# Joint UKBTS Professional Advisory Committee ([1])

**Position Statement**

**SARS-CoV-2/COVID-19 and the Safety of Blood, Tissues and Stem Cells**

**June 2020**

***Prepared by:*** The Standing Advisory Committees on Transfusion Transmitted Infections

## Background

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a recently emerged coronavirus, a pathogen of the respiratory tract, the spread of which has resulted in a global pandemic. Although the virus has been officially named as SARS-CoV-2 by the International Committee on the Taxonomy of Viruses (ICTV), the World Health Organization (WHO) has named the disease caused by the virus as COVID-19. It is important that this distinction is understood.

SARS-CoV-2 transmission is by the respiratory route during close unprotected contact between infected and uninfected individuals, primarily through droplet contact with infected secretions, directly or on surfaces.

Although coronaviruses are usually found in the upper and lower respiratory tract, at some point during infection virus may be found in the bloodstream. However, although there are a few reports of SARS-CoV-2 nucleic acid being found in the bloodstream, there are still limited data available regarding the presence of viable virus in blood, bodily fluids and various tissues and organs; to date virus has not been cultured from blood samples taken from laboratory confirmed infected individuals.

Although early investigations were performed on symptomatic individuals, more recently viral nucleic acid has been detected in the blood of asymptomatic individuals. Asymptomatic SARS-CoV-2 infection is an important aspect of virus infection and interaction with its human host which needs to be better understood. Initial data suggested that only a small proportion of cases would be asymptomatic, but more recent information, including data from the use of antibody testing, suggests that a much higher percentage of infections are asymptomatic.

Based on precedent, transmission of a respiratory virus by transfusion is very unlikely to result in an infection in the transfused patient; nonetheless, SARS-CoV-2 is a new human agent and the possibility of transmission has to be considered. It is important that blood donor deferrals to protect the blood supply are balanced with any negative impact on the ability to maintain a blood supply, and that actions taken are proportionate to the level of potential risk.

## Infection and viral persistence

Current estimates suggest a median incubation period from five to six days for SARS-CoV-2, with a range from one to up to 14 days. Comparisons with the two previous major coronavirus outbreaks (SARS from 2002 - 2004; MERS from 2007 and ongoing) have shown very similar incubation period distributions (3-10 days for SARS-CoV-1 and up to 14 days for MERS-CoV).

Virus can initially be detected in upper respiratory samples 1-2 days prior to symptom onset,

demonstrating the potential for transmission from infected individuals who are not displaying any symptoms, or in whom the symptoms are so mild and non-specific to not be noticed. The viral load profile of SARS-CoV-2 appears to be similar to that of influenza, peaking around the time of symptom onset. This is different to both SARS-CoV and MERS-CoV which peak at around 10 and 14 days respectively, after onset of symptoms. Testing of upper respiratory tract swabs for SARS-CoV-2 RNA using molecular techniques (reverse transcription polymerase chain reaction [RT-PCR]) has found persistence of viral RNA for 28 days post symptom clearance in moderate cases and for longer periods in more severe cases. However, infectivity decreases after 7 days and PCR detection of non-infectious virus genomes for several months has been shown for other viruses.

Most laboratory investigations are based on the use of RT-PCR to detect viral RNA in upper respiratory swabs. As well as the respiratory tract, viral RNA has been found in whole blood, serum, plasma, saliva, urine, semen and faeces; however, the presence of viral RNA does not necessarily equate with infectivity, and to date only viral nucleic acid, not infectious virus, has been found in blood.

## COVID-19 disease

Symptoms of COVID-19 disease are most commonly: cough, fever, loss or reduced sense of smell and taste, dyspnoea and tiredness, but other symptoms may occur, and include sputum production, headache, haemoptysis and diarrhoea. Clinical features include pneumonia, acute respiratory distress syndrome, acute cardiac and renal injury.

Most infected individuals experience no apparent or only mild symptoms, with recovery in 7 days. However, in other infected individuals, symptoms are more severe and life-threatening, with hospitalisation needed. In general, more severe symptoms and outcomes are associated with a range of pre-existing chronic conditions. Increasing age, male gender and ethnicity also appear to be associated with more severe outcomes. Case fatality rate increases with severity of symptoms, the time from onset of symptoms to death can be as long as 41 days, but in most cases is around 14 days.

