# COVID-19 infection and risk exposure

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**History of COVID-19 infection**

Collection should be deferred for at least 7 days after recovery from acute symptoms. For example, a donor who has a minor, non-productive cough but no other symptoms for the last 7 days may be accepted.

For asymptomatic infections, defer for at least 7 days after the first positive test result.

Most healthy young donors can be expected to recover within a week, so for scheduling purposes it would be reasonable to schedule (or reschedule) collection for 14 days following onset of symptoms or first 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 duration and severity of illness – in particular, any need for supportive hospitalisation, anti-viral or antibody treatment, and any ongoing sequelae.
- The date of full recovery.
- The results of any post-recovery testing.

**There is ample evidence that SARS-CoV-2 RNA can remain detectable by PCR in nasopharyngeal samples for an extended period after full recovery, but without being infectious. Nonetheless some institutions may still consider a donor with detectable nasopharyngeal SARS-CoV-2 RNA to be a public health risk.*

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

Collection should be deferred for 7 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. For example, many local guidelines will permit an early end to self-isolation if an asymptomatic contact of a COVID-19 case tests negative earlier than 7 days post-contact.

Risk assessment should be based on:

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

**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 is not 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, any such 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 as 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 antigen tests or collecting the 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 prior to transport may have additional advantages in relation to transport delays and travel restrictions.

Potential risks of cryopreservation include excessive cell loss and decline in viability after thawing, adverse reactions to the cryoprotectant (DMSO), and non-infusion of transported products. When considering cryopreservation, the transplant centre should perform a careful risk assessment weighing the risk of the unavailable or delayed product against the possibility of these risks.

Reassuringly, however, data published by the US National Marrow Donor Program (NMDP) showed no significant adverse effect on early transplant outcomes from cryopreserved product during the COVID-19 pandemic compared to the same months in 2019 [Stefanski et al, *Blood* (2021) 138 (Supplement 1): 478].

**Post-donation cryo-quarantine**

By delaying patient conditioning, cryopreservation will also delay product infusion for at least several days after donation. This means it becomes 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 could be denied HPC products unnecessarily as a result of COVID-19 exposure that occurred after collection.
- In the absence of symptoms, a positive nasopharyngeal swab on (for example) 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.
- Preliminary data from the NMDP/CIBMTR evaluated the effects of infusing products from COVID-19+ donors. No known infections of COVID-19 were reported among the patients who had products from COVID-positive donors infused. Moreover, there was no deleterious effects on neutrophil and platelet engraftment. The 3-month and 6-month overall survival were 100% (https://doi.org/10.1182/blood-2021-152952). This limited data reinforces that cryo-quarantine is NOT recommended.
- 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 cryo-quarantine by regulation.

**Summary table**

| **AFTER:** | **DONATION MAY BE COLLECTED:** |
|---|---|
| **COVID-19 infection** | • 7 days after recovery from acute symptoms.<br>• For asymptomatic infections, 7 days after the first positive test result.<br>• For scheduling purposes, a healthy young volunteer donor can be expected to recover within a week, so it would be reasonable to schedule HPC or MNC collection 14 days following the onset of symptoms or the first positive test result. |
| **Contact with COVID-19** | • 7 days after a donor's last contact with a person with COVID-19.<br>• Subject to risk assessment, a shorter waiting period may be considered – for example, where an asymptomatic donor tests negative after the minimum locally-required interval post-contact. |