Johnson & Johnson/Janssen COVID-19 Vaccine and Cerebral Venous Sinus Thrombosis with Thrombocytopenia – Update for Clinicians on Early Detection and Treatment

Clinician Outreach and Communication Activity (COCA) Webinar

Thursday, April 15, 2021

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- All participants joining us today are in listen-only mode.
- Using the Webinar System
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Today's Presenters

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  Centers for Disease Control and Prevention

Reports of cerebral venous sinus thrombosis with thrombocytopenia after Janssen COVID-19 vaccine

Clinician Outreach and Communication Activity (COCA)
April 15, 2021

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Vaccine Safety Team

Disclaimer

- The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC) or the U.S. Food and Drug Administration (FDA).
- Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC or FDA.

Topics

- Background
- Reports of cerebral venous sinus thrombosis (CVST) with thrombocytopenia (low platelets) following Janssen COVID-19 vaccine
- Summary

Background

Platelets and thrombocytopenia (low platelets)*

- Platelets (thrombocytes) are colorless blood cells that help blood clot; normal platelet count is 150,000–450,000 per microliter
- Platelets stop bleeding by clumping and forming plugs in blood vessel injuries
- Thrombocytopenia is a condition in which you have a low blood platelet count (<150,000 per microliter)
- Dangerous internal bleeding can occur when your platelet count falls below 10,000 platelets per microliter
- Though rare, severe thrombocytopenia can cause bleeding into the brain, which can be fatal

* Source: https://www.mayoclinic.org/diseases-conditions/thrombocytopenia/symptoms-causes/syc-20378293

AstraZeneca's COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots with low blood platelets

News 07/04/2021

EMA confirms overall benefit-risk remains positive

EMA's safety committee (PRAC) has concluded today that unusual blood clots with low blood platelets should be listed as very rare side effects of Vaxzevria (formerly COVID-19 Vaccine AstraZeneca).

In reaching its conclusion, the committee took into consideration all currently available evidence, including the advice from an ad hoc expert group.

EMA is reminding healthcare professionals and people receiving the vaccine to remain aware of the possibility of very rare cases of blood clots combined with low levels of blood platelets occurring within 2 weeks of vaccination. So far, most of the cases reported have occurred in women under 60 years of age within 2 weeks of vaccination. Based on the currently available evidence, specific risk factors have not been confirmed.

People who have received the vaccine should seek medical assistance immediately if they develop symptoms of this combination of blood clots and low blood platelets (see below).

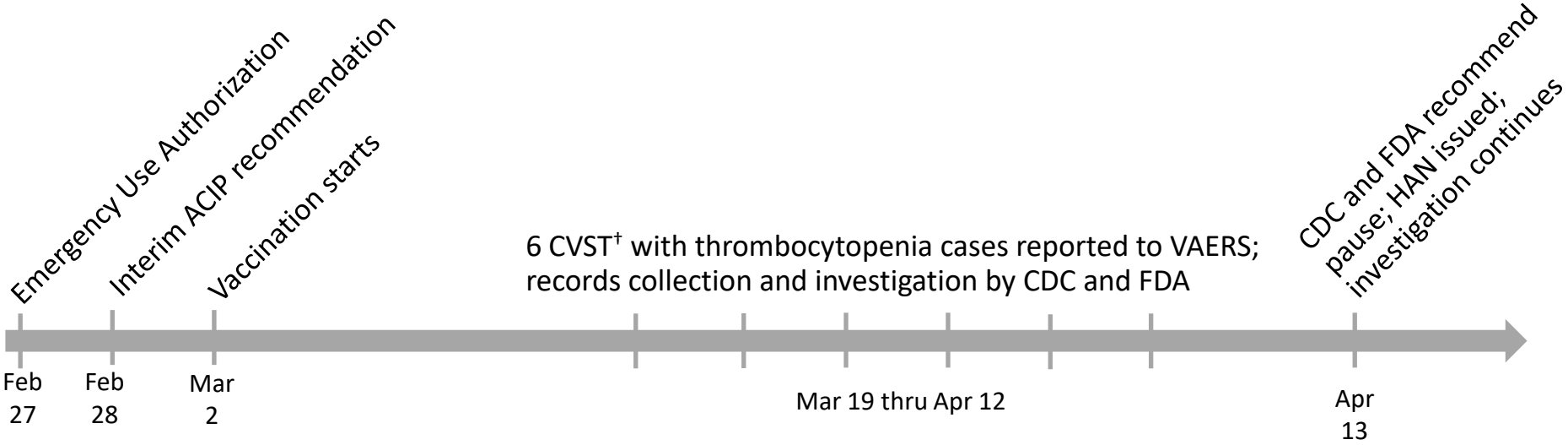
The PRAC noted that the blood clots occurred in veins in the brain (cerebral venous sinus thrombosis, CVST) and the abdomen (splanchnic vein thrombosis) and in arteries, together with low levels of blood platelets and sometimes bleeding.

The Committee carried out an in-depth review of 62 cases of cerebral venous sinus thrombosis and 24 cases of splanchnic vein thrombosis reported in the EU drug safety database (EudraVigilance) as of 22 March 2021, 18 of which were fatal.[1] The cases came mainly from spontaneous reporting systems of the EEA and the UK, where around 25 million people had received the vaccine.

COVID-19 is associated with a risk of hospitalisation and death. The reported combination of blood clots and low blood platelets is very rare, and the overall benefits of the vaccine in preventing COVID-19 outweigh the risks of side effects.

https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood

Janssen COVID-19 vaccine timeline* (2021)



* For illustrative purposes, not drawn to scale, † cerebral venous sinus thrombosis

This is an official

CDC HEALTH ALERT

Distributed via the CDC Health Alert Network
April 13, 2021, 1:00 PM ET
CDCHAN-00442

Cases of Cerebral Venous Sinus Thrombosis with Thrombocytopenia after Receipt of the Johnson & Johnson COVID-19 Vaccine

Summary
As of April 12, 2021, approximately 6.85 million doses of the Johnson & Johnson (J&J) COVID-19 vaccine (Janssen) have been administered in the United States. The Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA) are reviewing data involving six U.S. cases of a rare type of blood clot in individuals after receiving the J&J COVID-19 vaccine that were reported to the Vaccine Adverse Events Reporting System (VAERS). In these cases, a type of blood clot called cerebral venous sinus thrombosis (CVST) was seen in combination with low levels of blood platelets (thrombocytopenia). All six cases occurred among women aged 18–48 years. The interval from vaccine receipt to symptom onset ranged from 6–13 days. One patient died. Providers should maintain a high index of suspension for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the J&J COVID-19 vaccine. When these specific type of blood clots are observed following J&J COVID-19 vaccination, treatment is different from the treatment that might typically be administered for blood clots. Based on studies conducted among the patients diagnosed with immune thrombotic thrombocytopenia after the AstraZeneca COVID-19 vaccine in Europe, the pathogenesis of these rare and unusual adverse events after vaccination may be associated with platelet-activating antibodies against platelet factor-4 (PF4), a type of protein. Usually, the anticoagulant drug called heparin is used to treat blood clots. In this setting, the use of heparin may be harmful, and alternative treatments need to be given.