## Blood phase and potential for transmission through blood, tissues and stem cells

At the time of publication of this Position Statement, there have not been any reports of the transmission of any respiratory virus via blood, tissues or stem cells, although the identification of such infections would be difficult in a pandemic situation when there is ongoing transmission in the community and within healthcare environments. Limited data from South Korea suggest asymptomatic blood donors do not transmit SARS-CoV-2 to recipients, however, it is acknowledged that SARS-CoV-2 is a recent human infection and that evidence regarding the risk through transfusion and/or transplantation is limited. Well powered studies are needed to further evaluate the rate of detection of viral nucleic acids in donors, the viability of any virus detected in the blood of blood, tissue or cell donors and the

potential risk of transmission via transfusion/transplantation. In the US, 46,000 donations per month are being screened for SARS-CoV-2 RNA with very few showing any evidence or RNAaemia, and no infectious virus reported to date. Transfusion transmission studies in macaques, humanised ACE-2 receptor mice and other animal models are currently underway.

Nonetheless, the presence of coronavirus nucleic acids in the bloodstream of some infected individuals does indicate a potential risk, and the need for precautionary measures. Such measures include: the deferral of confirmed SARS-CoV-2 infected individuals until recovered, reminding donors to report post-donation illness, recall of donations from donors subsequently reporting confirmed infection or compatible symptoms and depending on the nature of the donors (e.g. live vs deceased) testing of the donor. In addition, for some tissue types, the processing of the tissue includes steps which may inactivate or physically remove any virus present. However, whilst Blood Services and Tissue Establishments may elect to test respiratory swabs/blood samples from donors of some product types for SARS-CoV-2 RNA it is noted that, at the time of publication of this Position Statement, the ECDC have not currently recommended screening of blood or plasma samples for SARS-CoV-2 RNA. It is currently unknown whether SARS-CoV-2 RNA may persist in certain organs and tissues, as well as other body fluids, longer than it is detectable in plasma and serum.

## Precautionary measures adopted by UK Blood Services

The UK Donor Selection Guidelines already include information on the identification and deferral of donors with acute infections. These are sufficient to deal with donors who provide information which would suggest recent or ongoing acute infection. It is unlikely that symptomatic live donors would attend to donate, but there is the potential for a live donor who is symptom free, but with virus circulating in the bloodstream, or a deceased donor with mild unidentified symptoms ante-mortem, to donate. Although there are no reports of the transmission of respiratory virus through blood, tissues and stem cells, precautionary measures have been adopted by the UK Blood Services.

An important issue to be considered in relation to donations which may be stored for some time prior to issue for clinical use, primarily some tissue and stem cell donations, is the timing of the spread of SARS-CoV-2 infection in the UK. The first cases of imported COVID-19 in the UK were identified on 31st January 2020 in two holiday makers from China. The Standing Advisory Committee on Transfusion Transmissible Infections (SACTTI) identified the 28th February 2020 as the date from when the UK is to be considered a country with sustained community transmission of SARS-CoV-2. On this date, the first case of COVID-19 transmitted in the UK was identified. Sequence analysis of UK SARS-CoV-2 samples indicate that China, where the virus originated, had a less than 1% impact on cases in the UK and that 80% of all those who came to the UK and spread COVID-19 arrived between 28 February and 29 March. Therefore, prior to the 28th February 2020, it is reasonable to consider that the majority of UK donors had not been exposed to the virus. UK Blood Services implemented specific measures to identify donors with risk of carrying SARS-CoV-2, including geographical deferrals from January 23rd, 2020.

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## The following measures apply to donors of blood, tissue and stem cells.

### Travel deferral

There is now significant sustained UK–wide transmission, and in addition all but essential international travel has ceased. Once locally acquired cases appear, the risk becomes more general and it is harder to identify individual at-risk donors. Whilst there is global transmission, country specific travel deferrals for SARS-CoV-2/COVID-19 have been removed. If the situation should arise whereby there were specific countries with high rates of ongoing transmission, and travel to and from such countries were to be allowed, travel deferral rules for SARS-CoV-2/COVID-19 would be applied to donors returning from these countries. It should be noted that, when applied, these rules are in addition to any existing travel related deferrals which may be in place;

- Donors who have been advised to isolate after travel can donate if at least 14 days have passed from the first day of isolation and the donor remains well.

- Donors recently returned from an area of ongoing transmission of SARS-CoV-2, and who have been laboratory confirmed to be infected with SARS-CoV-2, are deferred for 28 days from symptom resolution without the need for additional testing if the donor is otherwise well at the point of donation (3 months for stem cell donors due to donor safety-concerns).

