al., 2020). At this stage, it is not known what long-term impact there will be on the quality of teaching and learning anatomy. However, it is important for anatomists who value human dissection for teaching (Böckers et al., 2010; Ghosh 2017; Moxham and Pias, 2017; Ross et al., 2020) that the supply of human bodies for this purpose is ensured and that dissection for staff and students remains safe.

The coronavirus is not the first disease that has challenged the handling of human cadavers. For example, it is estimated that as many as 65% of individuals involved in unsafe burial practices during the Ebola outbreak in West Africa became infected (Hoffman and Healing, 2019). It needs to be emphasized, therefore, that the appropriate precautions to protect those staff who transport, prepare and embalm bodies for anatomical dissection should be adhered to rigorously and must include PPE and processes as outlined in the guidelines provided by the International Federation of Associations of Anatomists (IFAA, 2020). In particular, invasive procedures and the generation of aerosols should be avoided (Finegan et al. 2020; RCP 2020b). While some institutions have re-opened their laboratories for student dissection (e.g., Ross et al., 2020; University of the Witwatersrand, Johannesburg), the question remaining uppermost in many anatomists' minds is the adequate preservation of bodies for dissection in the future, due to risks from novel infectious diseases.

While it is appreciated that each institution will have Standard Operating Procedures and legal requirements that will affect issues, and while thus far the risk of transmission from handling of COVID-19-positive bodies is considered to be low (ECDC 2020), it is nevertheless recommended that, in general, bodies which are known to be COVID-19-positive should not be accepted into donor programs. It is appreciated that this raises some ethical concerns. For example, should a body be found to be COVID-19-positive after being admitted for anatomical examination,

who is then responsible for the body? In the case of bodies where the death certificate does not indicate whether COVID-19 was present at the time of death, it is recommended that testing should be undertaken. While testing (Ravi, 2020) or screening (AST, 2020) of bodies for coronavirus has been recommended prior to accepting bodies into a donor program, it is appreciated that the cost of testing all bodies may be prohibitive for some institutions in low resource settings and logistics could be complicated.

Even when testing is possible, as COVID-19 infection cannot be ruled out by a negative result on screening (Winichakoon et al., 2020), it is recommended that *all* bodies received in an anatomy department should be treated as if they were infectious, whether this be with a coronavirus infection or another infectious pathogen. There is an extensive array of inactivation procedures that have been suggested for enveloped viruses such as the coronavirus, but not all would be suitable for whole body fixation. The following inactivation methods have been proposed: Heat inactivation (Darnell et al., 2004), UV or gamma irradiation (Darnell et al., 2004; Kumar et al., 2015), phenol and guanidine isothiocyanate-based nucleic acid extraction agents (Darnell et al., 2004; Kumar et al., 2015) or fixatives such as formaldehyde, formalin, paraformaldehyde or glutaraldehyde (Darnell et al., 2004; Kumar et al., 2015; Bain et al., 2020) and ethanol (Shidham et al., 2020). Low alcohol concentrations in fixatives may not adequately inactivate the virus (Rossi et al., 2019; Gosney et al., 2020). Furthermore, those handling bodies in the early stages of donation should be trained (Finegan et al., 2020) and equipped with effective PPE (see CDPC, 2019; Finegan et al., 2020).

Embalming to contain infectious agents

Currently, there is no evidence in the literature to show that the COVID-19 virus is inactivated in a preserved body specifically, although Shidham et al. (2020) state that viral infectivity is greatly reduced by formaldehyde and ethanol. While embalming of COVID-19-infected bodies is not recommended by the WHO (2020), embalming cannot be avoided in anatomy departments.

However, through the use of adequate embalming, the risk of spreading infections from the cadaver to staff and students can be minimized (Demiryurek et al., 2004). Anatomy departments generally use embalming fluids which contain fixatives and disinfectants and comprehensive reviews of human body preservation are available in the literature (Demiryurek et al., 2004; Brenner, 2014).

Formaldehyde appears to be the chemical of choice for embalming (Brenner, 2014) and is the most widely used fixative for cadaver preservation in the US (Coskey and Gest, 2015). However, many other preservatives are also used (Brenner, 2014). Formalin is made as an aqueous solution from formaldehyde (37%). It has excellent tuberculocidal, bactericidal and virucidal properties which cause alkylation of groups of proteins and of some purine bases (Rutala, 1996). Its reaction with nucleic acids is important in attenuating viruses (Brenner, 2014). The use of formalin as a preservative has diminished in certain parts of the world, as formaldehyde above a certain level is known to compromise respiratory function (Akbar-Khanzadeh et al., 1994; Whitehead and Savoia 2008). While the adverse effects of formaldehyde in general have been widely reported (Khaliq & Tripathi, 2009; Ahmed, 2011; Raja & Sultana, 2012 ; Brenner, 2014; Sugata et al., 2016), formalin is still widely used as a preservative.

