

Good afternoon. I'm Commander Ibad Khan, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA Call: Johnson and Johnson Janssen COVID-19 Vaccine and Cerebral Venous Sinus Thrombosis with Thrombocytopenia -- Update for Clinicians on Early Detection and Treatment. Continuing education is not offered for this webinar. Closed captioning will not be available during today's webinar.

A transcript and closed-captioned video will be posted on the COCA Call webpage located at [emergency. CDC.gov/COCA/calls/2021/callinfo underscore 041521](https://emergency.cdc.gov/COCA/calls/2021/callinfo underscore 041521). ASP as soon as possible after today's live session. That web link can also be found at [emergency.cdc.gov](https://emergency.cdc.gov).

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I would now like to welcome our presenters for today's COCA Call. We are pleased to have with us Captain Tom Shimabukuro, a medical officer and the Vaccine Safety Team lead as part of CDC's COVID-19 response. And Lieutenant Commander Sara Oliver, a medical officer and co-lead for the Advisory Committee for Immunization Practices COVID-19 Vaccines Workgroup as part of CDC's COVID-19 response. I would now like to turn it over to Captain Shimabukuro. Captain Shimabukuro, please proceed.

Thanks. I just want to check that you have sound before I began.

Yes, Captain.

Okay, great. Thanks for having me today. It's a pleasure to present to the group. Today I'll be discussing some background on the CVST situation and then move into a description of the reports of cerebral venous sinus thrombosis with thrombocytopenia following the Janssen COVID-19 vaccine. And then I'll summarize our preliminary findings.

Next slide. Next slide. So just some basic information. So, platelets, also called thrombocytes, are colorless blood cells that help blood clot, and a normal platelet count is 150,000 to 450,000 per microliter. Healthcare providers, which most of us usually shorthand that, just say 150 to 450.

Platelets stop bleeding by clumping and forming plugs in blood vessel injuries. And thrombocytopenia is a condition in which you have low blood platelet count, defined as less than 150. Dangerous internal bleeding can occur when your platelet count falls below 10,000 or below 10 platelets per microliter. Though rare, severe thrombocytopenia can cause bleeding into the brain which can be fatal. Next slide.

So, the discussion around this issue or awareness of this issue originated from reports of a rare but serious condition following AstraZeneca's COVID-19 vaccine, and this condition initially recognized was CVST in the presence of thrombocytopenia, so, blood clots in the brain with low platelets. The Europeans have looked into this and have issued several guidance documents both broadly, you know, the European Medicines Agency and also, individual countries have issued documents stating their findings about a possible link between this rare condition and vaccination with AstraZeneca's COVID-19 vaccine. Next slide. So this is a timeline of the Janssen

vaccine. And I just want to -- I should have mentioned on the previous page that the AstraZeneca vaccine is a chimpanzee adenoviral vector vaccine.

The Janssen vaccine is a human adenoviral vector vaccine. So, the Janssen vaccine timeline is as follows. On February 27th, FDA issued an emergency use authorization. The following day ACIP issued interim recommendations for vaccination. A couple days later, those were published in the MMWR and became official.

But vaccination started March 2nd. On March 19th, CDC and FDA received the first CVST with thrombocytopenia case report to VAERS. And these continued to be submitted to VAERS. The latest report for this analytic period was received April 12th. The investigation has continued.

And on April 13th, CDC and FDA recommended a pause in the Janssen vaccine. A HAN was issued, that's health alert notification, issued by CDC notifying healthcare providers of this pause. And our investigation continues. I'll mention that we were on the lookout for these reports based on the situation in Europe. And were actually pre-screening or doing a preprocessing review of these VAERS reports as they came in to the VAERS system and identifying reports suspicious of this condition prior to them going through sort of the routine VAERS report processing process.

And we're doing an expedited collection of records. Sometimes CDC folks actually reaching out directly and almost immediately upon receiving these reports, gathering these records, and doing physician reviews of these records. And also engaging our Clinical Immunization Safety Assessment Project here at CDC to pull in experts in vaccinology and subspecialists in hematology to help with the review of these reports. Next slide. So, this is a screenshot of the CDC health alert that went out.

