

COVID-19 Vaccination with Special Reference to Adenoviral Vectors, Clotting Disorders and Old Age

Letter to the Editor

Compulsory vaccination with new vaccines harbors potential risks due to known and unknown health consequences. On the other hand, vaccination for threatened parts of the population may be recommended if a communicable disease with clinically severe forms occurs and its epidemic spread is to be expected. In the author's opinion, COVID-19 is an overestimated cause of death [1]. When the number of deaths is discussed, the co-morbidity is often disregarded. "Died with COVID-19" is not the same as "died of COVID-19". The economic damage from excessive anti-epidemic measures and lockdowns can damage public health more than SARS-CoV-2 itself. The irrational use of health resources hinders the scheduled patient care. In retrospect, the increase in mortality from various causes will probably be ascribed to COVID-19, and subsequent mortality decrease will be attributed to "successful" anti-epidemic measures including vaccinations. Long-term consequences of vaccinations are largely unknown. It is hardly feasible today to distinguish epidemiologically how many people die from COVID-19, how many "with it" or from medical, economical or social consequences of the pandemic, vaccinations or anti-epidemic measures. The topic is inflated and mixed with politics, which is not necessarily always unfavorable: more order is indicated in our age of overpopulation and mass migrations. However, these problems should be openly addressed [2] instead of using pandemics as a pretext for the tightening of screws. As usual, it is difficult to separate group interests from those of civilization and humanity. The question 'cui bono?' (to whose benefit?) should be tackled to clarify motives behind some COVID-related restrictive policies. In the author's opinion, partly based on the observations inside Russia, the restrictions, supervision and control measures are used to encroach upon civil liberties and to distract people from internal problems such as shortcomings of the healthcare system. Travel restrictions and suppression of individual tourism in the vast country help to conceal voluntarism, corrupt or particularistic policies [3]. The long-term social distancing has detrimental effects on physical and mental health [4], especially of elderly people living with frailty and multimorbidity, contributes to loneliness and depression [5].

Influenza spreads around the world in yearly outbreaks, resulting in millions of cases of severe illness. Presumably, seasonal flu kills 250-500 thousand people yearly, which may be an underestimation [6]. Influenza pandemics resulted in millions of deaths [7,8]. The effectiveness of travel restrictions, quarantines, and contact tracing appears questionable because SARS-CoV-2 is already spreading worldwide like influenza did repeatedly in the past. The spread around the world is putting into question the usefulness of travel bans. Historical data over recent centuries suggest no change in the speed of flu spread despite the proliferation of travel and human



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contacts. The travel restrictions might delay international spread only if instantaneous and 100% effective [7]. Numerous mild and asymptomatic cases will be inevitably missed. In terms of excess years of life lost, because of the mean age (80 years) of COVID-19 fatalities, the current pandemic would presumably score lower or similarly to the 1957 and 1968 influenza pandemics [9].

Statistics about potential side effects of COVID-19 vaccination are of questionable reliability; adverse effects may be missed, ascribed to other causes or obfuscated. Under these circumstances, the role of theoretic argumentation based on pathophysiological and biochemical mechanisms increases. For example, effects of the spike protein (SP) observed in COVID-19 patients can be expected to occur to some extent also after injections of vaccines containing SP (inactivated viral vaccines) or nucleic acids inducing the synthesis of SP by cells. SP can damage vascular endothelial cells by down regulating angiotensin-converting enzyme 2 (ACE2) and consequently inhibiting mitochondrial function [10]. SARS-CoV-2 uses ACE2 as a cellular receptor, which may lead to the ACE2 degradation and angiotensin-II-mediated lung injury in COVID-19 [11]. SP is presented to the immune system inducing immune reactions and binds to ACE2 receptors on platelets activating them [11]. The endothelial damage together with the platelet activation would result in thromboses and thrombocytopenia wholly expressed in the entity known as vaccine-induced thrombotic thrombocytopenia [12]. Of note, D-dimer level is usually high in patients with postvaccinal clotting disorders [12,13]. Thrombosis and thrombocytopenia may be caused not only by SP but also by adenoviral vectors in vaccines [14]. The vectors elicit cellular and humoral immune responses, bind to circulating platelets, inducing their activation and aggregation. There is evidence in favor of synergistic effects of SP and adenoviral vector in vaccines. These mechanisms may explain the comparatively high prevalence of thromboses and thrombocytopenia following application of adenoviral vector-based anti-SARS-CoV-2 vaccines e.g. cerebral and splanchnic vein thrombosis, pulmonary embolism and disseminated intravascular coagulation [14]. Moreover, SP has been shown in vitro to enter cell nuclei and to impair DNA repair [15], which may have far-reaching consequences to be studied in future.

SP binds to T cell receptors thus activating them and enhancing immune responses [16,17]. Endothelial cells laden by SP or other viral antigens would be attacked by the host immune defense. In the brain it may result in vasculitis and perivascular encephalitis. Proven cases of postvaccinal encephalitis after the ChAdOx1 nCoV-19 vaccination with an adenoviral vector have been recorded [18]; but subclinical cases must be more frequent considering headache as a typical postvaccinal symptom. Another concern is vaccine-associated myocarditis, whose potential long-term consequences are understudied [19,20]. The vaccine quality e.g. undeclared components may be a problem in this connection. In addition to the adenovirus vector, vaccines contain various substances of human and viral origin [14]. Officially tested preparations are not necessarily equal to those administered to the broad public. Political pressures for rapid approval of vaccines can result in distribution of products of unstable quality [3]. There have been singular reports from Russia about coagulation-related, cardiovascular and other adverse events after injections of the Gam-COVID-Vac (Sputnik V) and other vaccines [13,21,22]. It should be noted that reliability of the documentation of side effects remains questionable, as it has been the case with some other medical statistics in Russia [21-24]. Apparently, the problem is understudied and underestimated globally.

In conclusion, effects of SP, recorded in COVID-19 patients, can to some extent be present also after injections of vaccines containing SP or inducing its synthesis. In addition, adverse events after vaccination may be caused by adenoviral vectors, other components, admixtures and contaminations in vaccines, which depends on the manufacturing standards. The clotting disorders are of particular importance for elderly patients with comorbidities and restricted mobility as well as for other risk groups for thrombosis [25]. A promising research direction would be experiments in animals and human volunteers using SP preparations or vaccines comparing with controls of average D-dimer levels and other relevant markers.

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