CDC will convene an emergency meeting of the Advisory Committee on Immunization Practices (ACIP) on Wednesday, April 14, 2021, to further review these cases and assess potential implications on vaccine policy. FDA will review that analysis as it also investigates these cases. Until that process is complete, CDC and FDA are recommending a pause in the use of the J&J COVID-19 vaccine out of an abundance of caution. The purpose of this Health Alert is, in part, to ensure that the healthcare provider community is aware of the potential for these adverse events and can provide proper management due to the unique treatment required with this type of blood clot.

Background
VAERS is a national passive surveillance system jointly managed by CDC and FDA that monitors adverse events after vaccinations. The six patients (after 6.85 million vaccine doses administered) described in these VAERS reports came to attention in the latter half of March and early April of 2021 and developed symptoms a median of 9 days (range = 6–13 days) after receiving the J&J COVID-19 vaccine. Initial presenting symptoms were notable for headache in five of six patients, and back pain in the sixth who subsequently developed a headache. One patient also had abdominal pain, nausea, and vomiting. Four developed focal neurological symptoms (focal weakness, aphasia, visual disturbance) prompting presentation for emergency care. The median days from vaccination to hospital admission was 15 days (range = 10–17 days). All were eventually diagnosed with

https://emergency.cdc.gov/han/2021/han00442.asp

Cerebral venous sinus anatomy

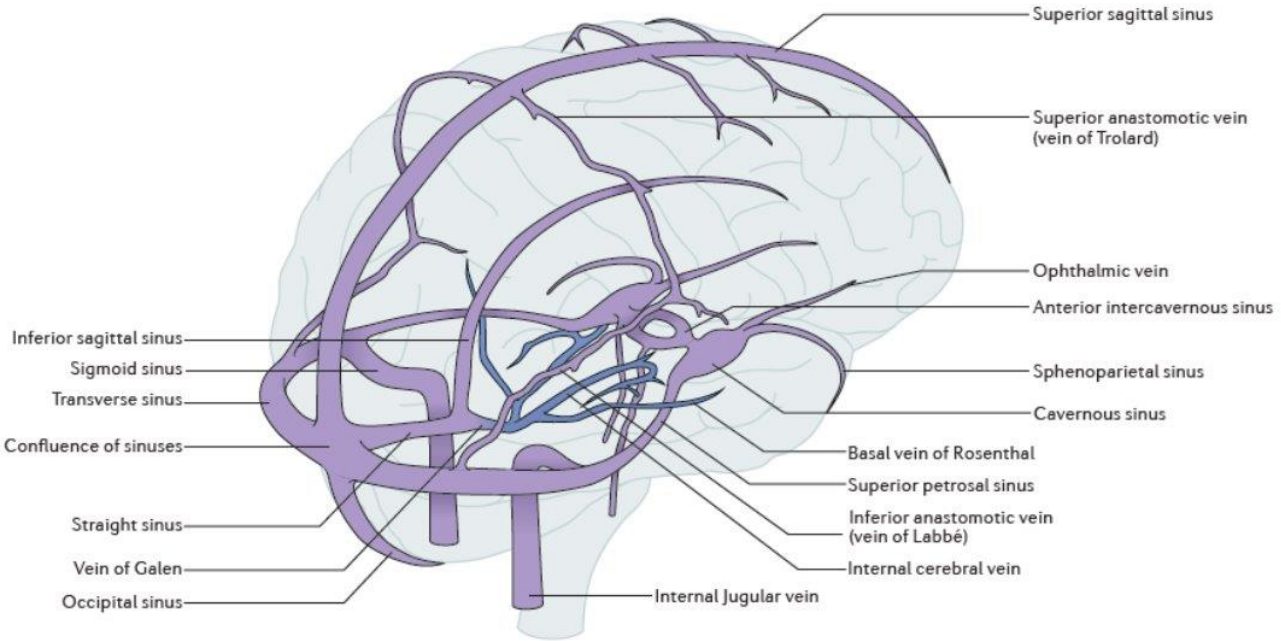


Figure 1 | **Anatomy of the cerebral venous system.** Diagram showing the main components of the cerebral venous system. Blue vessels represent the deep venous system.

Silvis SM et al, Nature Reviews Neurology 13, 555-565(2017)

Cerebral venous sinus thrombosis (CVST)

Background epidemiology[1-3]

- Rare, 0.22–1.57 per 100,000, ~0.5-1% of all strokes
- Median age 37 years
- 8% of patients >65 years
- Female:male ratio of 3:1

Risk factors[4]

- Prothrombotic conditions (genetic or acquired)
- Oral contraceptives
- Pregnancy and the post-partum period
- Malignancy
- Infection
- Mechanical precipitants (lumbar puncture)

[1] Cerebral vein and dural sinus thrombosis in Portugal: 1980-1998. Ferro JM, Correia M, Pontes C, Baptista MV, Pita F, Cerebral Venous Thrombosis Portuguese Collaborative Study Group (Venoport) Cerebrovasc Dis. 2001;11(3):177.
[2] The incidence of cerebral venous thrombosis: a cross-sectional study. Coutinho JM, Zuurbier SM, Aramideh M, Stam J. Stroke. 2012 Dec;43(12):3375-7..
[3] Cerebral Venous Sinus Thrombosis Incidence Is Higher Than Previously Thought: A Retrospective Population-Based Study. Devasagayam S, Wyatt B, Leyden J, Kleinig T. Stroke. 2016 Sep;47(9):2180-2.
[4] Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Saposnik G, et al. 2011;42(4):1158.