It went out April 13th. And I think the main messages or one of the main messages in here was that the CDC was going to convene the ACIP, and they did that yesterday to further review these cases and potential implications on vaccine policy. FDA was continuing its investigation. And until the process is complete, CDC and FDA are recommending a pause in the use of the J&J or Janssen COVID-19 vaccine out of an abundance of caution. The purpose of the health alert is in part to ensure that the healthcare provider community is aware of the potential for these adverse events and could provide proper management due to the unique treatment required with this type of blood clot.

And I'll get into that a little in some later slides. Next slide. So, this is a three-dimensional view of the brain demonstrating the venous drainage. And as you know, the brain is a vascular organ and therefore, has extensive venous drainage. And you can see these large sinuses draining sort of into these common areas and providing the drainage system for the brain.

And a cerebral venous sinus thrombosis would be a blood clot in some of these large venous sinus formations here. Next slide. So, I'm going to give you a little background epidemiology on CVST. I do want to mention that this is the epidemiology for CVST in general, not for CVST with thrombocytopenia. That condition, CVST with thrombocytopenia is really a very rare condition nested in a rare condition.

And the epidemiology of that condition, CVST with thrombocytopenia, is not that well understood, certainly not as well understood as CVST in general. But the background epidemiology for this condition is it is rare, around. 22 to 1. 57 per 100,000. It's implicated in about.

5 to 1% of all strokes. It is a disease of younger people. The median age is 37. Although it is not unheard of in older individuals, you see 8% of patients greater than 65. And there is a female to male ratio of three to one.

Risk factors include genetic or acquired prothrombotic conditions, oral contraceptive use, pregnancy and the postpartum period, malignancy, infection and mechanical precipitants. Next slide. So, the more common

presentations are isolated intracranial hypertension syndrome, includes headache with or without vomiting, papilledema, and visual problems, focal syndrome, and encephalopathy. More rare presentations include cavernous sinus syndrome, subarachnoid hemorrhage and cranial nerve palsies. Next slide.

Next slide. So the system we use to capture the data for this presentation is the Vaccine Adverse Event reporting System, otherwise known as VAERS, more commonly by its acronym VAERS is a spontaneous reporting or passive surveillance system that is managed by CDC and FDA. And as a passive surveillance system, VAERS depends on individuals to send reports to CDC. And anyone can report to VAERS -- patients, parents, caregivers, healthcare providers. Manufacturers are required to report to VAERS.

And certainly, for rare serious conditions like CVST, we really do depend on astute healthcare providers to recognize these potential adverse events and promptly report to VAERS. Healthcare providers are our partners in vaccine safety monitoring, especially during times like this, where we have a national immunization program where we're vaccinating large numbers of individuals rapidly. We really do depend on our partners out there on the front lines to recognize potential vaccine adverse events and to report those to VAERS. Now, VAERS is designed specifically to rapidly detect rare, serious adverse events that might indicate a safety problem. As a spontaneous reporting system, it's not designed to assess causality, but it is designed to detect safety signals.

And in this case, I think this is a great demonstration of the robustness of VAERS, the robustness of the US vaccine safety monitoring system, that we were able to rapidly detect a concerning number of these reports early on and rapidly assess the signal. And that's to say that VAERS performed exactly as intended, and the US vaccine safety surveillance system performed exactly as intended. We were able to quickly detect this problem, assess it, and now we're in the process of doing a more refined assessment to provide the necessary data to CDC and to FDA and to the Advisory Committee on Immunization Practices to make evidence-based recommendations. Next slide. So, this is just an overview of the reports -- a high-level overview of the reports for the three authorized COVID-19 vaccines.

And starting off with Janssen vaccine. So, during this analytic period, we have detected six reports -- we've confirmed six reports of CVST with thrombocytopenia following 6.86 million doses administered. This is a reporting rate of 87 cases per million doses administered.

In contrast, for the Pfizer BioNTech vaccine, there have been zero reports following 97.9 million doses administered. And for the Moderna vaccine, three reports following 84.7 million doses administered. However, all three of those reports after the Moderna vaccine had normal platelet counts.

So essentially, after about 180-plus million doses administered of the mRNA vaccines, we have no reports of this rare condition CVST with thrombocytopenia. And after about 6.9 million doses of Janssen, we have six reports. We consider this an imbalance in reporting rate for this condition for these vaccines. Next slide.

