NHSBT-TES POSITION STATEMENT

The Risk of Transmission of the SARS-CoV-2 Virus via Tissue Allografts

Background

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, emerged in December 2019 in Wuhan, China. The World Health Organization (WHO) has declared that the outbreak of COVID-19 constitutes a Public Health Emergency of International Concern. COVID-19 is an acute respiratory disease caused by a single-stranded RNA virus.

SARS-CoV-2 is a respiratory virus, which normally affects the airways. There is limited data available regarding the presence of viable virus in blood, bodily fluids and various tissues and organs; in data collected to date, the detection rate for viral nucleic acid in the blood of symptomatic patients ranged from 15% (1) to 1% (2). However, there is no data available on viraemia in the incubation period, during asymptomatic infection, or after the resolution of symptoms. There have been no documented cases of transmission of similar viruses, SARS-CoV and MERS-CoV, through transplantation or transfusion. Therefore, based on currently available knowledge and taking into account the processing applied to the majority of tissues, the risk of COVID-19 transmission via tissue allografts is theoretical.

The Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) Standing Advisory Committee on Transfusion/Transplantation Transmissible Infections (SAC-TTI) is currently undertaking a full risk assessment for COVID-19 for blood, tissue and cell transfusion and transplantation. This position statement will be reviewed when this is available.

Tissue safety measures

Donor Selection: Respiratory viruses are not known to be transmitted via tissue allografts, however until the pathogenesis of this new Coronavirus is known, precautionary measures are being applied; any potential tissue donor with confirmed or suspected COVID-19 infection will not be accepted until at least 14 days after the symptoms have resolved. Similar restrictions are applied to potential donors who may have been in contact with a person with COVID-19 (3,4). There is a possibility that asymptomatic, undiagnosed donors with COVID-19 may be accepted for tissue donation, however further safety measures are in place as detailed below

Donor Testing: There are currently no validated tests available for screening blood samples from deceased or living tissue donors for SARS-CoV-2. In the UK, organ donors are currently tested for SARS-CoV-2 by combined nose/throat swab and endotracheal aspirate and are accepted with a negative nucleic acid testing (NAT) result. Therefore, tissue donors who are also organ donors are tested for SARS-CoV-2 (see Appendix 2).

Currently, there is no consistency in international practice with respect to screening tissue donors for COVID-19. The European Centre for Disease Control (ECDC) does not currently recommend the screening of tissue donors for COVID-19 (5). They have recommended that “Viruses may be inactivated during processing of some types of tissues (e.g. processed bone and decellularised tissues). Tissue establishments should assess the risk and evaluate the ability of such processes to inactivate/eliminate the SARS-CoV-2 in tissues” In line with this recommendation, a risk assessment has been performed and is included as Appendix 1.
Retrieval & Processing: Tissue allografts generally undergo processing, decontamination and preservation protocols to prepare them for short- or long-term storage. Many of these processes have antiviral properties. Depending on the process in question, these can reduce or eliminate the theoretical risk of viral transmission via tissue allograft transplantation. For example, there is evidence that treatment with biocidal agents such as ethanol, povidone iodine and hydrogen peroxide inactivate coronaviruses at the concentrations that are used in routine tissue allograft retrieval and processing protocols. Some tissues are also sterilised with high dose gamma irradiation, which has been shown to inactivate coronaviruses. These methodologies, and their potential impact on tissue safety, are described in more detail in Appendix 1. During retrieval and processing activities, staff observe strict aseptic technique, use personal protective equipment, and work in controlled processing environments to minimise the risk of contamination.

Clinical Use: In contrast to solid organ transplants, most tissue allograft recipients do not routinely require immunosuppression, and therefore these grafts are unlikely to pose additional risk to recipients. Clinicians will be aware of other co-morbidities that put their patients at higher risk of severe COVID-19 and are expected to assess any risk accordingly. Hospitals should communicate post-transplant infection in recipients, in accordance to established procedures for reporting post-transplant serious adverse event/reactions.

Current activity: Due to pressure on NHS Resources caused by the ongoing COVID-19 pandemic, all planned non-emergency surgical procedures have been cancelled in NHS hospitals. This has resulted in reduced clinical requirement for tissue allografts, with transplant programs restricted to urgent procedures such as emergency cornea and heart valve transplants. To ease pressure on NHS hospitals, living donor programs for bone and amniotic membrane have been temporarily suspended. Deceased tissue donation activity has also been reduced in line with surgical demand, and is under continual review.