CVST signs and symptoms

- More common presentations
  - Isolated intracranial hypertension syndrome (headache with or without vomiting, papilledema, and visual problems)
  - Focal syndrome (focal deficits, seizures, or both)
  - Encephalopathy (multifocal signs, mental status changes, stupor, or coma)

- Rare presentations
  - Cavernous sinus syndrome
  - Subarachnoid hemorrhage
  - Cranial nerve palsies

Data source and case reports

VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

Reports of CVST to VAERS after COVID-19 vaccines as of April 12, 2021

- Janssen COVID-19 vaccine
  - 6 reports of CVST with thrombocytopenia (platelet counts <150K/mm^3) following 6.86 million doses administered
    - Reporting rate of 0.87 cases per million doses administered
- Pfizer-BioNTech COVID-19 vaccine
  - 0 reports following 97.9 million doses administered
- Moderna COVID-19 vaccine
  - 3 reports following 84.7 million doses administered
  - All 3 with normal platelet counts; onset 2, 6, and 12 days after vaccination

Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations

Reports of CVST to VAERS after COVID-19 vaccines as of April 12, 2021

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    - Reporting rate of 0.87 cases per million doses administered
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  - 0 reports following 97.9 million doses administered
- Moderna COVID-19 vaccine
  - 3 reports following 84.7 million doses administered
  - All 3 with normal platelet counts (150–450K/mm3)

Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations

Characteristics of patients with CVST and thrombocytopenia* after Janssen COVID-19 vaccine, N=6

- Median age 33 years (range 18–48)
- Median time to symptom onset 8 days (range 6–13 days)
- All cases occurred in white females
- Current estrogen/progesterone use (n=1)
- Pregnant or post-partum (n=0)
- Pre-existing conditions
  - Obesity (n=3)
  - Hypothyroidism (n=1)
  - Hypertension (n=1)
  - Asthma (n=1)
  - Coagulation disorders (none known)

* Note: Thrombosis usually does not occur in the presence of low platelets; these case presentations are atypical and consistent with cases observed after AstraZeneca COVID-19 vaccine

Initial and late signs and symptoms among CVST patients*, N=6 (patients listed in no particular order)

	Initial features	Late features
Patient 1	Headaches, lethargy	Severe headache, left-sided weakness, vomiting
Patient 2	Headaches	Severe headache, aphasia
Patient 3	Headaches, vomiting, fever	Left arm weakness, right gaze deviation, left neglect
Patient 4	Headaches, chills, myalgias	Severe abdominal pain and fever
Patient 5	Headache, chills, dyspnea, fever	Bruising, unilateral leg swelling, loss of consciousness
Patient 6	Back pain, bruising	Headache, abdominal pain

*All were hospitalized and admitted to the intensive care unit

Locations of CVST, intracerebral hemorrhage, and other thromboses, N=6

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Location of CVST	Right transverse sinus and right sigmoid sinus	Left transverse sinus, left sigmoid sinus, confluence of sinuses, and straight sinus	Superior sagittal sinus, inferior sagittal sinus, and straight sinus	Right transverse sinus and right sigmoid sinus	Right transverse sinus and right sigmoid sinus	Right transverse sinus
Location of intracerebral hemorrhage	Right temporo-parietal lobe	Left temporal lobe	Bilateral frontal lobes, intraventricular	None	None	Occipital lobe
Locations of other thromboses	None	None	None	**Portal vein and right pulmonary artery**	**Bilateral lower extremity VTE, right internal jugular vein**	**Portal vein**

SARS-CoV-2 test results among CVST patients, N=6

	SARS-CoV-2 viral test	SARS-CoV-2 serology
Patient 1	Negative	Not documented
Patient 2	Negative	Nucleocapsid Ab negative
Patient 3	Negative	Not documented
Patient 4	Negative	Not documented
Patient 5	Negative	Unspecified COVID Ab negative
Patient 6	Negative	Unspecified COVID Ab negative

Hematology test results among CVST patients, N=6

	Lowest platelet value (per mm^3)	PF4 HIT* antibody test result(s)
Patient 1	12,000	Not done
Patient 2	69,000	Positive
Patient 3	18,000	Positive
Patient 4	127,000	Positive
Patient 5	10,000	Positive
Patient 6	14,000	Positive

*Platelet factor 4 heparin induced thrombocytopenia

Treatment and outcomes among CVST patients, N=6

- Treatment
  - Heparin (n=4)
  - Nonheparin anticoagulants (n=5)
  - Platelets (n=3)
  - Intravenous immunoglobulin (n=3)
- Outcomes
  - Death (n=1)
  - Remain hospitalized (n=3)
    - Intensive care unit (n=2)
  - Discharged home (n=2)

* All 5 of these patients received Argatraban

Observed vs. expected CVST cases following Janssen COVID-19 vaccine

- Estimated annual incidence of CVST ~0.5–2 cases per 100,000 population*
- Assumed risk period of 5.6% of a calendar year: (41 days/2) ÷ 365 days
- Doses administered among women aged 20–50 years = 1,402,712 doses (as of Apr 12)

Est. annual background incidence	Obs. cases in women aged 20–50 yrs	Exp. cases in women aged 20–50 yrs	Reporting ratio, women aged 20–50 yrs
0.5 per 100K	6	0.39	**15.4**
1.0 per 100K	6	0.79	**7.6**
1.5 per 100k	6	1.18	**5.1**
2.0 per 100k	6	1.58	**3.8**

* https://www.hopkinsmedicine.org/health/conditions-and-diseases/cerebral-venous-sinus-thrombosis, http://www.med.umich.edu/1libr/Stroke/SinusVeinThrombosis.pdf, https://www.nejm.org/doi/10.1056/NEJMra042354?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub, https://www.ahajournals.org/doi/pdf/10.1161/STROKEAHA.116.013617, https://www.nature.com/articles/nrneurol.2017.104

Summary

Summary

- CVST is rare, but clinically serious, and can result in substantial morbidity and mortality; not usually associated with thrombocytopenia
- Observed cases following Janssen COVID-19 vaccines appear to exceed expected based on background rates of CVST among women aged 20–50 years (3-fold or greater)
  - All 6 reports were in women age range 18–48 years, all with thrombocytopenia
  - No obvious patterns of risk factors detected
- CVST with thrombocytopenia has not been observed after the two authorized mRNA vaccines
  - 182 million mRNA COVID-19 doses administered with no reported cases to date
- Clinical features of Janssen cases are similar to those observed following the AstraZeneca COVID-19 vaccine in Europe
- Both Janssen and AstraZeneca vaccines contain replication-incompetent adenoviral vectors (human [Ad26.COV2.S] for Janssen and chimpanzee [ChAdOx1] for AstraZeneca)

Summary (cont.)

- **For clinicians**
  - Maintain a high index of suspicion for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the Jansen COVID-19 vaccine, including severe headache, backache, new neurologic symptoms, severe abdominal pain, shortness of breath, leg swelling, petechiae (tiny red spots on the skin), or new or easy bruising. Obtain platelet counts and screen for evidence of immune thrombotic thrombocytopenia.
  - In patients with a thrombotic event and thrombocytopenia after the Jansen COVID-19 vaccine, evaluate initially with a screening PF4 enzyme-linked immunosorbent (ELISA) assay as would be performed for autoimmune HIT. Consultation with a hematologist is strongly recommended.
  - Do not treat patients with thrombotic events and thrombocytopenia following receipt of Janssen COVID-19 vaccine with heparin, unless HIT testing is negative.
  - If HIT testing is positive or unable to be performed in patient with thrombotic events and thrombocytopenia following receipt of Jansen COVID-19 vaccine, non-heparin anticoagulants and high-dose intravenous immune globulin should be strongly considered.
  - Report adverse events to VAERS, including serious and life-threatening adverse events and deaths in patients following receipt of COVID-19 vaccines as required under the Emergency Use Authorizations for COVID-19 vaccines.

