

Coronavirus - SARS-CoV-2 & COVID-19

BACKGROUND

A novel coronavirus (later named SARS-CoV-2, with the resulting illness named COVID-19) emerged in late 2019, with WHO declaring a global health emergency on 30 January 2020. The epidemic has since spread to all populated continents, with a global pandemic declared on 11 March 2020.

Public health measures against the COVID-19 pandemic have varied widely in strategy and success around the world. Travel restrictions in particular are presenting major challenges in logistics and transport for donated haemopoietic progenitor cells. Meanwhile there remains no evidence that SARS-CoV-2 is transmissible via blood or HPCs from a healthy donor lacking symptoms of COVID-19.

AT VERIFICATION TYPING OR WORKUP

History of COVID-19

Collection should be deferred for at least 14 days after recovery. For asymptomatic infections, defer for at least 14 days after the most recent positive test result.

If the patient's need for transplant is urgent, the donor is completely well and there are no suitable alternative donors, earlier collection may be considered if local public health requirements permit*, subject to careful risk assessment.

Risk assessment should be based on:

- The date of full recovery.
- The duration and severity of illness – in particular, the presence of any ongoing sequelae.
- The results of any post-recovery testing.

*There is evidence that SARS-CoV-2 RNA can remain detectable by PCR in nasopharyngeal samples for an extended period after full recovery, but nasopharyngeal shedding does not predict viraemia. In addition, other coronaviruses (including SARS and MERS) have not displayed any transmissibility via blood or HPC. Nonetheless a collection centre might consider a donor with detectable nasopharyngeal SARS-CoV-2 RNA to be a public health risk to staff and others at the facility.

Contact with COVID-19 – donors who report contact with a confirmed case

Collection should be deferred for 14 days after a donor's last contact with a person with COVID-19 either confirmed or clinically suspected by a health professional.

If the patient's need for transplant is urgent, the donor is completely well and there are no suitable alternative donors, earlier collection may be considered if local public health requirements permit, subject to careful risk assessment.

Risk assessment should be based on:

- The last date of contact.
- The nature of the contact.
- The results of any post-contact testing.

Geographical risk – donors residing in or returning from a high-incidence region

To identify countries where local transmission of SARS-CoV-2 is high, registries may refer to national health authorities and/or trans-national sources such as WHO and ECDC. Following the spread of the pandemic to nearly all developed countries, however, it may be more realistic to define geographical risk in terms of whether the donor's community exposure risk exceeds that of the patient.

In the absence of known contact with COVID-19, risk assessment should take into account:

- The level of risk and applicable public health restrictions in the donor's region.
- Any recent travel to higher-risk regions within the same country or other countries.
- Any contact with a person with known SARS-CoV-2 infection.
- The nationally required quarantine period.

Donor preparation

For at least 14 days prior to donation, donors in a region with ongoing local transmission should be advised to practice good hygiene and to socially isolate as much as possible. Unnecessary travel should be avoided.

In a healthy donor without symptoms, routine pre-donation testing should not be considered necessary as there is no known benefit to the recipient. Meanwhile the potential value of avoiding G-CSF exposure in a donor who is incubating SARS-CoV-2 has not been supported by case reports to date.

However, it is acknowledged that many jurisdictions have recommended or even mandated routine pre-donation screening of HPC donors. Depending on the stipulated purpose for testing, this testing should be performed early enough to forestall patient conditioning, donor mobilisation or collection.

Donation collection

In the absence of symptoms, testing the donor for COVID-19 at the point of collection – or testing the donation itself – is not recommended because:

- There is no benefit to the patient because a validated blood test for infective SARS-CoV-2 is not available, and there is no evidence that detectable nasopharyngeal RNA is associated with infectious viraemia in a pre-symptomatic or symptomless SARS-CoV-2 infection.

- There is no benefit to the donor or to collection staff if a result is not available early enough to prevent collection.

It may be possible to obtain an earlier result with rapid testing assays or collecting a donor sample one or two days prior to collection. Whether the result is available before or after collection, however, the following should be considered before cancelling or rejecting the donation:

- The donor is a volunteer who in most cases has already started or completed G-CSF conditioning.
- There is a possibility of false positive results with rapid or instant screening assays.
- The blood phase of COVID-19 is known to be difficult to detect in symptomatic patients, rarely detectable in pre-symptomatic patients, and there is no evidence for its infective potential.
- Any delay in transplant that results from the cancellation or rejection of the donation will therefore disadvantage the patient with no known or likely risk of COVID-19 transmission.

Planned cryopreservation

If there is concern that the donor is at high risk of community-acquired infection between work-up and collection, pre-planned cryopreservation will allow patient conditioning to be delayed until successful donation and delivery are confirmed.

Cryopreservation at the collection site may have additional advantages in relation to transport delays and travel restrictions.

It has become evident during this pandemic that cryopreservation can have several disadvantages such as the inevitable cell loss and decline in viability after thawing, adverse reactions to the cryoprotectant (DMSO), and collected products that are not used. When considering cryopreservation, the transplant centre should perform a careful risk assessment weighing the risk of the unavailable product against the risks of cryopreservation.

Post-donation cryo-quarantine

By delaying patient conditioning, cryopreservation will also delay product infusion for at least several days after donation. This means it is possible for the transplant centre to be warned if the donor develops COVID-19 symptoms shortly after donating.

Applying a formal post-donation “cryo-quarantine” period, however - whereby a donation will only qualify for release if the donor tests negative or remains symptom-free at the end of a cryo-quarantine period - is not recommended because:

- Patients might be unnecessarily denied HPC products as a result of COVID-19 exposure that occurred after collection.
- In the absence of symptoms, a positive nasopharyngeal swab on Day 14 post-collection or later is not consistent with the presence of pre-symptomatic COVID-19 infection at the time of collection.
- Failed qualification due to the possibility of pre-symptomatic COVID-19 infection at the time of donation is not supported by evidence of transmissibility via blood or HPC during the pre-symptomatic phase.
- Therefore withholding a donation for failed quarantine is detrimental to the patient because they lose their first-choice donor, and detrimental to the donor because their donation and associated community exposure has been in vain.

Nonetheless, it is acknowledged that certain jurisdictions may require such “cryo-quarantine” by regulation.

RATIONALES

There is convincing evidence that person-to-person transmission can occur during the pre-symptomatic phase of COVID-19, and indeed may be a major contributor to community spread. However, respiratory transmissibility does not necessarily equate to transmissibility via blood or HPC.

Studies of the blood phase of COVID-19 have so far shown limited SARS-CoV-2 RNA detectability in symptomatic infection and very limited RNA detectability in pre-symptomatic and symptomless infection, while any correlation between detectable RNA in the blood and actual infectivity is yet to be established. This is consistent with findings for previous coronaviruses, including SARS and MERS, that have not displayed transmissibility via blood or HPC.

Beyond the possibility of blood or HPC transmission risk, there are also important public health considerations and a variety of community measures around the world that are having a major impact on HPC donors and collection facilities. Also taking into consideration the limited evidence base in this rapidly evolving pandemic, individual cases should ideally be assessed in consultation with infectious disease and/or public health experts.

REFERENCES

WHO: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>

ECDC: <https://www.ecdc.europa.eu/en/publications-data/risk-assessment-outbreak-acute-respiratory-syndrome-associated-novel-1>

EBMT: <https://www.ebmt.org/covid-19-and-bmt>

COVID-19 is presenting major logistical challenges in managing and assessing HPC donors and in collecting and transporting HPC products. WMDA has developed a publicly-available resource page at <https://share.wmda.info/x/Yj6OF>.