And as such, I'm going to focus on the Janssen reports for the rest of this presentation. Next slide. So, here's some of the general characteristics of the CVST with thrombocytopenia reports after Janssen vaccine. The median age is 33, ranging from 18 to 48. Median time from symptom onset was eight days, ranging from six to 13 days.

So, about these tend to become symptomatic around one to two weeks after vaccination. All cases occurred in white females. In one case, the woman was taking estrogen and progesterone. There were no pregnant or postpartum women. And then you see some of the other preexisting conditions there.

I just want to note, with respect to these cases, thrombosis usually does not occur in the presence of low platelets. So, these case presentations are atypical, and they were consistent with cases observed after

AstraZeneca COVID-19 vaccine. Next slide. So here are some of the initial and late signs and symptoms. They're numbered patient one through six, but they're listed in no particular order.

So, the initial features largely included some general and nonspecific symptoms, but most importantly, headache. Headache is most common initial presenting symptom. You see in one patient there was back pain and bruising. I think what's important here is that, given the situation we're in, it's important that healthcare providers maintain a high index of suspicion when individuals show up and there is a history of Janssen COVID-19 vaccination. If you look at some of these symptoms, headache, lethargy, and some GI symptoms, chills, myalgias, you know, these are pretty common in patients seeking healthcare.

And unless you maintain that level of suspicion, it's possible that some of these patients may be sent home. In fact, that's what has happened in some cases. And then you see on the right-hand side, there are some of the later features which are a little more focal and tend to be more severe. Next slide. So, I apologize that this table is in a different orientation.

But I think this orientation highlights the important part of this -- important part of this table a little more clearly. And I want you to focus on the bottom right-hand side of the slide where I have circled in red some of these locations of other thromboses. I just think it's important to note that in three out of these six patients, there was clotting in other large vessels -- the portal vein, the pulmonary artery, bilateral lower extremity BTE's, right, internal jugular vein and portal vein. So, this syndrome appears to be a problem with clotting in general in the presence of thrombocytopenia. CVST is what I think brought these to our attention.

But clearly there are other clotting issues going on, at least in some of these patients. And as a result, as we further refine our investigation, I think we are going to broaden what we're looking for to include clotting in other large vessels, not just limited to the cerebral venous sinuses. Next slide. I show you this slide just to show SARS-CoV-2 testing history. COVID-19 disease has been implicated in clotting problems and thrombotic events.

But if you look at the testing here, it's fairly unremarkable in this case series of patients. None of these individuals was actively infected. And where testing was done for serology, it was negative in three out of the six. The other three weren't tested, or weren't documented, at least. Next slide.

Here's the hematology test results among the case patients. All had thrombocytopenia, and many of them had severe thrombocytopenia, so less than 50 platelets. And five out of the six had platelet factor four heparin-induced thrombocytopenia antibody testing done. And in all five where testing was done, it was positive. Next slide.

So, here's some of the treatment and outcomes of these patients. Four of the patient's got heparin, and that's problematic. And I'll explain that a little bit later. Five got non-heparin anticoagulants. Many of these were switched to these non-heparin anticoagulants after recognition of what was going on.

Three got platelets, three got IVIG. There was one death. Three of these cases at the time of this analysis remained hospitalized to an intensive care and two had been discharged home. Next slide. So, in order to put what we are observing into context for what we would expect, we did a quick and I'll say relatively crude observe versus suspected analysis.

And I'll just walk you through how we came to our numbers. First thing we wanted to do was get a handle on the estimated annual incidence of CVST. And again, this estimated annual incidence is based on CVST in general, because that's where we have the data. CVST with thrombocytopenia, again, is a rare condition on top of a rare condition, and there's really limited data available on the incidence of that specific condition. But for CVST, our estimates range from about.

5 to 2 cases per 100,000 population. We assume a risk period of 5.6% of a calendar year. We arrived at that based on assuming that vaccination began on March 2nd, which it did, and then ran through the analytic period, that's 41 days. We make the assumption -- we didn't know at the time when these individuals were vaccinated.

So, we made the assumption they came in halfway through the period. That is the days follow up. And then we have to divide that by 365, because they're not being followed up for a full calendar year. Then we look at the doses administered in the risk group that we identified, which is women 20 to 50 years, and that's about 1.4 million doses.

And then, on the table below, we're basically, breaking the estimates of background incidence into chunks. 5, 1, 1.5 and 2 per 100,000. We know what the observed is, that's the six cases. The expected observed -- the expected counts are based on the calculations I just explained above.