Summary (cont.)

- **For public health**
  - Encourage healthcare providers and the public to report all serious and life-threatening adverse events and deaths following receipt of COVID-19 vaccines to VAERS as required under the EUAs for COVID-19 vaccines.
  - Disseminate information to healthcare providers in your jurisdictions.
- **For the public**
  - If you have received the Janssen COVID-19 vaccine and develop severe headache, abdominal pain, leg pain, or shortness of breath within three weeks after vaccination, contact your healthcare provider, or seek medical care.
  - Report adverse events following receipt of any COVID-19 vaccine to VAERS.
  - If you are scheduled to receive the Janssen vaccine, please contact your healthcare provider, vaccination location, or clinic to learn about additional vaccine availability.

How to report an adverse event to VAERS

- Go to vaers.hhs.gov
- Submit a report online
- For help:

  Call 1-800-822-7967

  Email info@VAERS.org

  video instructions https://youtu.be/sbCWhcQADFE

- Please send records to VAERS ASAP if contacted and asked
  - HIPAA permits reporting of protected health information to public health authorities including CDC and FDA

Next steps

- Continue enhanced monitoring in VAERS and other vaccine safety systems (e.g., Vaccine Safety Datalink [VSD])
  - VSD: ~113K Janssen doses administered, 0 cases in risk interval(s)
- Investigate potential cases through detailed clinical reviews/chart reviews
- Refine analyses to better quantify risk

Acknowledgments

We wish to acknowledge the contributions of investigators from the following organizations:

Centers for Disease Control and Prevention

COVID-19 Vaccine Task Force

COVID-19 Vaccine Task Force, Vaccine Safety Team

Immunization Safety Office

Division of Healthcare Quality Promotion

Clinical Immunization Safety Assessment Project

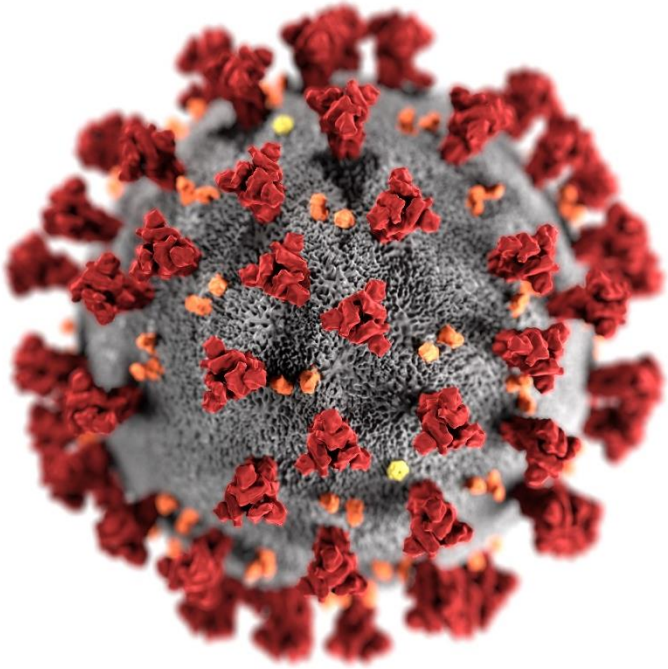
Vaccine Adverse Event Safety Network

Additional report of patient with non-CVST thromboses and thrombocytopenia after Janssen COVID-19 vaccine*

- 50s y/o female
- History coronary artery disease, hypertension, asthma, COPD
- Developed bruising and leg swelling 11 days after vaccination with Janssen vaccine
- Hospitalized with hematologic event that is non-CVST
  - Left lower extremity deep venous thrombosis
  - Right superficial femoral artery and bilateral iliac artery thrombosis (non-CVST)
- Thrombocytopenia of 15,000/mm^3

*Assessment based only on VAERS report; investigation in-progress including obtaining and reviewing medical records

Thrombocytopenic thrombosis after Janssen vaccine



Sara Oliver MD, MSPH
COCA Call
April 15, 2021

Adenovirus vector vaccines

Adenovirus Vector

Janssen/J&J

AstraZeneca

Janssen

One dose
Human Adenovirus 26 vector
EUA in the US issued Feb 2021
EMA authorized for Europe
Doses not yet delivered/administered

AstraZeneca

Two doses
Chimp adenovirus vector
Awaiting EUA application in the US
Approved in UK, Europe

- Concerns for rare clotting events seen after COVID-19 adenovirus vector vaccines
- Clinical syndromes after both vaccines appear similar
- However, extent to which the cases seen after both adenovirus vector vaccines represent the same syndrome is unknown

EUA: Emergency Use Authorization; EMA: European Medicines Agency

AstraZeneca (AZ) vaccine

- Last week, EMA's safety committee (PRAC) released report concluding:
  - **Strong association** and **probable causal link** between the AZ vaccine and rare clotting events

From the European Union:

- 62 cases of CVST & 24 cases of splanchnic vein thrombosis with thrombocytopenia; 18 were fatal
- Most in females <60 years of age
- Within 2 weeks of AZ vaccine receipt
- Due to different ways vaccine used in each country, cannot exclude age/gender as risk factors

From the United Kingdom:

- 79 cases of thrombosis + thrombocytopenia; 19 were fatal
- 44 cases of CVST (14 fatalities) & 35 cases of other clots (5 fatalities)
- 51 cases were female; 28 were male
- 20.2 million doses given. Estimated risk ~4 per million pop. ('slightly higher incidence' in younger age groups)

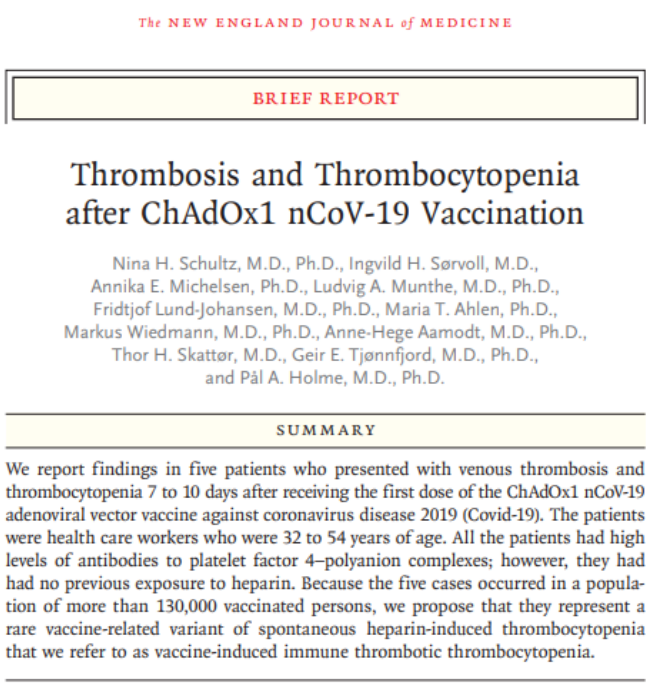
CVST: Cerebral Venous Sinus Thrombosis

https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood

https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement/jcvi-statement-on-use-of-the-astrazeneca-covid-19-vaccine-7-april-2021