### Illness deferral

The UK Blood Services have broadly aligned with the ECDC guidance on coronavirus disease and donation of substances of human origin, updated in April 2020.

- Donors with a laboratory confirmed diagnosis of infection with SARS-CoV-2 are deferred for 28 days from symptom resolution.

- Donors with SARS-CoV-2 symptoms but who have not been tested for SARS-CoV-2 RNA are deferred for 28 days from symptom resolution.

- Donors with upper respiratory tract symptoms but who have been confirmed to be negative for SARS-CoV-2 by laboratory testing of an upper respiratory tract sample are deferred for 14 days from symptom resolution.

### Post-donation reporting

An important safety measure which has been used for many years by the UK Blood Services is to ensure that any live donor with symptoms appearing in the 14 days post donation immediately contacts the appropriate Blood Service and reports the symptoms:

- All donors are reminded to report any illness arising in the 14 days after donation. This reminder is given at the point of donation, and for blood donors, at every

donation. Full details of the symptoms and accurate timings are required. This requirement applies to blood donors, living tissue donors and stem cell/cord blood donors.

- All components/donations from donors who are laboratory confirmed infected with SARS-CoV-2 or have clear diagnostic symptoms of COVID-19, within 5 days of donation/harvest, will be recalled/removed from inventory. If the components/donations have been administered/transplanted, the clinician responsible for the recipient should be informed. Confirmation of diagnosis should be attempted whenever possible.

- It is recommended that the archive sample of the index donation be tested for SARS-CoV-2 RNA.

This approach is precautionary, and predicated on the current, albeit limited, data available on duration of RNAaemia in infected individuals; viral load in respiratory tract peaking just prior to the appearance of symptoms and then starting to fall as symptoms appear. RNAaemia has been detected in 1-15% of clinical samples from hospitalised COVID-19 patients and to date has been reported to be associated with more severe symptoms. However, in those individuals in whom viral RNA has been detected, the viral load has been very low.

Although the above approaches help reduce risk of transmission via transfusion/transplantation, there are further options for tissue and cell donors/donations:

**Living tissue donors and cord blood donors**

- Living tissue donors are treated in a similar fashion to blood donors, with no requirement for anything other than the standard donor questioning and deferral. However, as living tissue donors are all hospital inpatients at the time of donation, they are likely to have a respiratory swab taken and tested for SARS-CoV-2 RNA on admission, depending on national and/or local hospital policy applicable at the time of donation; however, there will be a cohort of live tissue donors who donated during the early stages of the pandemic where donation proceeded in the absence of swab testing for the virus. As long as the donor does not report diagnosis of COVID-19 or symptoms suggestive of COVID-19 in the 2 weeks post-donation the donation can be released for clinical use.

- Mothers who donate cord blood or amnion may also have been subject to testing of respiratory swabs for SARS-CoV-2 RNA on hospital admission and post donations history applies in the same way as blood donors.

- Due to the severe immune-suppression that is likely in the setting of cord blood transplantation, the cord blood donation itself, depending on updated evidence in the intervening period, could be screened alongside the other screening performed when the donation is selected for use in the future - this may be some years after donation.

## Deceased tissue donors

- The standard donor selection process cannot be applied in the same way with deceased tissue donors. However, these donors going forward are likely to be subject to testing on a respiratory swab for SARS-CoV-2 RNA either on admission to hospital, or as part of the organ donation pathway. All organ donors are being tested for SARS-CoV-2 since 19th March 2020 (including islet donors), and about half of deceased tissue donors are also organ donors. However, a number of donations may have been progressed during the early stages of the pandemic when testing for SARS-CoV-2 RNA would not have been carried out prior to donation.

- A number of tissue types undergo processing prior to clinical release. If the processing is considered to be effective in the inactivation of any virus that may be present testing respiratory swabs for SARS-CoV-2 RNA would not be necessary in the case of donors where only such processed products are being donated. However, if the testing of respiratory swabs from any deceased tissue donor for SARS-CoV-2 RNA is readily available, SACTTI considers that this information can be used. In these cases, a positive result is a contraindication for donation.

- All deceased donors donating tissue types (e.g. heart valves) which do not undergo processing which would be considered to inactivate any virus present, should going forward have a respiratory swab tested for SARS-CoV-2 RNA.