And then you just do the arithmetic and you come up with a reporting ratio. And that ratio, depending on what you assume the background incidence, is ranges from 3.8-fold increase up to a 15.4-fold increase. Next slide.

Next slide. So just to sum things up, CVST is rare, but clinically serious and can result in substantial morbidity and mortality. It's not usually associated with thrombocytopenia. The observed cases following Janssen COVID-19 vaccine appear to exceed expected based on background rates of CVST among women aged 20 to 50 years, threefold or greater, as I just showed on the previous slide. All six of these reports are in women aged 18 to 48, all with thrombocytopenia, and there are no obvious patterns of risk factors detected.

CVST with thrombocytopenia has not been observed after the two authorized mRNA vaccines, so, 182 million doses of these mRNA vaccines administered with no reported cases to date. The clinical features of the Janssen cases are similar to those observed following the AstraZeneca COVID-19 vaccine in Europe. And both Janssen and AstraZeneca vaccines contain replication and competent adeno viral vectors -- a human for Janssen and a chimpanzee for AstraZeneca. Next slide. This is copied straight out of the CDC health alert notice.

And I think the important points are this, what I mentioned before, clinicians should maintain a high index of suspicion and do not treat patients with thrombotic events and thrombocytopenia following receipt of Janssen COVID-19 vaccine with heparin unless HIT testing is negative. Next slide. And for our public health partners, we encourage healthcare -- please encourage healthcare providers and the public to report all serious and life-threatening adverse events and deaths to VAERS as required under the EUA's. And for the public, if you ever received the Janssen COVID-19 vaccine and develop a severe headache or other symptoms, please seek healthcare. Next slide.

And I want to finish up by emphasizing the importance of reporting to VAERS. And here's some information on how to report to VAERS. Again, healthcare providers out there seeing patients, out there treating patients, out there on the front lines are our partners in vaccine safety monitoring. We depend on you. We depend on astute healthcare providers to recognize possible adverse events and to report those to VAERS.

I want to reinforce that for serious adverse events, you will likely be contacted by VAERS or by CDC to request medical records. And I want to reassure you that HIPAA permits reporting of protected health information, so, of providing medical records to CDC, to VAERS, providing this information to public health authorities, including CDC and FDA. There are no HIPAA issues with providing this information to CDC, and we appreciate your cooperation and we appreciate the prompt reporting that we have received of these medical records when requested throughout the pandemic. Next slide. So, some next steps.

We're going to continue our enhanced monitoring VAERS and other vaccine safety monitoring systems like the Vaccine Safety Datalink. Just to note, in our Vaccine Safety Datalink, we've had relatively small number of Janssen doses administered, but zero cases of CVSD so far. We'll investigate potential cases through detailed

clinical reviews and chart reviews. And we'll better refine -- and we'll refine analyses to better quantify risks. The observed versus expected I showed you made a lot of assumptions.

We're working on a more a more robust analysis where we have individual level data on when people got vaccinated so we can calculate our numerators in our follow up time a little bit better, so there'll be better information coming on that particular analysis. Next slide. I just want to acknowledge the contributions of the investigators from the following organizations. And with that, I'll turn it over to my colleague, Dr. Sara Oliver.

Great. Thanks, Dr. Shimabukuro. I am happy to go over similar events but with a focus on the vaccine policy aspects of it. Next slide.

But again, just to back up slightly and talk about these adenovirus vector vaccines -- there are two adenovirus vector vaccines used either in the US or in Europe, the Janssen Johnson & Johnson vaccine and AstraZeneca vaccine. Dr. Shimabukuro briefly went over some of this, but the Janssen vaccine is one dose, uses a human adenovirus 26 vector. An EUA was issued in the US in February of 2021. And the EMA has authorized this for Europe, but doses have not yet been delivered or administered.

The AstraZeneca vaccine is two doses, a chimp adenovirus vector, and has a waiting EUA application in the US, but it is approved and has been in use in the UK and Europe. Clots seen after both of these COVID ad vector vaccines, the clinical syndrome seen after both vaccines appear similar. However, we're still learning the extent to which these cases represent the same syndrome. Next slide. So last week, the European Medicines Agency or the EMA released a report that concluded a strong association and probable causal link between the AstraZeneca vaccine and rare clotting events.