Vaccine-induced immune thrombotic thrombocytopenia

Reports of low platelets (thrombocytopenia) and blood clots (thrombosis) after AZ vaccine in Europe



The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination

Nina H. Schultz, M.D., Ph.D., Ingvild H. Sørvoll, M.D., Annika E. Michelsen, Ph.D., Ludvig A. Munthe, M.D., Ph.D., Fridtjof Lund-Johansen, M.D., Ph.D., Maria T. Ahlen, Ph.D., Markus Wiedmann, M.D., Ph.D., Anne-Hege Aamodt, M.D., Ph.D., Thor H. Skattør, M.D., Geir E. Tjønnfjord, M.D., Ph.D., and Pål A. Holme, M.D., Ph.D.

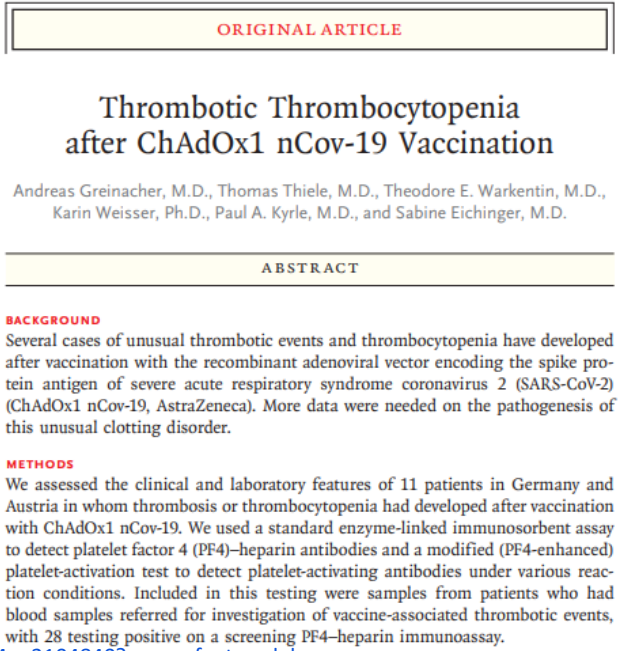
SUMMARY

We report findings in five patients who presented with venous thrombosis and thrombocytopenia 7 to 10 days after receiving the first dose of the ChAdOx1 nCoV-19 adenoviral vector vaccine against coronavirus disease 2019 (Covid-19). The patients were health care workers who were 32 to 54 years of age. All the patients had high levels of antibodies to platelet factor 4–polyanion complexes; however, they had had no previous exposure to heparin. Because the five cases occurred in a population of more than 130,000 vaccinated persons, we propose that they represent a rare vaccine-related variant of spontaneous heparin-induced thrombocytopenia that we refer to as vaccine-induced immune thrombotic thrombocytopenia.

Two publications describing cases of thrombotic thrombocytopenia from Germany & Austria, and Norway

Many cases had platelet activating antibodies directed against platelet factor 4 (PF4)

Authors propose syndrome entitled “Vaccine-induced immune thrombotic thrombocytopenia” (**VITT**)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination

Andreas Greinacher, M.D., Thomas Thiele, M.D., Theodore E. Warkentin, M.D., Karin Weisser, Ph.D., Paul A. Kyrle, M.D., and Sabine Eichinger, M.D.

ABSTRACT

BACKGROUND

Several cases of unusual thrombotic events and thrombocytopenia have developed after vaccination with the recombinant adenoviral vector encoding the spike protein antigen of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (ChAdOx1 nCov-19, AstraZeneca). More data were needed on the pathogenesis of this unusual clotting disorder.

METHODS

We assessed the clinical and laboratory features of 11 patients in Germany and Austria in whom thrombosis or thrombocytopenia had developed after vaccination with ChAdOx1 nCov-19. We used a standard enzyme-linked immunosorbent assay to detect platelet factor 4 (PF4)–heparin antibodies and a modified (PF4-enhanced) platelet-activation test to detect platelet-activating antibodies under various reaction conditions. Included in this testing were samples from patients who had blood samples referred for investigation of vaccine-associated thrombotic events, with 28 testing positive on a screening PF4–heparin immunoassay.

https://www.nejm.org/doi/full/10.1056/NEJMoa2104882?query=featured_home

https://www.nejm.org/doi/full/10.1056/NEJMoa2104840?query=featured_home

AstraZeneca (AZ) vaccine:
Recommendations for use

- EMA's Pharmacovigilance Risk Assessment Committee (PRAC) does not make vaccine policy for the EU; each country weighs the risks and benefits of AZ vaccine individually
- Many countries have adopted age-based recommendations
  - UK: Adults ≥30 years of age; April 7, 2021
  - Australia: Adults ≥50 years of age; April 8, 2021
  - Other European countries: Adults ≥55 to ≥70 years of age

EMA: European Medicines Agency

Discussion by the Work Group

- Benefit/risk balance for use of the Janssen COVID-19 vaccine

- Review of cerebral venous sinus thrombosis (CVST) cases
- Risk of COVID-19 disease, by sex and age
- COVID-19 vaccines administered, by age
- Janssen vaccine doses administered to date
- Projected supply of COVID-19 vaccines in the US

- Policy options for updated recommendations for use for Janssen COVID-19 vaccine

CVST cases reviewed by the Work Group

- 6 cases of CVST reported to VAERS
  - All 6 among women 18-48 years of age
  - Interval from vaccine receipt to symptom onset ranged from 6-13 days

