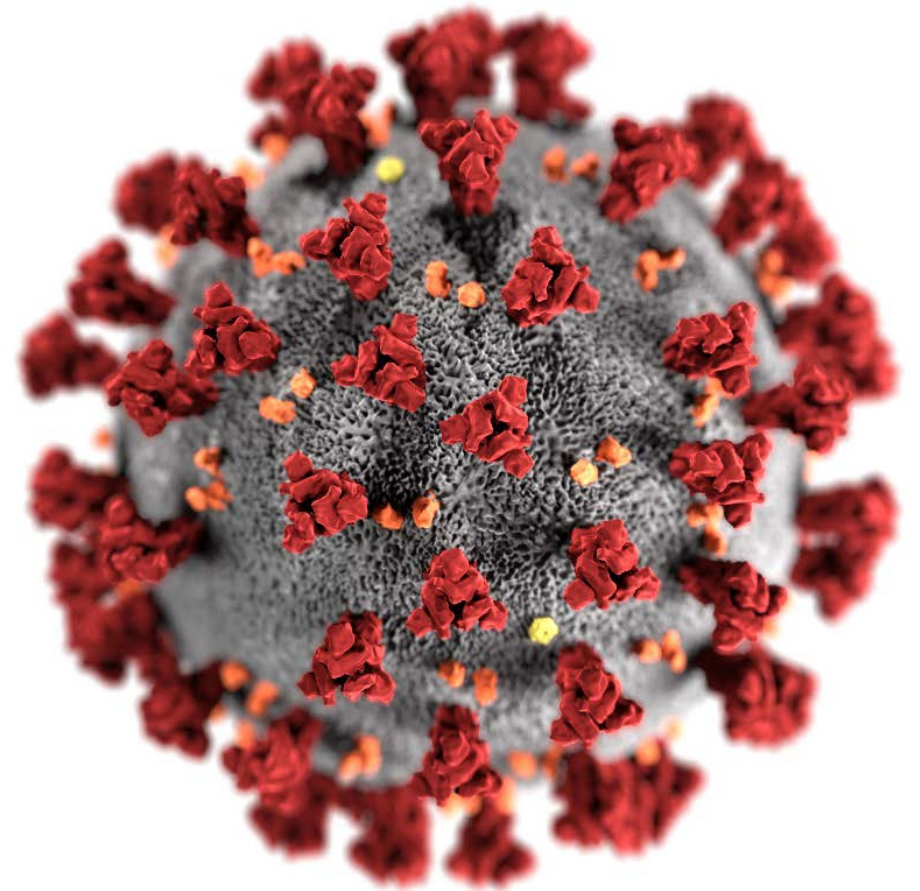


ACIP COVID-19 Vaccines Work Group

Dr. Beth Bell, Work Group Chair

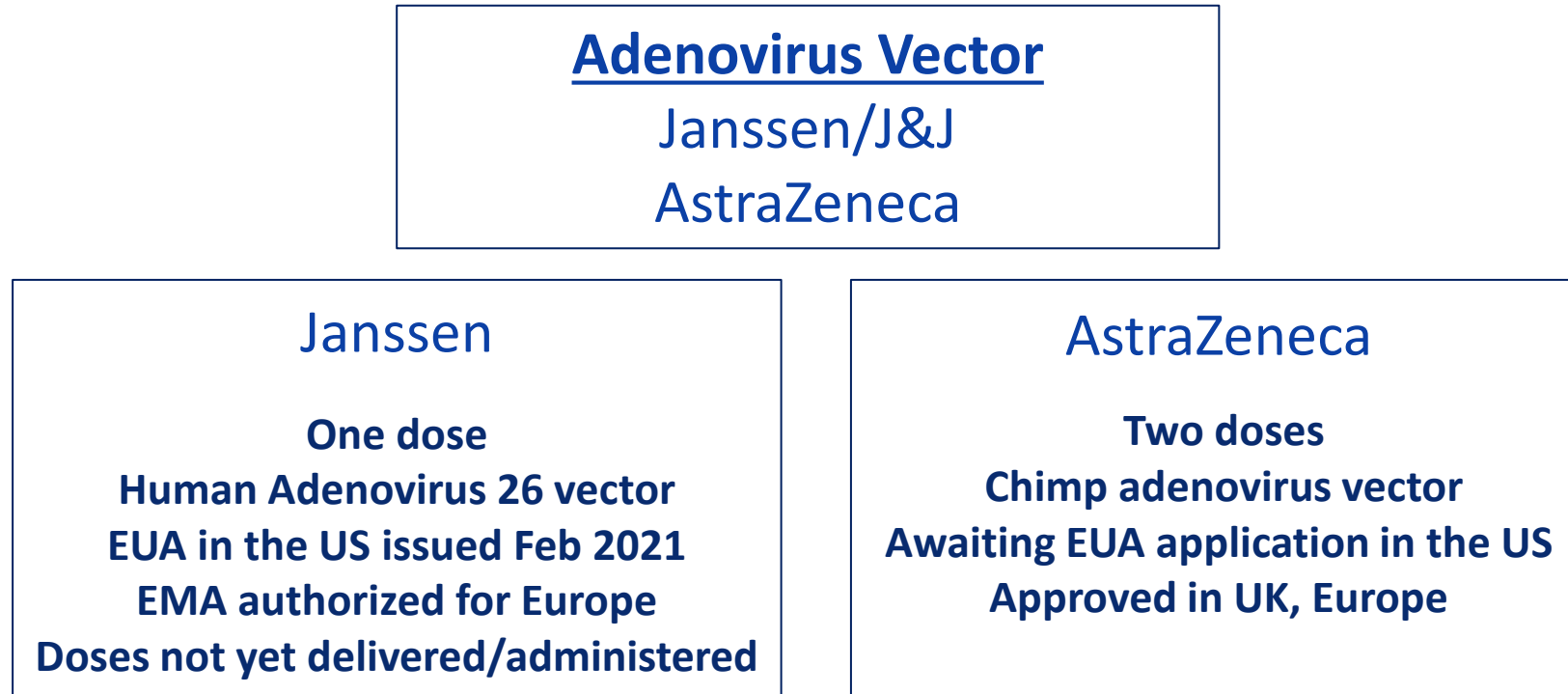
April 14, 2021



Overview

- Review of adenovirus vector COVID-19 vaccines
- Descriptions of rare clotting events seen after adenoviral vector vaccines:
 - Events after AstraZeneca vaccine in Europe
 - Events after Janssen vaccine in US
- ACIP Response
- Today's Agenda

Adenovirus vector vaccines



- 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