In the EU, they had 62 cases of CVST and 24 cases of splenic vein thrombosis both with thrombocytopenia, and 18 of those were fatal. Most -- [ Inaudible ] However, due to different ways the vaccine has been used in each country, they can't draw specific conclusions on age or gender as risk factors. From the US -- I mean, from the UK, there were 79 cases of thrombosis and thrombocytopenia. 19 were fatal. 44 were CVST.

35 were other clotting events. 51 were male and 28 were female. They estimate the risk at 4 per million, but acknowledge that it's slightly higher in younger age groups, and a specific rate wasn't supplied. Next slide. There were two papers released in the New England Journal of Medicine earlier this week that both described case series with clinical and lab findings of these thrombocytopenic thrombotic events after the AstraZeneca vaccine, one from Germany and Austria, one from Norway.

Many had platelet activating antibodies directed against this platelet factor four. And again, it's a phenomenon that looks like HIT or heparin induced thrombocytopenia, but these individuals had not received heparin prior to developing clots. So, the authors of these papers propose a new syndrome entitled vaccine induced immune thrombotic thrombocytopenia or VITT as the name of this emerging syndrome. Next slide. So, the EMA Safety Committee does not make vaccine policy for the EU, and each country has to weigh the risks and benefits individually.

Many countries have adopted an age-based recommendation for the AstraZeneca vaccine, and they're listed here. Next slide. So next, moving to the policy discussions over the past week regarding the specific issues with the Janssen COVID-19 vaccine, both discussed in the workgroup and then yesterday at the ACIP meeting. This included the risk benefit balance, which evaluated the review of this CVST cases, risk of COVID disease by age and sex, COVID-19 vaccines administered, Janssen doses administered to date, projected supply of COVID-19 vaccines. And then policy options were discussed for use of the Janssen vaccine, which we'll walk through as well.

Next slide. So, the workgroup reviewed the six cases of CVST reported to VAERS that were just described all among women 18 to 48 years of age, with an interval of vaccine receipt to symptom onset ranging from six to 13 days. There was also a case of CVST reported in the Janssen phase three trial in a 25-year-old male. He developed symptoms nine days after vaccination, and on day 21 was diagnosed with the CVST and ultimately found to be anti-PF-4 positive as well. Next slide.

So next, just briefly walking through overall COVID epi. It's difficult because the exact risk factors for CVST are unknown. So, we can't highlight the epi among the specific population only at risk for CVST. But we can discuss the epi by sex and by age. This slide shows COVID cases and deaths by age -- I mean, by sex.

Overall, females represent a slightly higher proportion of overall cases on the left in blue, and a slightly smaller proportion of COVID deaths on the right in red. Next slide. And this slide shows COVID cases and deaths by age group. The bars in blue on the left show percent of cases by age. You can see that the younger population represents a higher proportion of COVID cases relative to the percent of the US population shown in gray.

However, on the right in red, we see deaths by age group. And as we're all familiar with these days, the oldest population represents a substantial portion of deaths from COVID relative to the younger populations. Next slide. So, then if we move to overall COVID vaccination coverage by age, you can see here that among the oldest population, those 65 years of age and older, nearly 80% of that population has received at least one dose. 40 to 50% of adults age 60 to 64 years of age have received at least one dose.

And then 25 to 30% of those 18 to 39 years of age have received at least one dose of a COVID vaccine. So, this highlights the proportion of the population who has yet to be vaccinated with any COVID vaccine. Next slide. To date, there have been over 7.2 million doses of the Janssen vaccine administered to date.

And if we limit the population to females 18 to 50 years of age, there have been approximately 1.5 million doses to date. Next slide. However, there's another way to think through the doses that have been administered. From currently available data, thrombocytopenic thrombotic events developed six to 13 days after vaccine received.

And we know there's around 7.2 million doses administered. So, if we think through those doses from the beginning of the program, the Janssen vaccination program -- so early in March through March 30th, there were 3.4 million doses for 48% of all doses administered. With a risk window of up to two weeks after the dose administered, it's likely that if these vaccine recipients were to develop thrombocytopenic thrombotic events post-vaccine, they likely would have already occurred.