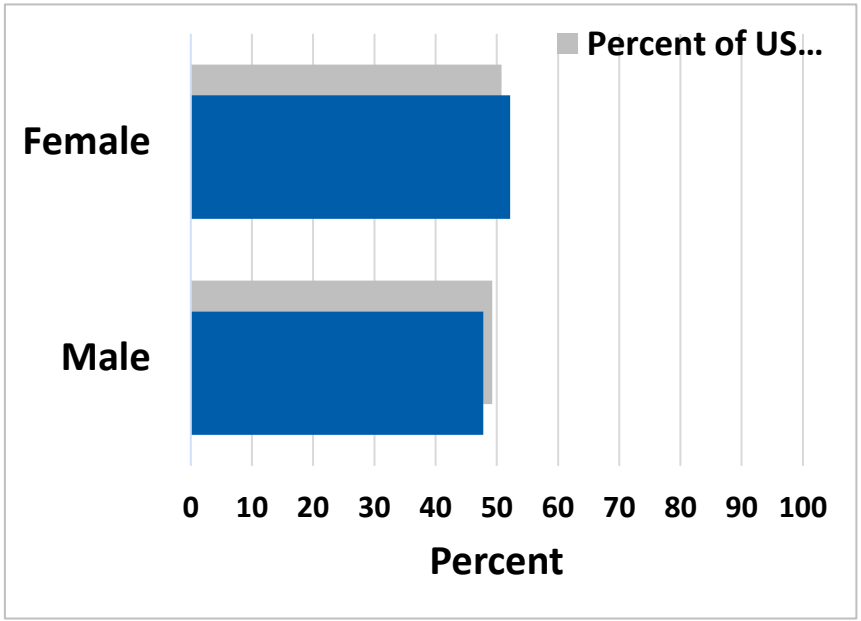
- 1 case of CVST reported in the Phase 3 clinical trial
  - 25-year-old male, no previous medical history, no medications
  - Day 9 after vaccination: fever, headache
  - Day 19 after vaccination: seizure, CT with cerebral hemorrhage
    Day 21 after vaccination: CVST diagnosed, anti-PF4 positive

HAN Archive - 00442 | Health Alert Network (HAN) (cdc.gov) https://emergency.cdc.gov/han/2021/han00442.asp

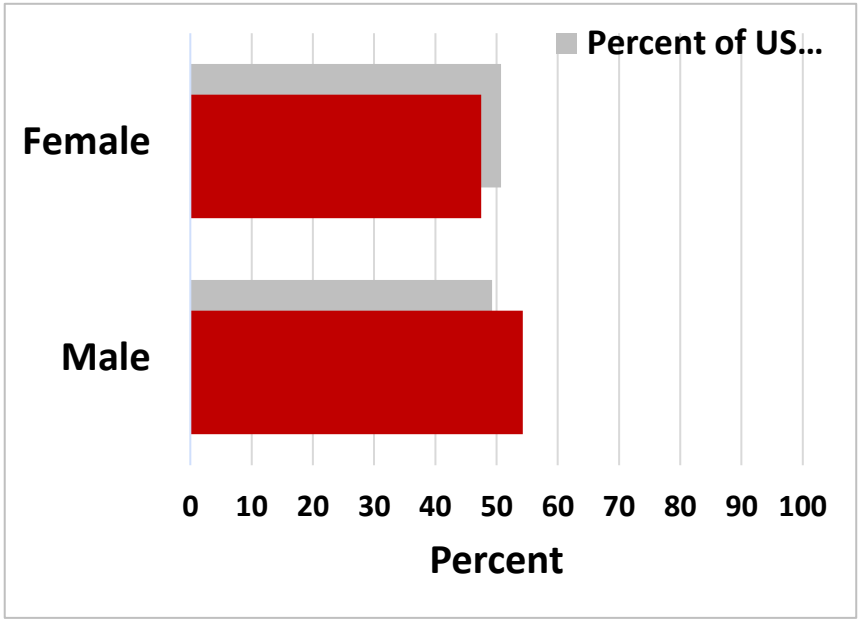
CVST: Cerebral Venous Sinus Thrombosis

COVID-19 Cases and Deaths by Sex

COVID-19 Cases by Sex,
January 22, 2020 – April 12, 2021



COVID-19 Deaths by Sex,
January 22, 2020 – April 12, 2021

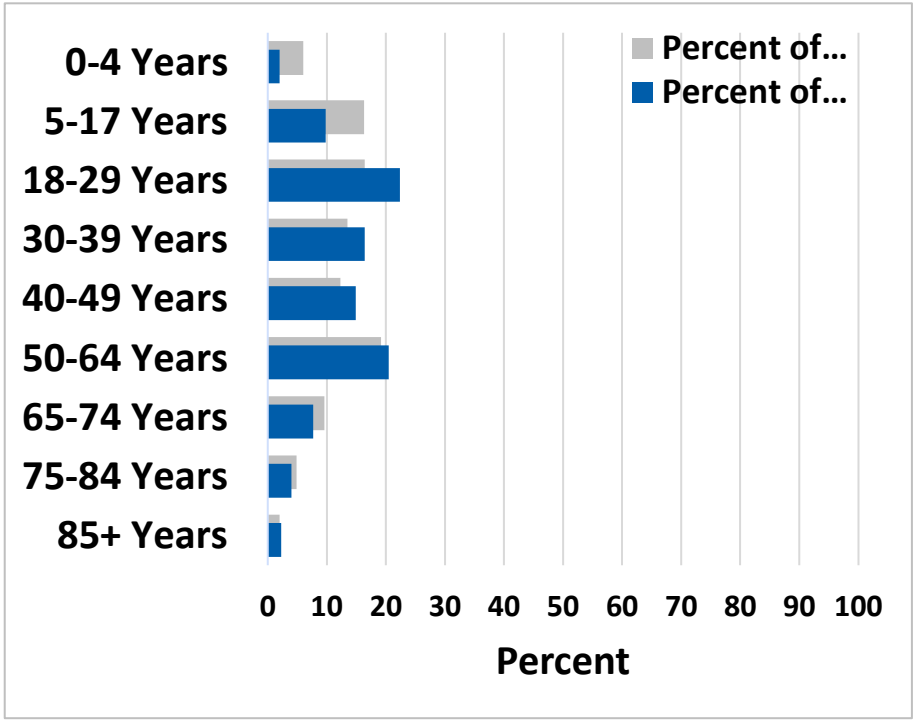


*Data from 24,349,551 cases, sex was available for 24,071,425
https://covid.cdc.gov/covid-data-tracker/#demographics

