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EDITORIAL

The COVID-19 pandemic: New global challenges for the haemophilia community

Over the past few decades, several blood-borne viruses have targeted haemophilia patients requiring treatment with clotting factors derived from human plasma.[1] Even today, many haemophilia patients and their families still retain painful and indelible memories of HIV and hepatitis C infections or are confronted with the progressive health consequences of these infections.

Long considered true enemies of haemophilia patients, viruses, at least some of them, have now become partners in the cure of haemophilia as demonstrated by the successes of gene therapy clinical trials.[2,3] It is indeed possible to cure haemophilia by using viruses, deprived of most their content and infectivity, as vectors to transport genetic material and permit long-term, endogenous production of factor VIII or factor IX by the transduced liver in quantities sufficient to maintain haemostasis.

Beyond these successes and reinforced by past experiences, the emergence of new infectious agents is a constant concern for the haemophilia community. For this reason, the last few decades have been devoted to improving the infectious safety of clotting factor concentrates derived from human plasma and especially to the development of clotting factor concentrates produced by recombinant DNA technology in the laboratory independently of the addition of any human or animal protein.[4-6]

A new disease (COVID-19) caused by a coronavirus (SARS-CoV-2) that appeared in China at the end of 2019 is currently invading the world[7] (Table 1). This emerging virus, spreading from person to person via respiratory droplets, is mainly responsible for respiratory tract infections and potentially fatal pneumonia in more frail patients.[8] Current available data show that the mortality is very low in those <20 year of age but much higher, up to 20%, in older patients presenting with comorbidities. The pandemic is not short term. The current containment measures aim at decreasing the rate of new infections so that enough ventilators are available to support patients who need them.

It is impossible to estimate at the present time how many patients with haemophilia will become infected and whether their factor deficiency and their treatment could influence the manifestations of the infection, its natural course, treatment and consequences.

It seems clear, however, that the current pandemic will have definite consequences, direct or indirect, immediate or delayed, on the management of haemophilia worldwide. In this context, it seems appropriate to try to identify these likely consequences in order to best manage the current challenges and anticipate major difficulties in the longer term.

The major concern and priority are to ensure access to haemophilia treatment. The delivery of replacement therapies through pharmacies, hospitals or home delivery programs could be impacted. Haemophilia treatment centres are working hard to avoid such problems. The situation is totally different for the many countries whose only supply relies on the WFH humanitarian aid program.[9] The current paralysis of air transport may slow or impede the transport of replacement products and access to treatment for an undefined period of time.

The production of recombinant DNA produced replacement products (ie FVIII, FIX, FVIIa, emicizumab) is not expected to be affected by the pandemic unless production plants run out of components of the production process, which seems unlikely. There could be also be a major challenge if there is insufficient workforce available to continue production due to an expanding cohort of infected skilled workers. Contamination of the production lines of synthetic replacement products with SARS-CoV-2 from workers is highly unlikely.

The situation may be quite different for plasma-derived clotting factors if plasma donations are reduced due to the deferral of infected donors and fear of donating blood and plasma. Already, as happened with the HIV epidemic in the 1980s, blood and plasma donations are down due to the mistaken understanding donors may be at increased risk of COVID-19. Viral inactivation during the production process of plasma-derived clotting factors eliminates SARS-CoV-2, a lipid-enveloped virus like HIV.[10]

The increasing containment and mobilization of hospitals to treat patients infected with CoV-2-SARS worldwide will make access to treatment centres difficult, if not impossible. This may have consequences on medical follow-up, assessment consultations, specific treatments (immune tolerance induction), therapeutic education programs and diagnostic procedures including laboratory testing. Treatment centres must rapidly adapt to this reality by taking advantage of all means of distance communication such as telemedicine and maintain regular contacts with patients, especially those who require more attentive and regular follow-up.[11] Elective surgeries have been postponed in areas where hospitals need conserve resources for the overwhelming onslaught of COVID-19 patients.

Clinical research programs are negatively impacted by the pandemic. This includes the initiation and continuation of clinical studies. It is currently not possible to initiate new studies or to recruit new patients, for both logistical and health reasons. Haemophilia centres are taking steps to adapt the monitoring of patients currently included in clinical studies by ensuring access to treatment and appropriate follow-up. In practice, as a consequence of these

TABLE 1 Online important sources of accurate information on COVID-19

Centers for Disease Control and Prevention (US)	https://www.cdc.gov
World Health Organization	https://www.who.int/emergencies/diseases/novel-coronavirus-2019 https://www.who.int/health-topics/coronavirus
EU Center for Disease Prevention and Control	https://www.ecdc.europa.eu/en/novel-coronavirus-china
National Institutes of Health	https://www.nih.gov/health-information/coronavirus
Global data	https://www.worldometers.info/coronavirus/
New England Journal of Medicine summaries	https://www.nejm.org/coronavirus
World Federation of Hemophilia	www.wfh.org
Plasma Protein Therapeutics Association	https://www.pptaglobal.org/23-advocacy/access-to-care/1057-covid-19
International Society of Blood Transfusion	https://www.isbtweb.org/

major disruptions, some experimental therapies will be evaluated with delays, some clinical trials may be interrupted or stopped, and the introduction of many new treatments will likely be postponed.

The pandemic will also result in the cancellation of many educational or research activities planned for the year 2020 (expert and consensus meetings, congresses, patient training camps, community support groups etc) that are essential to advancing the knowledge and care of haemophilia throughout the world. These are all lost opportunities that will have to be reactivated. Even if communication technologies make it possible to maintain interactions between major stakeholders, they do not replace the richness of direct human-to-human contacts. However, efforts should move toward optimizing virtual meetings since this pandemic will not disappear soon.

The economic and social consequences of the pandemic will be major. It is impossible today to evaluate the impact on the funding of haemophilia worldwide, both in terms of reimbursement for treatments and financial support for haemophilia centres. It seems obvious that the entire community must prepare for a difficult financial situation. Many patients already socially and/or professionally weakened by haemophilia could suffer even more from the economic and social consequences of the crisis. They will have to be helped so as not to add financial, social and professional difficulties to the burden of the disease and its treatment.

This text is not intended to be pessimistic but realistic. The current situation requires us to be vigilant, to be proactive in monitoring the situation on a daily basis, to anticipate for a long duration a 'new-normal', to work closely together, and to be innovative. Our bleeding disorders' global community has experienced more than one crisis. This one is as different as it is unexpected. Together, we can all face it and learn the necessary lessons from it.

DISCLOSURES

This letter reflects the positions of Cedric Hermans Editor-in-Chief of the Haemophilia Journal and Medical Member of the Board of the WFH, Alain Weill President of the WFH, and Glenn Pierce Medical Vice-President of the WFH.

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