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Addressing the Elephant in the Room: Intravenous Injection of Coronavirus Disease 2019 mRNA

To the Editor—We read with great interest the article by Li et al who found that inadvertent intravenous (IV) injections of coronavirus disease 2019 (COVID-19) messenger RNA (mRNA) vaccines may cause acute myopericarditis in a murine model [1]. Although pertinent, we suggest that their findings be interpreted in the context of certain limitations and weighed against the broader context.

Safety monitoring of the millions of doses of COVID-19 mRNA vaccines administered worldwide has found a generally low incidence of myocarditis among vaccine recipients, at 2 to 4 cases per 100 000 persons [2, 3]. Younger males appear to be at the highest risk of post-vaccination myocarditis [3].

In the present in vivo study, only the IV group showed histopathological changes of myopericarditis, not the group that received the intramuscular BNT162b2 mRNA COVID-19 vaccine. However, it is important to note that the authors administered 0.25 μg of BNT162b2 per gram of body weight to the mice, which is a much larger dose per body weight than would be used in humans. These doses were meant to elicit an immune response similar to that observed in humans [1]; however, reactogenicity and the appearance of vaccine-related adverse events only correlates weakly to immunogenicity [4]. Additionally, it is likely that the same antibody response could be induced with a smaller dose. Walsh et al found that two 20-μg doses of BNT162b2 elicit a similar protective response in those aged 18 to 55 years compared with two 30-μg doses [5]. Given that the average adult weighs an estimated 62 kg [6], the dose administered to mice is thus disproportionately higher. Accordingly, we may expect a much greater inflammatory response, albeit the mechanism for post-vaccination myocarditis remains elusive. Complicating the applicability of the murine model in determining the ideal human dose would be the difficulty in extrapolation due to the size difference and attendant differences in metabolism [7]. The authors could have experimented with a larger range of doses and with more weight-comparable dosing as the focus was on post-vaccination myopericarditis rather than antibody levels per se.

Perhaps out of an abundance of caution, the authors also suggested that aspirating during vaccination may be a possible way to reduce such risks. However, this is not standard practice as the COVID-19 vaccines are routinely injected over the deltoid muscles, which do not have any major blood vessels or nerves nearby. With proper technique and localization, it is unnecessary for aspiration to be performed. There is no evidence that it is effective or that failing to do so causes harm to patients [8, 9].

In this context, although the risks of post-vaccination myocarditis are duly noted, no change is needed to current protocols when vaccinating the population against COVID-19. An abundance of caution with the brief withdrawal of the syringe plunger to exclude blood aspiration is unlikely to yield benefits.

Note

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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