- Tissue donations progressed during the early stages of the COVID-19 pandemic where routine testing of deceased donors for SARS-CoV-2 on an upper respiratory tract was not carried out will require a case-by-case assessment and can be released for clinical use if the donor did not have symptoms suggestive of COVID-19.

## Stem cell donors

- Stem cell donors have a respiratory swab taken and tested for SARS-CoV-2 RNA on the day of donation.

- For stem cell donations collected in the early stages of the pandemic, before routine testing of stem cell donors for SARS-CoV-2 PCR was put in place, if the donation remains in storage, testing the blood sample taken at the point of donation for the virus would be a sensible approach.

## Retrospective testing (tissues/stem cells)

In the situation where donations have been retrieved/harvested, but not yet released and transplanted, there is the possibility of retrospective testing using the stored plasma archive sample. There are limited data on the presence and significance of viable virus in the bloodstream. It is considered likely that virus will not be present in the majority of cases as most donors are anticipated to be asymptomatic at the point of donation;

- Prior to the 28th February 2020, SACTTI considered that sustained community transmission in the UK was not present. Therefore, it is reasonable to consider that prior to the 28th February 2020 the majority of donors had not been exposed to the virus.

- Although SACTTI suggests that the retrospective testing of any donations collected before that date, and currently stored ready for release, is not mandatory, it acknowledges that individual UK Blood Services may elect to test for SARS-CoV-2 RNA to assist in their risk assessments to mitigate the risk of virus possibly being present in donations collected prior to 28th February 2020.

- For tissues collected from deceased donors after 28th February 2020, SACTTI considers that there are limited data on the presence and significance of virus in the bloodstream and there are no reports to date of transmission of the virus via tissue transplantation. Although, as SARS-CoV-2 is a new human agent and the ACE-2 receptors used by the virus to enter cells are present on certain tissue types, the possibility of transmission has to be considered. The processing applied to some tissue types should inactivate any virus present in those tissues, however, it is noted that processing may not be applied to all types of retrieved tissues e.g. no viricidal processing is applied to heart valve tissue. Individual risk assessment will be required to release non-processed tissues without a negative SARS-CoV-2 respiratory swab test. There are currently no CE-marked SARS-CoV-2 RNA assays for samples collected from deceased donors but if/when such an assay becomes available, individual UK Blood Services may elect to test for SARS-CoV-2 RNA to assist in their risk assessments to mitigate the risk of virus possibly being present in donations where the donor has not been tested for the virus on an upper respiratory swab. The caveat regarding possible persistence of SARS-CoV-2 RNA in tissues/other body fluids longer than it is detectable in plasma and serum applies.

- For stem cells collected after the 28th February 2020, because of the potential consequences of infection in such heavily immunosuppressed individuals, in addition to the pre-donation testing of a respiratory swab for SARS-CoV-2 RNA, SACTTI considers that, if fully validated testing of blood samples becomes available, testing a serum/plasma sample for SARS-CoV-2 RNA may be considered, particularly for any collections still in storage prior to routine respiratory swab testing having been put in place.

## Antibody response to SARS-CoV-2

Although specific SARS-CoV-2 antibody assays are under evaluation and starting to become available they have limited value in assuring the safety of donations at this stage.

However, the use of plasma from individuals who have recovered from SARS-CoV-2 infection, and who have developed sufficient level of antibody against the virus (convalescent OR immune plasma), is currently under investigation. There are trials underway to determine if the antibody produced is neutralising and can help currently infected individuals to clear the virus more quickly.

## Resources

ECDC produces regular situation updates for coronavirus in the EU/EEA and the UK
https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea

ECDC has produced guidance on coronavirus and the safety of SoHO
https://www.ecdc.europa.eu/en/publications-data/coronavirus-disease-2019-covid-19-and-supply-substances-human-origin

WHO has a dedicated section to all aspects of the coronavirus pandemic
https://www.who.int/emergencies/diseases/novel-coronavirus-2019

WHO has produced a document on maintaining a safe blood supply during the pandemic
https://www.who.int/publications-detail/maintaining-a-safe-and-adequate-blood-supply-during-the-pandemic-outbreak-of-coronavirus-disease-(covid-19)

The JPAC Geographical Disease Risk Index (GDRI) is regularly reviewed and updated with appropriate deferrals
https://www.transfusionguidelines.org/dsg/gdri/guidelines

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