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MAYO CLINIC

Vaccination Safety: Don't Toss the Champagne With the Cork

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Vaccines have formed a rare bright spot in the ongoing COVID-19 pandemic. The rapid and successful deployment of several new vaccines offers a way out of this crisis, now threatened more by vaccine hesitancy than anything else. Unfortunately, recent reports of thromboembolic (TE) events with both adenoviral vector vaccines, cerebral venous sinus thrombus (CVST) with Johnson and Johnson/Janssen (JJ) vaccine, and other clotting concerns with the Oxford AstraZeneca (AZ) may amplify vaccine hesitancy.

The CDC has recommended a "pause" to the roll out of the JJ vaccine to thoroughly investigate a small number of cerebral venous thrombosis (CVT) events (6) in women between the ages of 18 and 48, 6 to 13 days after vaccination.[1] To date, these are the first reported TE complications attributed to the vaccine, despite the administration of nearly 7 million doses. Additional analysis and review also found laboratory work consistent with heparin-induced thrombocytopenia (HIT) in these patients. Details about these events are scarce, as more in-depth review by manufacturers and authorizing agencies to further investigate this suspected association begins.

If these events are as rare as currently reported, this would be consistent with a generally safe vaccine with very rare side effects. However, the larger concern with this pause is that these represent the tip of the iceberg, with more cases or similar pathology going unrecognized. We reviewed the >7000 patients who were vaccinated with the JJ vaccine within the Mayo Clinic for newly recorded thrombotic complications of any kind in the electronic medical record. Although this number is small, if there were a significant risk of thrombotic complications that was going unseen, we may see evidence of unprovoked events. To understand a baseline rate of complications to be expected after a routine vaccination, we also extracted the same set of 30-day new-onset thrombotic complications from all patients who received influenza vaccines from April 1, 2018, to April 1, 2021 (approximately 361,000 patients).

Serious TE events were seen in 7 cases. Five were pulmonary emboli and deep vein thrombosis, and the other 2 were non-CVST thrombotic complications. All these events were in some way provoked and related to an underlying etiology fulfilling the Virchow triad: that is, venous stasis, activation of blood coagulation, and vein damage.

In recent large-scale studies reviewing more than 500,000 COVID-19 infections, the risk of CVST is 39 in 1 million cases, 2 weeks from infection.[2] Compared with this, European agencies have estimated that risk of CVST following the AZ vaccine is approximately 5 per million doses.[2] In our population, the observed rate of all-cause 30-day thrombotic complications was lower than observed in the past 3 years of influenza vaccinations 0.32 (95% confidence interval, 0.17 to 0.69). The influenza data are a crude all-cause thrombosis measure, and although there is likely an artifact related to the small number of JJ vaccines, it is reassuring to see an event rate lower than "background."

In addition, the relative risk of venous thromboembolism with smoking in the general population per various studies is anywhere between 1.3 and 3.3.[3,4] Studies also estimate that the risk of venous thromboembolism in women with current oral contraceptive pill users is 3-fold compared with

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those not exposed to oral contraceptive pills.[5]

Close to 7 million doses of the JJ vaccine have been administered, of which only 6 documented cases of TE events have been observed. Further in-depth review of these cases is needed to ascertain if causality with the administration of vaccine can be established or if these patients had alternative etiologies for having these events. However, if current numbers hold, the risk from the JJ vaccine is lower than oral contraceptives, smoking, and—perhaps most notably—symptomatic COVID-19 infection itself. The single-dose vaccine regimen and less stringent storage requirements make the JJ vaccine a critical tool in the fight against COVID-19. Although stringent monitoring of vaccine safety is critical, we must be careful to not contribute to vaccine hesitancy by conveying impressions of excess risk where it has not been established. More targeted approaches to restricting the vaccine during investigations—such as pausing for women of childbearing age, the only group with any demonstrated risk—would have been more appropriate. Rapid review of any and every adverse event, communication to the public, and return to use of the vaccine is critical to getting back on track.

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