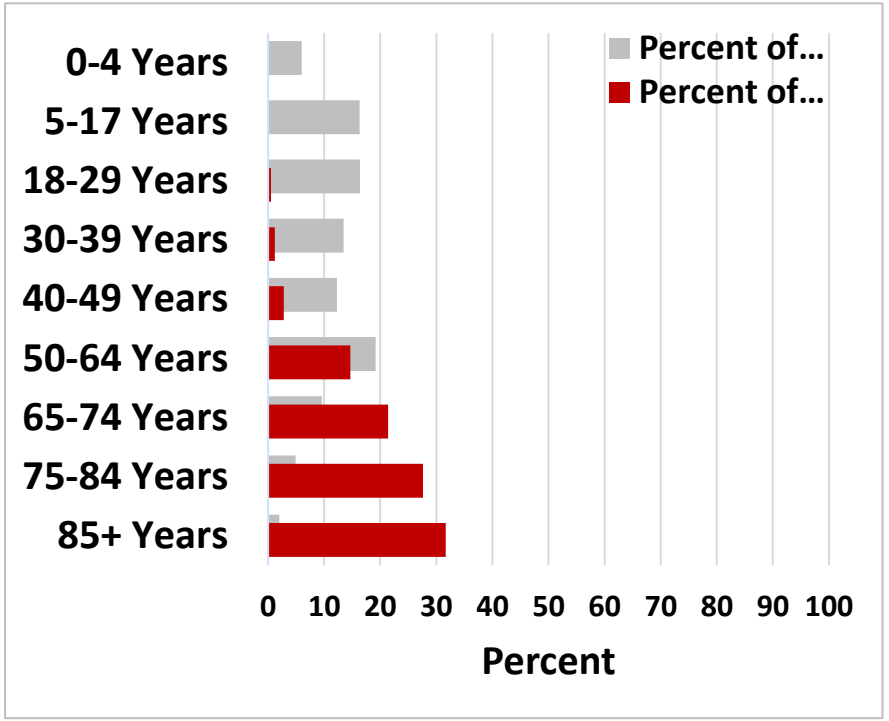
*Data from 433,171 deaths, sex was available for 432,059

COVID-19 Cases and Deaths by Age Group

COVID-19 Cases by Age Group
January 22, 2020 – April 12, 2021



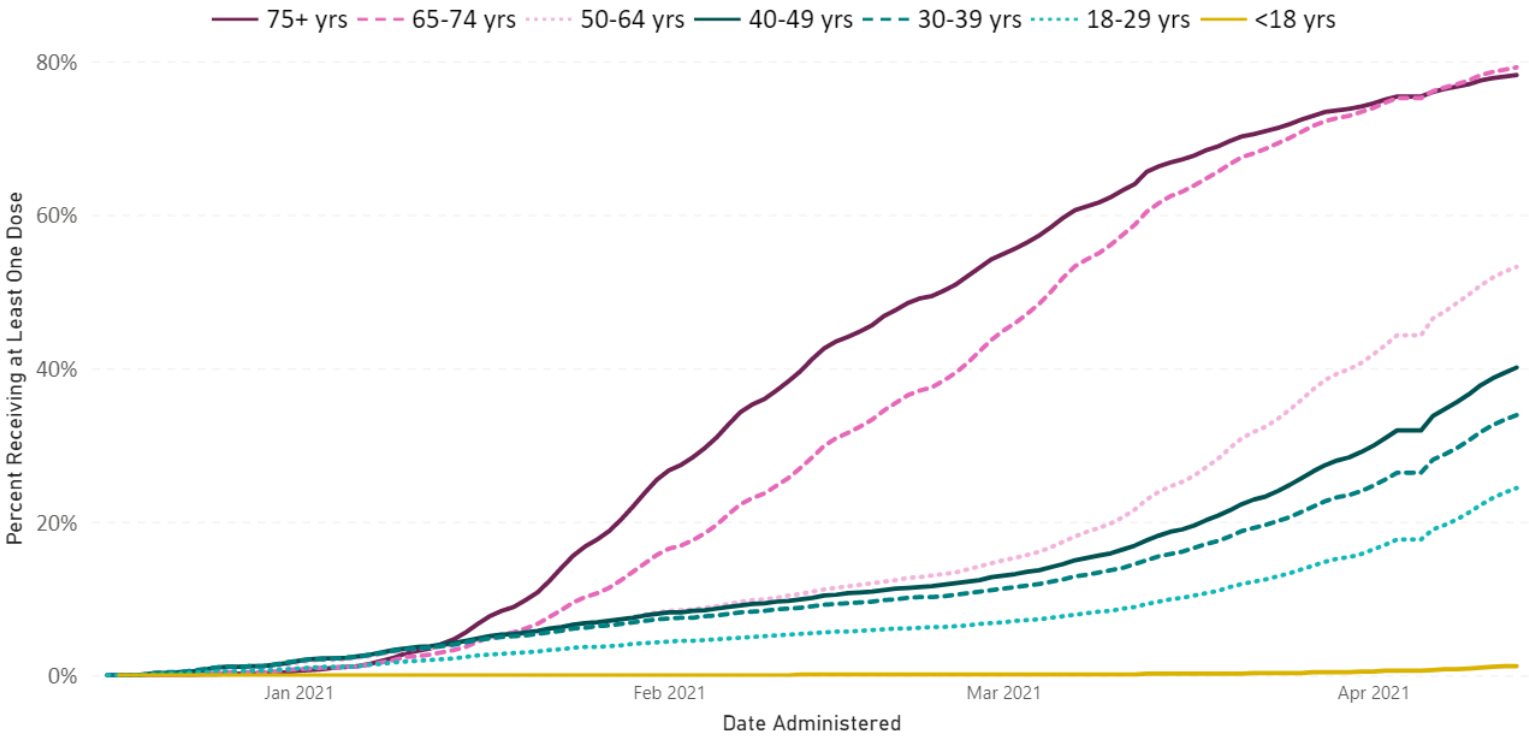
COVID-19 Deaths by Age Group
January 22, 2020 – April 12, 2021



https://covid.cdc.gov/covid-data-tracker/#demographics

Data from 24,349,551 cases. Age group was available for 24,176,192

COVID-19 Vaccination Coverage by Age – United States



Percent Receiving ≥1 dose

≥75 years	78.2%
65-74 years	79.2%
50-64 years	53.2%
40-49 years	40.1%
30-39 years	33.9%
18-29 years	24.4%

Data as of April 13, 2021; age available for 92% of doses administered.
https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic

Janssen Doses Administered to Date

- 7,233,726 Janssen doses administered to date
  - 1,495,400 Janssen doses administered to females 18-50 years of age*

Source: CDC Immunization Data Lake; Includes data reported to CDC as of 4/13/2021 at 6:00 am

***Data stratified by age and sex does not include Texas.**

Janssen Doses Administered to Date

Thrombocytopenic thrombotic events develop ~6-13 days after vaccine receipt

7,233,726 doses administered in the United States

Prior to March 30:

3,466,166 Janssen doses administered
48% of doses

Thrombocytopenic thrombotic events post-vaccine likely already occurred

March 30 to April 13

3,767,560 Janssen doses administered
52% of doses

Thrombocytopenic thrombotic events post-vaccine may still occur

Source: CDC Immunization Data Lake; Includes data reported to CDC as of 4/13/2021 at 6:00 am ***Data stratified by age and sex does not include Texas.**

What is known so far

- Thrombocytopenic thrombotic events after the AstraZeneca vaccine have occurred
- In the US, 6 cases of CVST reported after receipt of the Janssen COVID-19 vaccine.
- No cases of CVST with thrombocytopenia reported after receipt of either Pfizer and Moderna COVID-19 vaccines
- CVST cases have occurred primarily in younger adults, females
- CVST can be clinically devastating or fatal
- In the US, alternative COVID-19 vaccines (mRNA vaccines) are available
  - Based on current projections, supply of both mRNA vaccines fairly stable for near future