Summary

Based on the information summarised in this document, NHSBT-TES is satisfied that current tissue safety measures are adequate to mitigate the risk of COVID-19 transmission via tissue allografts.

Review

This document should be reviewed as and when relevant new information regarding SARS-CoV-2 and COVID-19 becomes available.

Date of preparation: 30th March 2020
Position Statement prepared by
Richard Lomas, Senior Clinical Development Scientist,
Paul Rooney, Head of R&D/ Principal Investigator
John Armitage, Head of Ocular R&D
Kyle Bennett, Head of Operations, TES
Akila Chandrasekar, Consultant in Transfusion Medicine
Ines Ushiro-Lumb, Consultant Virologist

Other contributors:
Helen Gillan, General Manager, TES
Ulrike Paulus, Consultant Haematologist
Angus Wells, Consultant in Donor Medicine
Su Brailsford, Consultant in Epidemiology and Health Protection
Pasco Hearn, Consultant Medical Microbiologist
Carl McDonald, Consultant Clinical Scientist

References
(3) Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee Donor Selection Guidelines for Deceased Tissue Donors. Available at: https://www.transfusionguidelines.org/dsg/ctd/guidelines/coronavirus-infection-1 (Accessed 27/03/2020)
(4) Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee Donor Selection Guidelines for Live Tissue Donors. Available at: https://www.transfusionguidelines.org/dsg/std/guidelines/coronavirus-infection-1/ (Accessed 27/03/2020)
(5) Coronavirus disease 2019 (COVID-19) and supply of substances of human origin in the EU/EEA. March 20th 2020, European Centre for Disease Control
### Appendix 1: Tissue & Eye Services, Tissue Retrieval and Processing Risk Reduction Measures for COVID-19

