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Reply to the letter "Venous sinus thrombosis after the second dose of SARS-CoV-2 vaccine administration" by Mungmunpuntipantip and Wiwanitkit

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Reply to the letter by Mungmunpuntipantip and Wiwanitkit

With want to thank Dr. Mungmunpuntipantip and Prof. Wiwanitkit for their valuable comments [1] regarding the article "Venous sinus thrombosis after the second jab of an mRNA-based SARS-CoV-2 vaccine" [2].

We agree that serum hyperviscosity could be one pathophysiological mechanism to explain the putative increased risk of arterial and venous thrombosis following SARS-CoV-2 vaccinations [3]. Increased serum hyperviscosity after SARS-CoV-2 vaccinations may result from increased titres of neutralising antibodies, from previously applied intravenous immunoglobulins, previous symptomatic or asymptomatic SARS-CoV-2 infections, from hyperbilirubinemia, or from other mechanisms. However, the index patient had not previously received immunoglobulins, had no previous symptomatic COVID-19 infection, and no hyperbilirubinemia. Antibody titres were not measured and a previous asymptomatic SARS-CoV-2 infection cannot be excluded. Previous traumatic brain injury is regarded irrelevant for a VST 15 years later.

We also agree that a causal relation between the vaccination and the venous sinus thrombosis (VST) cannot be definitively established. This is because of a lack of basic knowledge about the effects of SARS-CoV-2 vaccinations on the immune system, the vascular endothelial cells, the coagulation system, on serum viscosity, and on drug metabolism. However, the increasing num-

* Corresponding author at: Postfach 20, 1180 Vienna, Austria. *E-mail address:* fifigs1@yahoo.de ber of patients experiencing thromboembolic events timely to the vaccination, suggests that the vaccination can be causative.

Putative mechanisms other than hyperviscosity responsible for the inclination towards thromboses could be inflammation, endothelitis, hypercoagulability, thrombocyte dysfunction, or generation of antigen–antibody complexes but this has mainly been confirmed only for SARS-CoV-2 infections [4]. There are, however, some indications that complexes consisting of platelet factor-4 (PG4), polyanions, and anti-PF4/polyanion-reactive antibodies are produced by some vaccinees but not by others [5]. The different response may be due to variable genetic conditions of the human leukocyte antigen (HLA) system [5].

Currently unclear remains why some vaccinees experience thrombotic events, whereas others experience bleeding [6] or even thrombosis plus bleeding [7]. One explanation for the bleeding risk is vaccine-induced immune thrombotic thrombocytopenia, which can also manifest as isolated thrombocytopenia or massive headache and is related to the production of platelet activating anti-PF4 IgG antibodies [8].

In summary, SARS-CoV-2 vaccinations are unsafe for some subjects warranting research for those factors responsible for the individually increased risk of adverse reactions to SARS-CoV-2 vaccines.

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JF: design, literature search, discussion, first draft, critical comments

Declaration of Competing Interest

The authors declare that they have no conflicts of interests to this work. We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

Ethical statement and patient's consent

Informed consent was waived because of the retrospective nature of this study.

Consent for publication

The author have consented for publication of this manuscript.

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