Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

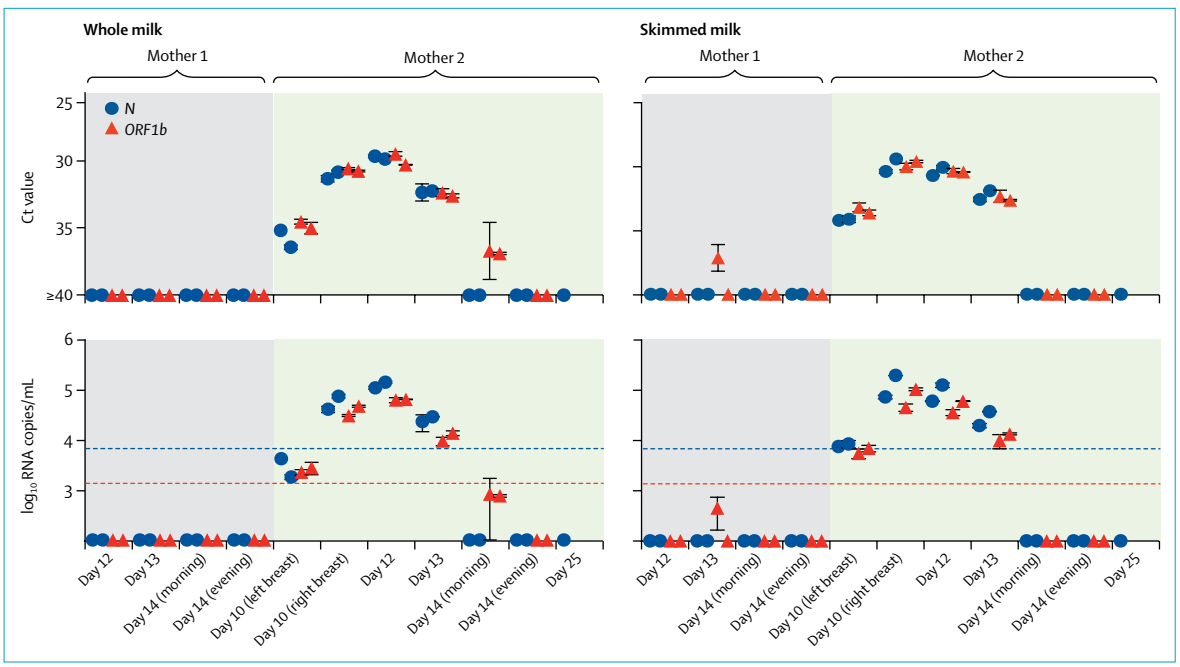

***Figure 2*: Detection of SARS-CoV-2 in breastmilk from an infected mother**
SARS-CoV-2 RNA was isolated from whole and skimmed breastmilk obtained at different timepoints and analysed by RT-qPCR, using primer sets targeting SARS-CoV-2 *N* and *ORF1b* genes. Samples and viral RNA standard were run in duplicates, and isolation and RT-qPCR were repeated in two independent assays. RNA in breastmilk from Mother 2 on day 25 was only isolated once and only analysed by RT-qPCR for SARS-CoV-2 *N*. Symbols at baseline indicate no amplification (or Ct>36·5 and no amplification in one replicate). Blue dashed line denotes quantification threshold for *N* (160 copies per reaction; Ct 34·2) and red dotted line for *ORF1b* (32 copies per reaction; Ct 35·9). Values below these lines but above baseline indicate amplification in both replicates, but no reliable quantification. Values shown represent mean (SD) from duplicates. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. Ct=cycle threshold.

and sterilisation of milk pumps and tubes). However, whether Newborn 2 was infected by breastfeeding or other modes of transmission remains unclear. Further studies of milk samples from lactating women and possible virus transmission via breastfeeding are needed to develop recommendations on whether mothers with COVID-19 should breastfeed.