Both antiviral and antimycosal effects have been ascribed to alcohols dependent on the concentration and conditions (Brenner, 2014). Ethanol is known to denature proteins and dissolve lipids and is thus effective in controlling bacteria and fungi, but not against non-enveloped viruses (Demiryurek et al., 2002). It can be used alone or with other antimicrobial agents (Demiryurek et al., 2002).

The saturated salt solution method and Thiel's method of embalming, both having relatively low concentrations of formalin (0.75% and 0.6% respectively; Hayashi et al., 2016), have been shown to be bactericidal (Hayashi et al., 2016) and virucidal (Benkhadra et al. 2009).

Phenol, which is a disinfectant, will at high concentrations destroy the entire cell, but at lower

concentrations and higher molecular weight is bacteriocidal (Prindle, 1983). Certain phenolic detergents have been shown to be bacteriostatic (Brenner, 2014), bactericidal, virucidal, and tuberculocidal (CDC, 2008).

The use of high concentrations of sodium hydroxide, together with autoclaving (which obviously cannot be applied in whole body fixation), have been suggested for prions, which are highly resistant to general methods of disinfection (Brown et al., 1982) and require unique methods of inactivation (Prindle, 1983). Although the use of formaldehyde may decrease infectivity of prions, the risk of transmission still remains (Sakudo, 2013).

While much is still to be learned about the appropriate disinfectants for COVID-19 specifically, Henwood (2020) has postulated that disinfectants such as 70% ethanol and 0.1% sodium hypochlorite utilized for other coronaviruses (e.g. SARS-CoV and MERS-CoV) should inactivate COVID-19 on surfaces and on skin.

Information about the fixation of COVID-19 in cultures and in histological tissues is limited. In culture, the MERS-CoV virus was inactivated when exposed to formaldehyde-based fixatives for 30 minutes or for 60 minutes in a methanol-acetone solution (Kumar et al., 2015). In the case of histological tissues, it has also been suggested that fixatives utilized for SARS-CoV and MERS-CoV should be adequate for COVID-19 (Henwood, 2020). The SARS-CoV virus is inactivated in tissue samples fixed in 10% neutral buffered formalin at room temperature for one day and by 70% ethanol (Darnell and Taylor, 2006). Temperature and time are important in the inactivation of SARS-CoV by formalin and glutaraldehyde (Darnell et al., 2004). At 25°C and 37°C respectively, the infectivity of the virus on day 1 of fixation by formalin was significantly decreased. However, by day 3 of fixation some virus still remained infectious (Darnell et al., 2004). SARS-CoV was inactivated by glutaraldehyde after an incubation of 1–2 days (Darnell et al., 2004). The immersion of tissue blocks (2cm³) in 10% formalin or phosphate buffered saline containing 4% paraformaldehyde for a period of 24 hours inactivates SARS-

CoV-2 (Bain et al., 2020). Although ethanol and formalin fixation may render the virus inactive (Barbareschi 2020), it should be borne in mind that low alcohol concentrations may not inactivate the virus (Gosney et al., 2020, Rossi et al., 2020).

The length of time for the fixation of viruses in large samples of tissue such as a whole body is of prime importance for anatomists, as specific viruses are known to remain viable in cadavers for some time after fixation (e.g., *Mycobacterium tuberculosis* for up to 48 hours; Weed and Baggenstoss, 1951). Prolonged periods of fixation prior to using whole bodies is thus preferable. Extended periods of fixation are said to reduce the risk of infection (Vigliar et al., 2020). Thus, increasing the period of fixation in formalin has been recommended for tissue blocks (Rossi et al., 2020). Prolonged fixation is also important, as it is known that tissue permeability rates vary for large pieces of tissue (Bain et al., 2020). The period for which bodies for dissection should be fixed to mitigate against infectious diseases needs investigation, but it is suggested that fixed bodies should remain undisturbed for prolonged periods of time (e.g., three months) to allow for permeation of the fixative to all tissues of the body.

Concluding remarks

In order to mitigate the transfer of any infectious disease from cadavers to staff and students within anatomy departments, safety measures must be implemented. Knowledge of preservatives and the time taken to adequately “fix” these infectious agents is helpful for those managing a donor programme or anatomy laboratory. Formalin, although known to be hazardous, appears to be the fixative with properties that would mitigate tuberculocidal, bactericidal and currently known virucidal infections. Unfortunately, there is no/little information in the literature with regards to the time needed for fixatives to permeate all regions of a whole body, and hence cause inactivation of any virus that may be present. Thus, bodies should remain undisturbed for as long as possible following preservation with an appropriate preservative/fixative in order to allow for permeation of the fixative to all parts of the body. The use of effective PPE for those

staff handling the body during the early stages of processing is essential.

Staff and students could thus be protected, while allowing body donor programs to continue and student training to ensue.

Those individuals, whether staff or students who come into contact with cadavers, should be vaccinated against hepatitis B and *M. tuberculosis*. It is also recommended that vaccination against COVID-19 be included in the vaccination protocol/regime for all staff and students in anatomy departments.

ACKNOWLEDGEMENTS

The authors acknowledge the generosity of the donors who bequeath their bodies for the training of health science professionals. Dr Tanya Augustine is thanked for comments on the manuscript.

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