However, if you think through the doses administered within the last two weeks from March 30th through April 13th, 3.7 million doses have been administered, or 52% of the doses overall have been given within these last two weeks. Therefore, the thrombocytopenic thrombotic events post-vaccine may still occur after these doses as they still remain within that risk window. Next slide. So just to summarize what we know so far, thrombocytopenic thrombotic events have occurred after the AstraZeneca vaccine.

In the US, we've seen six cases reported to VAERS of CVST and thrombocytopenia after receipt of a Janssen vaccine. No cases of CVST with thrombocytopenia have been reported after receipt of either Pfizer or Moderna vaccines. These cases have occurred primarily in younger adults and females. We know that CVST can be clinically devastating or fatal. And then it's also worth highlighting that in the US, alternative COVID-19 vaccines, the mRNA vaccines are available.

Based on current projections, the supply of both mRNA vaccines are expected to be fairly stable in the near future. Therefore, the choice may not be receipt of a Janssen vaccine versus remaining at risk for COVID. The decision may be receipt of the Janssen vaccine, or receipt of an mRNA vaccine. Next slide. However, we need to highlight what we don't know so far.

We don't know the true background incidents of CVST with thrombocytopenia. We don't know specific risk factors for these thrombocytopenic thrombotic events. We don't know the incidence of other thrombotic, so non-CVST cases with thrombocytopenia, after the Janssen vaccine. We don't know the ability to compare or generalize thrombotic cases after the AstraZeneca vaccine to the Janssen vaccine. And we don't know the true incidence of these thrombocytopenic thrombotic events and CVST after a J&J vaccine, as more cases may be identified in the coming days to weeks.

Next slide. So now just to highlight the policy options that were discussed yesterday by ACIP. Next slide. There were several overall discussion points that were highlighted when discussing the policy. First, that the reported CVST cases are rare.

But once limited to doses administered to the age and sex of CVST cases seen, the observed cases exceeded the expected cases. Given the timing of doses administered, additional cases may still be identified. But an emphasis that robust safety surveillance is critical. The fact that we've had these discussions so quickly after these cases were identified demonstrate that signal detection and evaluation of these cases occurred as planned, moving to public discussions of the safety issues and policy implications as soon as possible. Next slide.

So there really is a spectrum of policy options for the Janssen vaccine. ACIP has and will continue to discuss the entire spectrum of policy options with a full risk benefit assessment. So ACIP could decide that the risks outweigh the benefits and vote to not recommend use of the Janssen vaccine due to these safety concerns in any population. ACIP could decide that the benefits outweigh the risks overall, and recommend the use of the vaccine in all adults 18 years of age and older. However, there's an option in the middle of the spectrum as well, which could involve recommending use of the Janssen vaccine in some populations with potentially age or gender specific recommendations, such as adults 50 years of age and older or males only possibly.

Next slide. So, to walk through what is overall and recap what has happened so far this week on this issue, on Monday, the Vaccine Safety Technical Group met to discuss the safety signal identified. Tuesday, the ACIP COVID Vaccines Workgroup met to discuss these issues and policy options. And Wednesday, yesterday, we had the emergency ACIP meeting. And so, the purpose was to consider the implications of reported cases of thrombosis and thrombocytopenia after a Janssen vaccine on vaccination policy.

I'm sure some people were able to join the call yesterday, but what happened in summary yesterday was that ACIP had a thoughtful discussion of the data presented and heard from a variety of stakeholders on this issue. Ultimately, the committee agreed that more information is needed before a decision on vaccine policy could be made, and that CDC will collect additional information and convene another ACIP meeting as soon as possible within the next two weeks. During this time, CDC and FDA will continue to identify and evaluate any cases within the risk window, identify and evaluate any past cases that may come to light because of the recent notifications around this. We call this stimulated reporting. Formulate more precise data around observed versus expected rates, including for specific demographic populations.

And undergo a formal risk benefit analysis. Then this will be brought back before ACIP for additional discussion as soon as possible. Again, planning for that to occur within the next one to two weeks. Next slide. So, Dr.

Shimabukuro highlighted this, but I just want to end on these important notes from the HAN. As this is a clinician-focused call, so for diagnosis and treatment if there is concern that a patient could have CVST after receipt of the Janssen vaccine, evaluating the patient with the screening PS-4, ELISA assay, also known as the HIT assay, and consider consultation with a hematologist. And do not treat with heparin, unless the HIT testing is negative. In addition, what we've learned to date is that these patients are presented with thrombocytopenia. So, a screening CVC could also be informative to assess the likelihood that the patient has a specific thrombocytopenic thrombotic event.



