Position Statement

May 2024

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SARS-CoV-2/COVID-19 and the safety of substances of human origin (SoHO)

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 Organisation (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. SARS-CoV-2 RNA, and what are assumed to be virus particles, have been found in the bloodstream (viraemia) of symptomatic individuals. However, there are limited data available regarding the presence of viable virus in blood, bodily fluids and various tissues and organs, and to date virus has not been cultured from blood samples taken from laboratory confirmed infected individuals. In at least one published study SARS-CoV-2 RNA was detected in a significant proportion of hospitalised patients, including 100% of patients in ICU, the levels of SARS-CoV-2 RNA associating with disease severity.

Based on precedent, transmission of a respiratory virus by transfusion is very unlikely to result in an infection in the transfused patient, but SARS-CoV-2 is a novel virus and the possibility of transmission has to be considered. However, although SARS-CoV-2 RNA has also been found in a very small percentage of asymptomatic blood donors, transfusion transmission has not been reported.

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 to 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). As new variants have arisen, the average incubation period has shortened; 3.42 days for Omicron.

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 a small number of more severe cases. However, infectivity decreases after seven days and the detection of non-infectious virus genomes for several months post-recovery has been seen with a number of 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.

SARS-CoV-2/COVID-19 disease

Symptoms of SARS-CoV-2 infection 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.

Symptoms are likely to be less severe in individuals that have been vaccinated, received of a booster shot, or had COVID previously. However, a change to the immune system (e.g. pregnancy or a new medication or illness) can result in symptoms that may be more severe than experienced in previous infections.

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

At the time of publication of this Position Statement, with the exception of cases following lung transplantation, there have not been any reports of the transmission of SARS-CoV-2 via SoHO and plasma-derived medicinal products worldwide. There are reported cases of non-lung organs (and lungs) and stem cells being transplanted from individuals known to have tested positive for SARS-CoV-2 just prior to death, without reported transmissions. Limited data from the very few published case reports of donors identified as infected soon after donation suggest that asymptomatic blood donors do not transmit SARS-CoV-2 to recipients. In the US many thousands of donations were screened for SARS-CoV-2 RNA with very few showing any evidence or RNAaemia, and no infectious virus reported.

Nonetheless, the presence of SARS-CoV-2 RNA 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. The period during which donors should refrain from donating until after the resolution of clinical symptoms or clearance of test results, as recommended by various organisations, ranges from seven to 28 days. No transmission of SARS-CoV-2 infection has been reported in association with the application of any of the existing recommendations.

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 review 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. Based on available information on the initial spread of SARS-CoV-2 in the UK SACTTI considered that prior to the 28 February 2020 it is reasonable to consider that the majority of UK donors had not been exposed to SARS-CoV-2. UK Blood Services implemented specific measures to identify donors with a risk of carrying SARS-CoV-2, including geographical deferrals, from January 23 2020.

The measures put in place by the UK Blood Services to deal with the risk of transmission of SARS-CoV-2 through blood, tissue and stem cells, including eligibility to donate after receiving a SARS-CoV-2 vaccine, are available online in the UK Blood Services Donor Selection Guidelines: Whole Blood and Components; Tissue and Cells. **http://www.transfusionguidelines.org/DSG**

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 confirmed as infected with SARS-CoV-2, within 48 hours 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 unless a SARS-CoV-2 RNA test on the day of donation serum/plasma sample is negative.

This approach is precautionary and predicated on the current 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 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.

Retrospective testing (tissues/stem cells)

In the situation where tissue and cell donations have been retrieved/harvested, but not yet released and transplanted, there is the possibility of retrospective testing using the stored plasma archive sample. 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 28 February 2020, SACTTI considered that sustained community transmission in the UK was not present and therefore the majority of donors had not been exposed to the virus.

- Although it is acknowledged that Blood Services may choose to carry our retrospective testing archive sample from tissue or stem cell donations for SARS-CoV-2 RNA, SACCTI does not recommend it as a mandatory requirement.

Resources

ECDC produces regular situation updates for coronavirus in the EU/EEA and the UK
https://www.ecdc.europa.eu/en/covid-19

ECDC has produced guidance on coronavirus and the safety of SoHO, second update December 2020
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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