European panel concludes AstraZeneca vaccine is linked to blood clots in rare cases

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The European Medicines Agency (EMA) advisory panel concluded on Wednesday that there is a link between AstraZeneca's COVID-19 vaccine and a rare blood clotting disorder—cerebral venous sinus thrombosis (CVST), blood clots that occur in veins that drain blood from the brain, and splanchnic vein thrombosis (SVT), blood clots that develop in the veins of the liver, spleen, or intestines—that is accompanied with declines in platelet counts. Platelets are an essential blood component whose function is to react to blood vessel injury and bleeding by initiating a blood clot formation.

In their analysis, they reviewed 62 cases of CVST and 24 cases of SVT, of which 18 resulted in death. The statistics were obtained from the European Union drug safety database. These cases occurred among 25 million people who had received the AstraZeneca vaccine. Most occurred in women within two weeks of receiving their first injection. According to the website Center for Infectious Disease Research and Policy, published by the University of Minnesota, the European Union surveillance had received 169 reports of CVST and 53 reports of SVT among 34 million vaccinated individuals.

At the same time as EMA's press conference on AstraZeneca's vaccine was under way, the Medicines and Healthcare Products Regulatory Agency (MHRA), the UK's medicine regulator, announced that their review from last week had found 79 cases of severe blood-clotting complications out of 20 million doses of vaccines that had been administered. Regulators said that 19 patients had died days after having been inoculated. Much work remains to be done to determine the exact etiology of this adverse event, but they hypothesized it is most likely related to the immune system's reaction.

Dr. Jonathan Van-Tam, UK deputy chief medical officer, noted that the propensity for the complication was higher in younger people who have a lower risk of death with COVID-19 than older people. Based on a risk-benefit analysis of young people developing severe COVID-19 versus the small risk of blood clots from the vaccine, the UK health regulators have changed their recommendations that people under 30 should receive alternative vaccines, such as Pfizer or Moderna's COVID-19 vaccines. However, many EU nations such as Germany, France, Italy, Australia and Canada are placing higher age restrictions on the AstraZeneca vaccine.

Emer Cooke, executive director at the EMA, told reporters, "Our review has found that the AstraZeneca vaccine is not associated with an increased risk of overall thromboembolic events or blood clots, but there have been a small number of very rare but very serious clotting disorders which triggered a more focused review." She went on to add, "After a very in-depth review of reported cases of these unusual blood clots, the agency has decided that these should be listed as possible side-effects of the vaccine." The EMA, however, stopped short of recommending placing any limitations on the vaccine for a particular population by their age or gender. As Cooke explained, their review didn't indicate there was "any causal link between the different gender or age groups."

In this regard, Cooke went on to state, "It is very important to highlight when a country makes a decision about vaccination, they do that with the full knowledge of that particular population, of what is available and what the particular risk factors of that population are. The EMA's job is to look at the vaccine and to see whether it is safe and effective and if the benefit outweighs risk."

The chair of the EMA's Pharmacovigilance Risk Assessment Committee (PRAC), Dr. Sabine Straus, supplemented Cooke's remarks by adding, "We have been working around the clock on this review. Our conclusion is that benefit of the AstraZeneca vaccine is far greater than the risks. There is also no evidence of a quality issue with a particular batch of vaccine."

After explaining that the number of overall blood-clotting events after vaccination with the AstraZeneca vaccine is lower than would be expected in the population, she added, "As the vaccine is effective in reducing COVID-19, which itself causes an increased risk of blood clots, it is likely that vaccination will result in an overall reduction of blood clots." She estimated that the overall frequency for the condition is approximately one in 100,000.

They did advise that anyone who has recently received a dose of the AstraZeneca vaccine and develops shortness of breath, chest pains, leg swelling, persistent abdominal pain, severe headaches or blurred vision, or tiny blood spots under the skin at the injection site, occurring from four to 20 days following vaccination, should seek medical attention immediately to

determine if such a rare complication is developing. Though there have been fatalities associated with these rare blood clot events, the reaction is treatable. Mild and local side effects within two or three days from vaccination are expected and common.