And as always, if a case is detected, please report to VAERS. Next slide. I think that's my last slide. So, Dr. Khan, I'll turn it back over to you.

I'm happy to answer questions.

Thank you very much, presenters, for providing our audience with such beneficial information. We will now go into our Q&A session. Audience, please remember, you may submit questions through the webinar system by clicking the Q&A button at the bottom of your screen and then typing your question. Also, please understand that we receive hundreds if not more than 1,000 questions during some of these Q&A sessions. So, we simply cannot answer every question.

However, we will answer as many questions as we can during this part of the call. So, starting with our first question, we have in fact a couple of questions related to patients receiving dialysis. And the questions ask, should heparin be avoided in dialysis patients who have had the Johnson and Johnson vaccine? And should platelet counts be followed prospectively in dialysis patients who have received the Johnson & Johnson vaccine?

This is Dr. Oliver. I'm happy to attempt to take a stab at this and see if Dr. Shimabukuro has anything else to add. So ultimately, we would say we're not proactively saying everybody who has had a J&J vaccine, has had the Janssen vaccine needs to start getting serial CVC's or anything like that.

It's more if somebody presents for medical care with a concerning symptom, that is a test that could be done. In addition, the concern around heparin is, you know, once the clot has been identified, could the heparin make it worse if they have developed this condition? If there are specific concerns about the anticoagulation treatment for any specific patient, though, I would absolutely recommend consultation with a hematologist and additional discussions on that particular individual for what would be best for that. Dr. Shimabukuro, do you have anything else to add?

I agree. I don't have anything to add to that. Thanks.

Okay.

Thank you very much. Our next question asks, during the reviewing of the data that you received, did you notice any correlation with vaccine lots when it comes to these patients?

We did not. Keep in mind there are only six cases. So, it's hard to draw any conclusions about an N of six, but we did not observe any issues with any particular lot.

Thank you very much. Another question we received is when characterizing the headaches as a symptom that you mentioned, did the patients describe the headaches similar to what patients describe when experiencing an aneurysm or something similar?

I don't have the specifics of the narratives that were given either in the report of the medical record. But the initial -- from my understanding, talking to the reviewers, the initial presentation or the initial symptoms were not particularly notable. They were somewhat, you know, nonspecific headache and fatigue and just feeling unwell. But nothing that would really just stand out to make you think that, at least initially, that there was anything unique or special going on.

Great, thank you. Next question asks, can you elaborate what role can V-safe play in reporting an intervention?

So, V-safe is primarily a relationship between the V-safe system and the individual patient. And during the first week after vaccination, we do daily check ins, and we're asking -- we're soliciting symptoms. So, individuals will through an electronic survey report symptoms back to us. The value for V-safe in detecting clinically serious adverse events following vaccination is if a person does seek medical care, that information is transmitted to our

VAERS program, and VAERS would follow up to take a report. But as far as just the basic V-safe reporting, the V-safe process, it's probably less effective in monitoring these types of events.

Keep in mind these are very serious events. These people wind up in the hospital in the intensive care unit. And V-safe depends on people sending information to CDC. In that situation, we think it's unlikely that a person would be able to actually send this type of information. But again, if a person does report seeking medical care, we would reach out to that person and make an assessment.

Thank you, sir. Another question we received is, are you aware of any other adenovirus vector vaccines with similar adverse events?

So, there are other adenovirus viral vector vaccines, I believe. At least one of the Ebola vaccines is an adenovirus viral vector vaccine. Maybe Dr. Oliver can confirm that. Is that correct?

Yes, there's an ad-26 Ebola vaccine.

So, my understanding is these events were not observed after that vaccine, but that vaccine is not as widely used as the AstraZeneca vaccine and as the Janssen vaccine, I think maybe the use was on the order of hundreds of thousands. Here, you've got millions to tens of millions of doses. So, it's not necessarily surprising that you wouldn't have picked up these rare adverse events when the doses administered are not that great.

Thank you very much. Our next question asks, should patients who have had the Johnson and Johnson vaccine have any blood tests drawn prophylactically? And if not, are there any other proactive steps that they can take?

