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Coronavirus and Haematopoietic Stem Cell Transplantation

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Coronaviruses are a family of viruses which have previously manifested as worldwide public health issues of concern associated with significant morbidity and mortality as the Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).

Unfortunately, another novel strain of the coronavirus, currently thought to have likely originated from the Hubei province in China and termed Coronavirus 2019 (COVID-19), has at the time of writing on 17th Feb 2020, affected more than 70,000 individuals and resulted in 1770 deaths in China alone. As a comparison, the SARS-CoV outbreak led to 774 deaths out of 8,098 cases, according to figures from the World Health Organization (WHO).

Other neighbouring countries in Asia have also reported cases of COVID-19 including Singapore (77), Japan (77) and Hong Kong (60) amongst others with one death reported each in Japan and Hong Kong. There is also evidence of significant local transmission in these Asian countries putting them into a higher risk category while smaller numbers have also been reported worldwide including USA, France, Spain and UK. There are also concerns that the disease has been under-reported due to undetected cases not being tested.

In view of the risk of possible COVID-19 infection on haematopoietic stem cell transplant (HCT) donors and recipients, as well as the possible logistical issues involved in the transportation of donor stem cells due to various travel advisories and restrictions, the Worldwide Network for Blood and Marrow Transplantation (WBMT) have collated the current situation for stem cell transplantation in some of the most affected countries.

The measures outlined below illustrates the positions taken by each country in response to this outbreak. The differing measures taken are not necessarily or entirely based on specific evidence based infectious disease guidelines and are likely to include political and public health considerations. The evidence based guidelines for wearing of masks in the prevention of disease acquisition is a case in point which has differed between individual countries involved in this outbreak. It also reflects a rapidly evolving situation and highlights the significant challenges for individual countries to respond in terms of public health and preventive measures to contain the virus.

Areas with endemic or high frequency of COVID-19 infections (China).

All patients (or donors) must be evaluated by epidemiological investigation before any HCT-related procedures. Patients with fever, cough or other symptoms associated to coronavirus should be screened by clinical and laboratory testing for COVID-19, influenza or related viral illnesses.

All patients and family donors are subject to a 14-day home quarantine prior to collection of the stem cell product.

Stem cell harvesting for unrelated donors is still ongoing in most parts of mainland China except Hubei province. Extra protection of unrelated donors by special procedures have been introduced including special shuttle to and out of HSCT centers to avoid public transportation, as well as personal protection including surgical facemask and disinfectant. Currently, unrelated donor products are also transported by medical professionals rather than volunteers of the Chinese Marrow Donor Program (CMDP).

For cross border transportation of unrelated products, more than 80% of allogeneic HCT performed in China are from family donors (HLA identical and haploidentical). As a result, there has not been a major impact on unrelated HCT.

Overall, both autologous and allogeneic HCT may experience delays due to re-direction of medical and hospital resources towards the COVID-19 outbreak.

All clinical activities are to follow the National Health Commission's Novel Coronavirus Pneumonia Prevention and Control Strategy which is updated regularly.

Other countries in Asia with evidence of local transmission (Singapore, Japan, Hong Kong)

Singapore:

Recipients:

- a. Defer non-urgent autologous transplants and non-urgent allogeneic transplants as needed to manage bed capacity and blood product availability issues. This is likely applicable only in areas of endemic infection.

- b. Defer until beyond the incubation period (at least 14 days) any recipients, including planned PBSC mobilization who have:
 - i. Had close contact with a case of 2019 novel coronavirus infection (COVID-19) within the last 14 days or longer; or
 - ii. Had frequent or close contact during work with recent travelers from mainland China (within the last 14 days), defined by health authorities; or
 - iii. Have household members who returned from mainland China in the last 14 days or longer.

Donors:

- a. Defer until beyond the incubation period (14+ days) any donors:
 - i. Who have travelled to China in the preceding 14-21 days; or
 - ii. Who have had close contact with a case of COVID-19 infection; or
 - iii. Had frequent or close contact during work with recent travelers from mainland China (travel history in the last 14-21 days), as defined by health authorities; or
 - iv. Have household members who returned from mainland China in the preceding 14-21 days.

- b. For volunteer unrelated donors (URD) from other countries, especially from regions with high incidence/prevalence of COVID-19:
 - i. Consider pre-harvest and cryopreserve the graft to ensure that the product is safely on-site before starting the preparative regimen, in case of unforeseen travel disruption or donor illness.
 - ii. If this is not possible, ensure that an alternative stem cell source will be available within a reasonable time frame for the recipient should the product fail to arrive. This may include reserving a UCB with confirmatory typing completed, or an alternative donor who has completed infectious disease marker (IDM) testing.

Japan:

The Japanese Marrow Donor Program (JMDP) have just convened and are in the process of implementing actions to reduce the risk of COVID-19 infection. Currently, daily activities of JMDP have not been affected much.

At present, no specific testing or quarantine has been recommended by health authorities in Japan.

One of the member organizations with WBMT, the World Marrow Donor Association (WMDA) has also released a set of guidelines concerning potential donors for a stem cell transplant. These early guidelines have been based on previous guidelines for SARS-CoV and MERS-CoV but adjusted based on the characteristics of the current outbreak. These measures are:

- Similar to SARS-CoV and the possibility of prolonged post-infection viraemia; a 3-month standard deferral period has been recommended by bodies like European Centre for Disease Prevention and Control (ECDC).
- ECDC recommends a 3-week deferral period after contact or geographical exposure. Considering early indications of an incubation period of up to 14 days, WMDA recommends a 4-week deferral period to conservatively double the longest expected incubation period.
- There is already limited evidence of person-to-person transmission during the pre-symptomatic phase. This justifies the deferral of symptomless donors who report recent geographical risk or contact.

As this current outbreak is continuing and more evidence is being collected from infected cases and its transmissibility, additional recommendations will continue to be developed.

USEFUL REFERENCES:

World Health Organization (WHO):

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

European Centre for Disease Prevention and Control (ECDC):

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

World Marrow Donor Association (WMDA):

<https://share.wmda.info/display/DMSR/Coronavirus+-+2019-nCoV#/>

National Health Commission's Novel Coronavirus Pneumonia and Control Strategy (website in Chinese)

<http://www.nhc.gov.cn/jkj/s3577/202002/573340613ab243b3a7f61df260551dd4.shtml>

Centers for Disease Control and Prevention (CDC)

<https://www.cdc.gov/coronavirus/2019-nCoV/summary.html>