CVST: Cerebral Venous Sinus Thrombosis

What we do NOT know

- True background incidence of CVST with thrombocytopenia
- Specific risk factors for thrombocytopenic thrombotic events
- Incidence of other thrombotic (non-CVST) cases with thrombocytopenia after Janssen vaccine
- Ability to compare or generalize thrombotic cases after the AstraZeneca vaccine to Janssen vaccine
- True incidence of thrombocytopenic thrombotic events/CVST after a Janssen/J&J COVID-19 vaccine
  - More cases may be identified in the coming days/weeks

CVST: Cerebral Venous Sinus Thrombosis

Policy discussions from ACIP: Janssen/J&J COVID-19 vaccine

Policy options: Janssen/J&J COVID-19 vaccines

WG Discussion points

- While overall reported cases are rare, once limited to doses administered to age and sex of CVST cases seen, observed cases exceed expected cases

- Given the timing of doses administered (52% of doses administered in the previous 2 weeks), additional cases may be identified over the next 1-2 weeks

- Emphasis that robust safety surveillance is critical
  - Signal detection and evaluation of cases occurred as planned

Policy Options for Janssen Policy Recommendations

Do **not** recommend use of Janssen vaccine

Recommend use of Janssen/J&J COVID-19 vaccine in **some** populations

Recommend use of Janssen/J&J COVID-19 vaccine in **all adults** ≥18 years of age

Age or **gender** specific populations?

- Adults **50 years of age** and older only
- **Males** only

Janssen/J&J COVID-19 vaccine:

ACIP Response

- Monday 4/12: Vaccine Safety Technical Group (VaST) meeting
- Tuesday 4/13: ACIP COVID-19 vaccines Work Group meeting
- Wednesday 4/14: Emergency ACIP meeting

Purpose of Emergency ACIP meeting

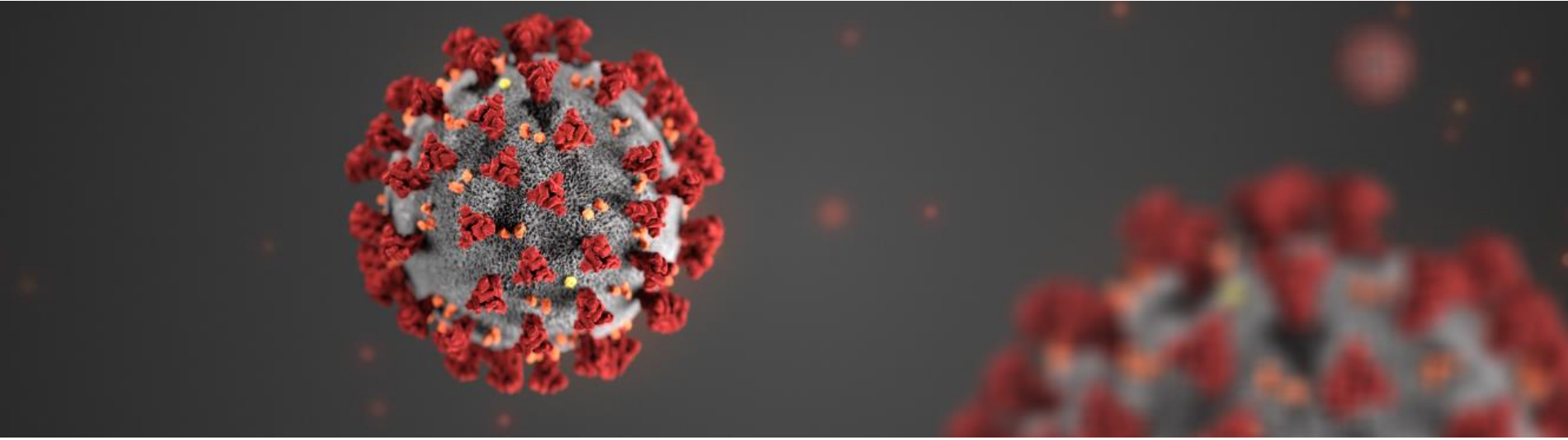
- Consider implications of reported cases of thrombosis and thrombocytopenia after Janssen/J&J vaccine on vaccination policy

Janssen/J&J COVID-19 vaccine:
HAN released April 13, 2021

Cases of Cerebral Venous Sinus Thrombosis with Thrombocytopenia after Receipt of the Johnson & Johnson COVID-19 Vaccine

- Recommendations for Clinicians: diagnosis and treatment
  - Evaluate patients with a screening PF4 enzyme-linked immunosorbent (ELISA) assay as would be performed for autoimmune HIT. Consultation with a hematologist is strongly recommended.
  - Do not treat with heparin, unless HIT testing is negative
- Recommendations for Public Health: case reporting through VAERS
  - Encourage healthcare providers and the public to report all serious and life-threatening adverse events and deaths following receipt of COVID-19 vaccines to VAERS
- Recommendations for the Public: clinical signs and symptoms to monitor
  - Contact healthcare provider, or seek medical care if you develop severe headache, abdominal pain, leg pain, or shortness of breath within three weeks after vaccination with the J&J COVID-19 vaccine

HAN Archive - 00442 | Health Alert Network (HAN) (cdc.gov) https://emergency.cdc.gov/han/2021/han00442.asp



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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  - Click on the “Q&A” button.
  - Type your question in the “Q&A” box.
  - Submit your question.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

- If you are a patient, please refer your question to your healthcare provider.

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- **What:** Video recording
- **Where:** On the COCA Call webpage at https://emergency.cdc.gov/coca/calls/2021/callinfo_041521.asp

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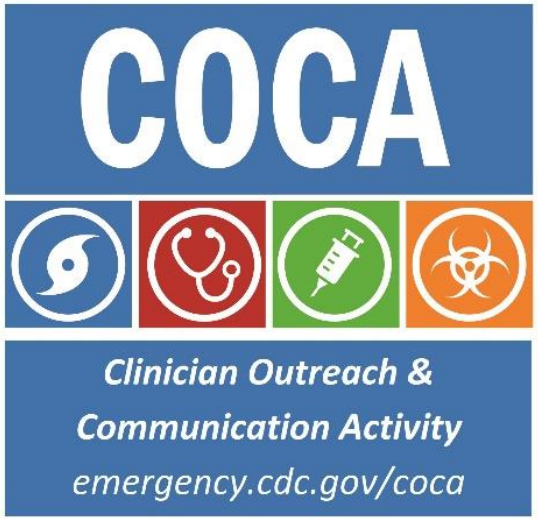

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