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 & Australia, 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

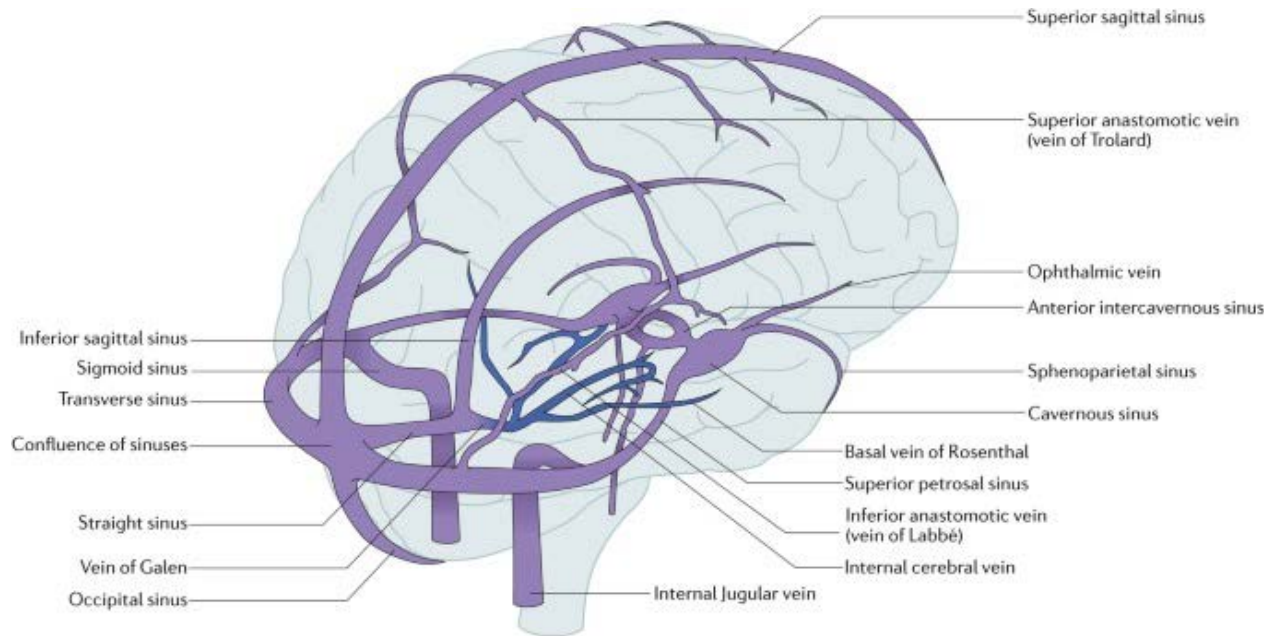
Several cases of unusual thrombotic events and thrombocytopenia have developed after vaccination with the recombinant adenoviral vector encoding the spike protein antigen of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (ChAdOx1 nCoV-19, AstraZeneca). More data were needed on the pathogenesis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