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Processing Step</th>
<th>Potential COVID-19 Risk Reduction</th>
<th>References</th>
<th>Level of risk reduction achieved by processing alone</th>
<th>Additional non-processing related risk reduction factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>All tissues</td>
<td>Aseptic retrieval, and all open processing steps take place in controlled environments</td>
<td>Reduces the possibility of environmental contamination of the tissue</td>
<td>TES Processing SOPs</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
| Cornea      | Polyvinyl Pyrrolidone (PVPI) rinse                                               | There is evidence that Polyvinyl Pyrrolidone inactivates a variety of both enveloped and non-enveloped viruses, including influenza A, MERS-CoV and SARS-CoV. PVPI at a concentration ranging from 0.23% to 7.5% is capable of inactivating at least 4 logs (99.99% inactivation) within 15 seconds at room temperature. | (1), (2), (3), (4)          | High                                              | 1) Some grafts obtained from organ donors, who are tested for SARS-CoV-2  
                                                      | Coverage of the donor face with an eye mask                                       |                                                                                   |                                           |                                                   |
| Skin        | Decontamination of the skin at retrieval using Hibiscrub and Hydrex (0.5% chlorhexidine gluconate in | Anti-viral effect of the 70% alcohol in the Hydrex. Note this is only a surface decontamination. | (2), (5)                  | Moderate (cryopreserved)                          | 1) Some grafts obtained from organ donors, who are tested for SARS-CoV-2  
<p>| | | | |
|                                                                                   |                                                                                   |                                           |                                                   |</p>
<table>
<thead>
<tr>
<th><strong>70% ethanol</strong></th>
<th><strong>Hydrex exposure is ~ 10 minutes, enough time for air drying</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For irradiated skin, the irradiation process (25-40 kGy gamma irradiation)</strong></td>
<td><strong>The dose required to achieve a 1 log reduction is less than 3.6 kGy, therefore a 25 kGy dose will inactivate at least 7 logs (10 million PFUs)</strong></td>
<td><strong>(6), (7)</strong></td>
</tr>
<tr>
<td><strong>Multiple rinsing protocols during the preparation protocol</strong></td>
<td><strong>Removal of residual donor blood, and surface contamination</strong></td>
<td><strong>TES Processing SOPs</strong></td>
</tr>
<tr>
<td><strong>Bone</strong></td>
<td><strong>Heat treatment / sonication</strong></td>
<td><strong>(2), (5)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Heating for 30 minutes at 56°C is highly effective in inactivating the virus in the absence of serum, if serum is present, increase heat to 60°C</strong></td>
<td><strong>High (processed)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Treatment with 3% hydrogen peroxide</strong></td>
<td><strong>Moderate (Massive allografts)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>A concentration of 0.5% hydrogen peroxide kills the virus in 1 minute</strong></td>
<td><strong>Low (Fresh frozen femoral heads)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Treatment with 70% ethanol</strong></td>
<td><strong>1) Some grafts obtained from organ donors, who are tested for SARS-CoV-2</strong></td>
</tr>
<tr>
<td></td>
<td><strong>70% ethanol, kills 3 logs in 10 minutes, higher concentrations of ethanol kill in 30 seconds</strong></td>
<td><strong>2) Note: Living donation program (for FFFH) currently suspended to ease pressure on NHS hospitals</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Irradiation at 25 kGy</strong></td>
<td><strong>(6)</strong></td>
</tr>
<tr>
<td>Tendon</td>
<td>All tendons - Treatment with 70% ethanol</td>
<td>70% ethanol, kills 3 logs in 10 minutes, higher concentrations of ethanol kill in 30 seconds</td>
</tr>
<tr>
<td>-----------------</td>
<td>------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Irradiated grafts only - Irradiation at 25 kGy</td>
<td>The dose required to achieve a 1 log reduction is less than 3.6 kGy, therefore a 25 kGy dose will inactivate at least 7 logs (10 million PFUs)</td>
<td>(6)</td>
</tr>
<tr>
<td>Multiple washing and rinsing during routine processing</td>
<td>Removal of residual donor blood, and surface contamination</td>
<td>TES Processing SOPs</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>For deceased donor hearts and arteries, the grafts are wrapped in Hydrex soaked gauze for up to 24 hours following retrieval</td>
<td>Anti-viral effect of the 70% alcohol in the Hydrex. Note this is only a surface decontamination.</td>
</tr>
<tr>
<td>Material</td>
<td>Treatment / Process</td>
<td>Surface Antiviral Effect</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------------------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>All hearts, including those from organ donors, are swabbed with Hydrex prior to dissection. Additionally the external myocardium is cut away before the dissection proper commences.</td>
<td>Anti-viral effect of the 70% alcohol in the Hydrex. Note this is only a surface decontamination. Physical removal of potentially contaminated tissue</td>
<td>(2), (5)</td>
</tr>
<tr>
<td>Multiple washing and rinsing during routine processing</td>
<td>Removal of residual donor blood, and surface contamination</td>
<td>TES Processing SOPs</td>
</tr>
<tr>
<td>Amniotic Membrane</td>
<td>Treatment with antibiotics, multiple washes and rinses</td>
<td>Physical removal of surface contamination</td>
</tr>
<tr>
<td>dCELL dermis</td>
<td>Decontamination of the skin at retrieval using Hibiscrub and Hydrex (0.5% chlorhexidine gluconate in 70% ethanol). Hydrex exposure is ~ 10 minutes, enough time for air drying</td>
<td>Anti-viral effect of the 70% alcohol in the Hydrex. Note this is only a surface decontamination.</td>
</tr>
<tr>
<td></td>
<td>Irradiation at 25-40kGy (gamma irradiation)</td>
<td>The dose required to achieve a 1 log reduction is less than 3.6 kGy, therefore a 25 kGy dose will inactivate at least 7 logs (10 million PFUs)</td>
</tr>
</tbody>
</table>
### Table: Anti-viral effect of Sodium Dodecyl Sulphate (SDS)

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
<th>Reference</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-viral effect of Sodium Dodecyl Sulphate (SDS)</td>
<td>SDS has recognised anti-viral effects on enveloped and non-enveloped viruses. (12), (13), (14)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Meniscus & osteochondral allografts                                   | Multiple washing and rinsing during routine processing                                               | Removal of residual donor blood, and surface contamination | TES Processing SOPs | Low | 1) Some grafts obtained from organ donors, who are tested for SARS-CoV-2 |

### References


Appendix 2: Testing Flowchart

Referral of Potential Deceased Tissue Donor

- Known confirmed COVID-19
  - Not Recovered: Exclude
  - Recovered (1): Patient can be carefully assessed for donation

- Meets any UK Gov 'Possible' COVID-19 definition (both hospital and community)
  - Not tested
    - Not Recovered: Exclude
    - Recovered (1): Patient can be carefully assessed for donation
  - Tested
    - COVID-19 Test result pending or Positive: Exclude
    - COVID-19 Negative
      - Patient can be carefully assessed for donation

- Has no clinical indication for testing and has not been tested for COVID-19
  - Patient can be carefully assessed for donation

- Consented COVID-19 Tested Organ donor
  - COVID-19 Test result Positive: Exclude
  - COVID-19 Negative
    - Patient can be carefully assessed for donation

(1) In line with JPAW guidelines, donors can be considered to have recovered if they were free of fever and respiratory symptoms for 14 days at the time of death.