This is Dr. Oliver. Yeah. So, we're not recommending any proactive prophylactic, you know, treatment or monitoring of CVCs. Again, if a patient develops or presents for medical care, because they're concerned that, you know, they have some symptoms, then I think CVC can be part of that initial evaluation.

But we're not recommending that otherwise people who feel totally healthy and are fine have, you know, serial monitoring of CVCs or -- you know, I saw in the chat people asking about taking aspirin or anything like that. We're not recommending that at this time. Tom, anything else to add to that?

No, I agree.

Thank you very much. Next question asks, were there any instances of orbital edema observed in any of the patients?

I'm not aware of that that was a sign in any of the case reports that we became aware of.

And a question I have from the audience is, can you elaborate on how long after receiving the vaccine these events took place for the various patients?

This is Tom. Let me find my -- I want to make sure I give you the right information. So, the median time to symptom onset was eight days, and it ranged from six to 13 days. So, I will caveat that by saying that determining symptom onset is part art, part science, and often involves the judgment of the person reviewing the records. Some of these symptoms can be somewhat insidious in onset.

But our review, and it's a detailed review of these reports and these medical records, leads us to believe that these cases occur within about one to two weeks. Or become symptomatic within about one to two weeks.

Thank you so much. Another question asks, have the CDC been able to draw any conclusions yet from any such cases from Johnson and Johnson's trial data?

There was one case from the clinical trials that was a male. Certainly, now one case in a clinical trial, does not definitively -- would not allow you to conclude that there is a safety problem. But there was one case observed. And because there were similar cases being observed in the post-authorization surveillance after AstraZeneca, and they both use adenovirus viral vectors, we were certainly looking for this. And so, we were doing enhanced monitoring in the United States during the post authorization.

So, I would say that the clinical trial data for the Johnson vaccine in combination with what was being observed following the AstraZeneca vaccine, and the fact that these are similar vaccine platforms, had us monitoring closely for this condition.

Thank you very much. Next question asks, do you have any advice for oncology patients that are on drugs which normally decrease their platelets?

I would say that any decisions about kind of treatments or anticoagulation should absolutely be made with people taking care of the patient, recommending consultation with a hematologist. I can say that we have been made aware that the American Society of Hematology will be releasing a resource on what we're seeing, this kind of thrombotic thrombocytopenic event within the next day or so. And we're happy to provide the link to where those will be posted. So that website link can be provided in the additional resources to the COCA Call. So, we can link to that.

I don't know that they'll specifically address oncology patients. But I know that we're partnering with other professional organizations that potentially can speak much more to kind of detailed treatment recommendations than we are able to.

Thank you, Dr. Oliver. And for our audience, to be able to find that resource that Dr. Oliver was referring to, please direct your browser to emergency. CDC.

gov/COCA and find this COCA Call's webpage and you will find that resource listed under additional resources. We will be posting it shortly. So, it might be an hour or two after the COCA Call where you will be able to find that resource. We have time for one last question. And the question is, since this is such a rapidly evolving situation and novel adverse event that's developing, what can clinicians do to get more information as things develop and evolve? And what would be the next steps that they should keep an eye out for?

So, this is Tom. And I will say we are committed to providing vaccine safety information in as timely and transparent a manner as possible. I know that the ACIP will be meeting on a more frequent schedule specifically to get updated information on the situation. The ACIP meetings are public and anyone can attend. And we will also -- CDC will also be, you know, making information available through its normal ways, whether that's online postings or conducting briefings such as this one.

We want to make sure that people get the most updated information that we have available in the most transparent manner as possible.

Thank you very much. I would like to thank everyone for joining us today with a special thanks to our presenters. Today's COCA Call will be available on demand a few hours after the live call. You can find the video recording of today's call at emergency. CDC.

gov/COCA. You will also be able to find those additional resources that Lieutenant Commander Oliver was referring to. Continue to visit emergency. CDC. gov/COCA to get more details about this COCA Call and other upcoming COCA Calls.

And please share the call announcements you receive with your clinical colleagues. You can also sign up to receive weekly COVID-19 science updates by visiting the link listed here in the slides. And you can also find this link in the slides posted at [emergency. CDC. gov/COCA](https://emergency.cdc.gov/COCA).

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Again, thank you for joining us for today's COCA Call and have a great day. .