Cerebral Venous Sinus Thrombosis (CVST) – a brief background

- Thrombosis within large vessels draining blood from the brain
- Mostly among people 20–50 years of age; female
- Risks: pregnancy, usual coagulation risks (e.g., oral contraceptives)
- Symptoms typically include headache, nausea, vomiting, other neurologic symptoms
 - Presentation acute → weeks, months



Nature Reviews | Neurology

<http://www.med.umich.edu%2F1libr%2FStroke%2FSinusVeinThrombosis.pdf&usg=AOvVaw3qjvm4UOFcHN-eR4O3Kyf8>

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
 - European countries: Adults ≥ 55 to ≥ 70 years of age

Janssen/J&J COVID-19 vaccine:

Joint CDC and FDA statement on Johnson & Johnson COVID-19 vaccine, April 13, 2021

- As of April 12, more than 6.8 million doses of the Johnson & Johnson (Janssen) vaccine have been administered in the U.S.
- CDC and FDA are reviewing data involving 6 cases of CVST in combination with low platelets
- “CDC will convene a meeting of the Advisory Committee on Immunization Practices on Wednesday to further review these cases and assess their potential significance”.
- “Until that process is complete, we are recommending a pause in the use of this vaccine out of an abundance of caution.”

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
- Recommendations for Public Health: case reporting through VAERS
- Recommendations for the Public: clinical signs and symptoms to monitor

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

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

Today's Agenda

Wednesday, April 14

- **Overview of safety with Janssen's COVID-19 vaccine, Ad26.COV2.S**
Dr. Aran Maree (Janssen Pharmaceuticals Companies of Johnson & Johnson)
- **Cerebral Venous Sinus Thrombosis with Thrombocytopenia after COVID-19 vaccines, VAERS, March 2-April 12, 2021**
Dr. Tom Shimabukuro (CDC)
- **VaST assessment**
Dr. Grace Lee (ACIP, VaST Co-chair)
- **Work Group interpretation**
Dr. Sara Oliver (CDC)
- **Public Comment**
- **Discussion**
- **VOTE:**
Janssen COVID-19 vaccine: Updated interim recommendations for use

Work group members

ACIP members

- Beth Bell (chair)
- Matthew Daley
- Grace Lee
- Jose Romero
- Keipp Talbot

Ex-officio/government members

- FDA: Doran Fink, Rachel Zhang
- NIH: Chris Roberts
- IHS: Thomas Weiser, Uzo Chukwuma
- DOD: Bryan Schumacher
- CMS: Jeff Kelman
- BARDA: Christine Oshansky
- HHS: David Kim