We declare no competing interests. RG, CC, and JAM contributed equally. This work was supported by the EU's Horizon 2020 research and innovation programme (Fight-nCoV, 101003555 to JM) and the German Research Foundation (CRC 1279 to SS, FK, and JM; and MU 4485/1-1 to JAM)

*Rüdiger Groß, Carina Conzelmann, Janis A Müller, Steffen Stenger, Karin Steinhart, Frank Kirchhoff, *Jan Münch*
jan.muench@uni-ulm.de

Institute of Molecular Virology (RG, CC, JAM, FK, JM) and Institute for Microbiology and Hygiene (SS), Ulm University Medical Center, Ulm 89081, Germany; and Administrative District Heidenheim, Public Health Office, Heidenheim, Germany (KS)

Published **Online** May 25, 2020
https://doi.org/10.1016/S0140-6736(20)31209-5

1 Lackey KA, Pace RM, Williams JE, et al. SARS-CoV-2 and human milk: what is the evidence? *medRxiv* 2020; published online April 20. DOI:10.1101/2020.04.07.20056812 (preprint).
2 Yang N, Che S, Zhang J, et al. Breastfeeding of infants born to mothers with COVID-19: a rapid review. *medRxiv* 2020; published April 19. DOI:10.1101/2020.04.13.20064378 (preprint).
3 Chen L, Li Q, Zheng D, Jiang H, et al. Clinical characteristics of pregnant women with Covid-19 in Wuhan, China. *N Engl J Med* 2020; published April 17. DOI:10.1056/NEJMc2009226.
4 Chu DKW, Pan Y, Cheng SMS, et al. Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia. *Clin Chem* 2020; **66:** 549–55.

COVID-19-associated hyperviscosity: a link between inflammation and thrombophilia?

Reports of thrombotic complications in patients with COVID-19 are increasingly prominent, and these reports include patients receiving therapeutic anticoagulation.[1,2] At our institution, multiple occurrences of anticoagulation failure prompted us to search for alternative aetiologies contributing to refractory hypercoagulability. Here we describe COVID-19-associated hyperviscosity, a potentially severe consequence of infection with severe acute respiratory syndrome coronavirus 2, in 15 patients tested to date. This work was done ethically in accordance with institutional review board approval.

All patients were critically ill with COVID-19 pneumonia and admitted to the medical intensive care unit. 14 patients had acute respiratory distress syndrome requiring intubation, 14 patients were encephalopathic, 12 patients had shock requiring vasopressors, and 11 patients had renal failure requiring continuous renal replacement therapy (CRRT). All patients received anticoagulation according to an institutional protocol based on

data suggesting increased venous thromboembolism rates when D-dimer concentrations exceed 3 µg/mL.[2] Five patients with D-dimer concentrations of 3 µg/mL or higher and known (or highly suspected) thrombosis received therapeutic anticoagulation. Two of the patients received intravenous heparin, and three patients received a direct thrombin inhibitor (argatroban or bivalirudin) because of heparin resistance or concern for heparin-induced thrombocytopenia. Four patients with D-dimer concentrations below 3 µg/mL received low-dose thromboprophylaxis with low-molecular-weight heparin (LMWH) or subcutaneous heparin. Six patients with D-dimer concentrations of 3 µg/mL or more and without known thrombosis received intermediate dosing (ie, subtherapeutic) of LMWH or intravenous heparin.

The 15 patients had plasma viscosity exceeding 95% of normal, as determined by traditional capillary viscometry, ranging from 1·9–4·2 centipoise (cP; normal range 1·4–1·8). Notably, the four patients with plasma viscosity above 3·5 cP had a documented thrombotic complication: one patient had pulmonary embolism, one patient had limb ischaemia and suspected pulmonary embolism, and two patients had CRRT-related clotting. Plasma viscosity and Sequential Organ Failure Assessment scores, a measure of illness severity, were strongly correlated (Pearson's r=0·841, R^2=0·7072, p<0·001; appendix).