Following suit, the COVID-19 subcommittee of the World Health Organization's (WHO) Global Advisory Committee on Vaccine Safety (GACVS) published their statement based on a review of the investigations conducted by the EMA and MHRA. They wrote, "Based on current information, a causal relationship between the vaccine and the occurrence of blood clots with low platelets is considered plausible but is not confirmed. Specialized studies are needed to understand the potential between vaccination and possible risk factors fully."

The WHO said that 200 million doses of the AstraZeneca vaccine had been given so far out of a total of 710 million COVID-19 vaccine doses worldwide. They also pointed to the grim statistics noting that almost 2.9 million people had succumbed to COVID-19 in the 16 months since the first death from the infection was reported.

Dr. Andreas Greinacher from the University of Greifswald's Institute for Immunology and Transfusion Medicine named the rare disorder as vaccine-induced prothrombotic immune thrombocytopenia (low platelet count).

The dominant theory about this rare blood-clotting event is that it resembles a condition known as heparin-induced thrombocytopenia (HIT) but caused by an immune reaction elicited by the vaccine. Heparin is a medication used to prevent or treat blood clots. In rare instances, the drug can cause the immune system to form antibodies against it when bound to a protein called platelet factor 4 (PF4). These antibodies bind to platelets, activating them, which initiates the formation of aberrant blood clots. At the same time, platelet numbers drop, causing thrombocytopenia.

Heparin was first discovered more than 100 years ago. Clinical trials only commenced in the mid-1930s and the drug has been a critical component of the medical armamentarium since. On June 1, 1957, Dr. Roger Weismann and Dr. Richard Tobin presented a report on ten patients at their scientific meeting of the International Society of Angiology in New York. These patients had developed unusual arterial blood clots after having been on heparin therapy. Finally, after platelet measurement counts became routinely performed by the 1970s, the condition's pathogenesis began to be understood.

In a preprint report first posted on March 29, 2021, Greinacher et al. published their investigation of nine cases of rare blood clots from Germany and Austria after receiving the AstraZeneca vaccine. Eight of the patients were female, with a median age of 36, ranging from 22 to 49. Seven patients had CVST, one had a pulmonary embolism, and one had SVT. Four of those who died had also tested strongly for the HIT antibodies leading to their conclusions. What precisely is triggering the formation of this immune-mediated pathway remains to be determined.

Medications have been an essential adjunct in modern medicine to improve people's lives from infections, high blood pressure, blood clots and diabetes, to name just a few. Vaccines have been critical in response to potential pandemic pathogens and community scourges like tuberculosis, typhus, cholera and dysentery. Life expectancy has doubled over the past 200 years, having reached close to 80 in the US. The most significant gains occurred between 1880 and 1920, as implementation of public health measures helped improve control of infectious disease, particularly provisions for more abundant and safer food and water.

Yet, the very same medications that have provided these social gains have been known to cause harm and be fatal to a small subset of people. Severe allergic reactions to antibiotics that may lead to a respiratory arrest are one typical example of this. No one, however, questions the benefits antibiotics have had for society. With regard to the COVID-19 vaccines, the clinical phase three trials found no such safety concerns. It required a vigilant pharmaceutical monitoring program to capture these rare events in the population where millions were being inoculated.

But it is precisely in this context that society's benefits have to be balanced with risks to a tiny minority of people. As the *Guardian* recently noted, "We pay disproportionate attention to rare events precisely because they are exceptional. Politics often exploit that cognitive weakness. Emotion and drama crowd out reflection and reason. That has been the hazard throughout the pandemic."

It becomes imperative that vaccines are not politicized nor commoditized, and communities remain in constant engagement with their health systems to learn more about the nature of these decisions made by their regulatory agencies. However, with the nature of the herd immunity policy and amidst the utter disregard exhibited by governmental and public health officials for the lives of the population, the working class is pitted in an adversarial position with the infrastructure that claims to have its best interest.