CDC Lead

- Sara Oliver

Liaisons

- AAFP: Jonathan Temte
- AAP: Sean O’Leary
- ACOG: Denise Jamieson (primary), Laura Riley (alternate)
- ACP: Jason Goldman
- AGS: Ken Schmader
- AIM: Rob Shechter (primary), Jane Zucker (alternate)
- AMA: Sandra Fryhofer
- ANA: Kendra McMillan (primary), Ruth Francis (alternate)
- APhA: Michael Hogue
- ASTHO: Marcus Plescia
- CSTE: Susan Lett (primary), Christine Hahn (alternate)
- IDSA: Jeff Duchin (primary), Carol Baker (alternate)

Liaisons, cont’d

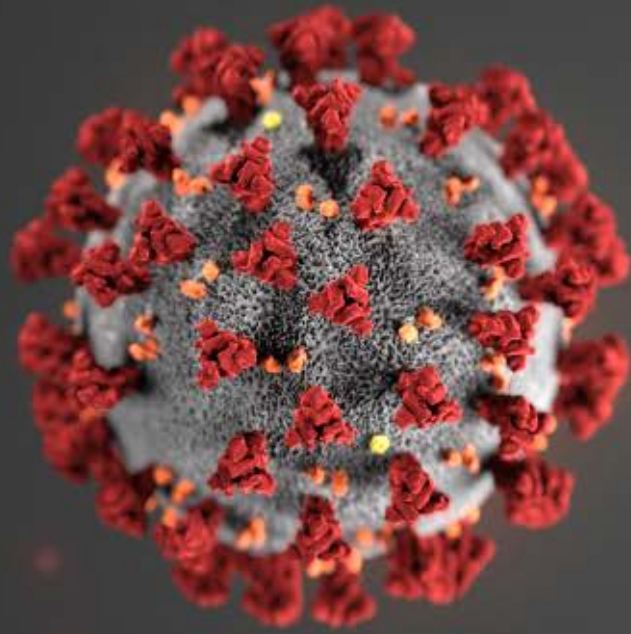
- NACCHO: Matt Zahn (primary), Jeff Duchin (alternate)
- NACI: Matthew Tunis
- NFID: Bill Schaffner (primary), Marla Dalton (alternate)
- NMA: Oliver Brooks
- SHEA: Marci Drees

Consultants

- Ed Belongia
- Kathy Kinlaw
- Dayna Matthew
- Kathleen Neuzil
- Stanley Perlman
- Peter Szilagyi

CDC participants

- Amy Blain
- Doug Campos-Outcalt
- Mary Chamberland
- Thomas Clark
- Amanda Cohn
- Jean Cox-Ganser
- Jonathan Duffy
- Kathleen Dooling
- Anthony Fiore
- Mark Freedman
- Julia Gargano
- Sue Gerber
- Jack Gersten
- Susan Goldstein
- Sam Graitcer
- Lisa Grohskopf
- Julie Garon
- Stephen Hadler
- Rita Helfand
- Susan Hiers
- Terri Hyde
- Cynthia Jorgensen
- Erin Kennedy
- Sarah Kidd
- Ram Koppaka
- Megan Lindley
- Nicole Lindsey
- Ruth Link-Gelles
- Jessica MacNeil
- Lauri Markowitz
- Mona Marin
- Sarah Mbaeyi
- Nancy Messonnier
- Danielle Moulia
- Rebecca Morgan
- Titilope Oduyebo
- Anita Patel
- Janell Routh
- Stephanie Schrag
- Heather Scobie
- Edwin Shanley
- Tom Shimabukuro
- Heidi Soeters
- Mark Sotir
- Stephanie Thomas
- Natalie Thornburg
- Jennifer Verani
- Megan Wallace
- Annemarie Wasley
- Cindy Weinbaum
- Melinda Wharton
- Yon Yu



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.



COVID-19 Work Group activities – March, April 2021

- COVID-19 Vaccine Work Group meets weekly
- Topics covered:
 - COVID-19 variants and impact on vaccine policy
 - Review of ‘real world’ vaccine effectiveness studies
 - Updates on pediatric clinical trials
 - Safety updates