Hyperviscosity damages endothelium and is a known risk factor for thrombosis.[3] It can result from increases in cellular components or plasma proteins, such as fibrinogen or immunoglobulin, as seen in Waldenström macroglobulinaemia. Consistent with reports of hyperfibrinogenaemia in patients with COVID-19, our patients had substantially increased fibrinogen concentrations (median 708 mg/dL, range 459–1188; normal reference range 200–393).[4] Further study is needed to evaluate which plasma components, including acute phase proteins such as fibrinogen, contribute to COVID-19-associated hyperviscosity.

Our novel observation might provide an important link between inflammation and coagulopathy in critically ill patients with COVID-19. We are actively exploring any beneficial role of therapeutic plasma exchange, a highly effective treatment for symptomatic hyperviscosity in other conditions such as hypergammaglobulinaemia, in the clinical management of these patients.[5] Finally, any causal relationship between hyperviscosity and thrombotic complications in COVID-19 warrants immediate investigation given the potential to impact clinical care.

We declare no competing interests.

Cheryl L Maier, Alexander D Truong, Sara C Auld, Derek M Polly, Christin-Lauren Tanksley, Alexander Duncan
cheryl.maier@emory.edu

Department of Pathology and Laboratory Medicine, Center for Transfusion and Cellular Therapies, (CLM, AD) and Emory Critical Care Center, Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Department of Medicine (ADT, SCA, C-LT), Emory University School of Medicine, Atlanta, GA30322, USA; and Department of Pharmacy, Emory University Hospital Midtown, Atlanta, GA, USA (DMP)

1 Wichmann D, Sperhake J, Lutgehetmann M. Autopsy findings and venous thromboembolism in patients with COVID-19. *Ann Intern Med* 2020; published online May 6. DOI:10.7326/M20-2003.
2 Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost* 2020; **18:** 1094–99.
3 Gertz M, Kyle R. Hyperviscosity syndrome. *J Intensive Care Med* 1995; **10:** 128.
4 Ranucci M, Ballotta A, Di Dedda U. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. *J Thromb Haemost* 2020; published online April 17. DOI:10.1111/jth.14854.
5 Padmanabhan A, Connelly-Smith L, Aqui N, et al. Guidelines on the use of therapeutic apheresis in clinical practice – evidence-based approach from the Writing Committee of the American Society for Apheresis: the eighth special issue. *J Clin Apher* 2019; **34:** 171.

Caution against corticosteroid-based COVID-19 treatment

Published Online
May 25, 2020
https://doi.org/10.1016/S0140-6736(20)30749-2

In December, 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, Hubei province, China, and COVID-19 has become a threat to global public health.[1]

Use of corticosteroid-based therapy to reduce inflammatory-induced lung injury has been described for patients with severe COVID-19,[2,3] similar to the use of corticosteroids to treat severe acute respiratory syndrome (SARS) during the SARS outbreak in 2003.[4] However, improper use of systemic corticosteroids can increase the risk of osteonecrosis of the femoral head (ONFH).

In a retrospective study of 539 patients with SARS who received corticosteroid therapy,[5] the incidence of steroid-induced ONFH was 24%, and increased incidence of steroid-induced ONFH was associated with total corticosteroid dose and the use of more than one type of corticosteroid. Improper or delayed treatment of steroid-induced ONFH can cause hip pain, claudication, and even disability of the lower limbs.

Overall, we call for caution in the use of corticosteroids for COVID-19 and do not recommend this as a routine treatment. To prevent steroid-induced ONFH, corticosteroids should be considered only for patients undergoing septic shock, or in critical cases.[6,7] Corticosteroids should be minimised in dose and duration, and the use of multiple types should be avoided. We believe that bisphosphonates and vitamin E should be prescribed to patients who are undergoing corticosteroid treatment; anticoagulants, vasodilators, and traditional Chinese medicine could also be considered.[8–10] Close follow-up should be conducted after discharge, with MRI as the best option for early detection of ONFH. Physical therapy

See Online for appendix