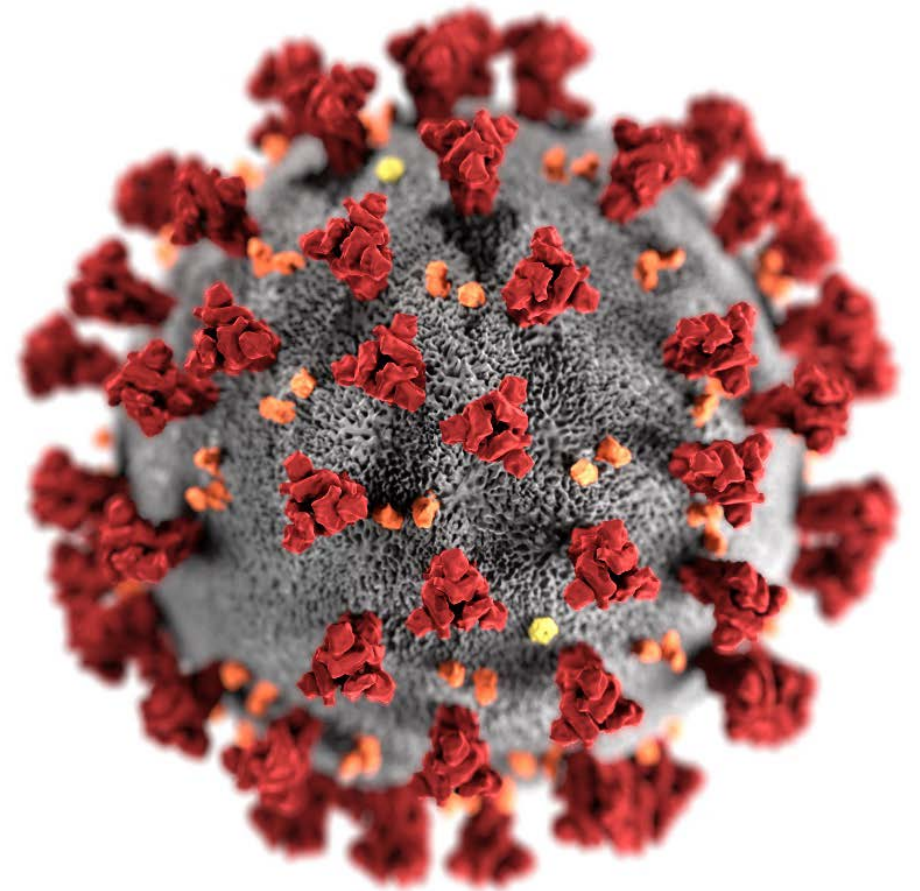


# ACIP COVID-19 Vaccines Work Group

**Dr. Beth Bell, Work Group Chair**

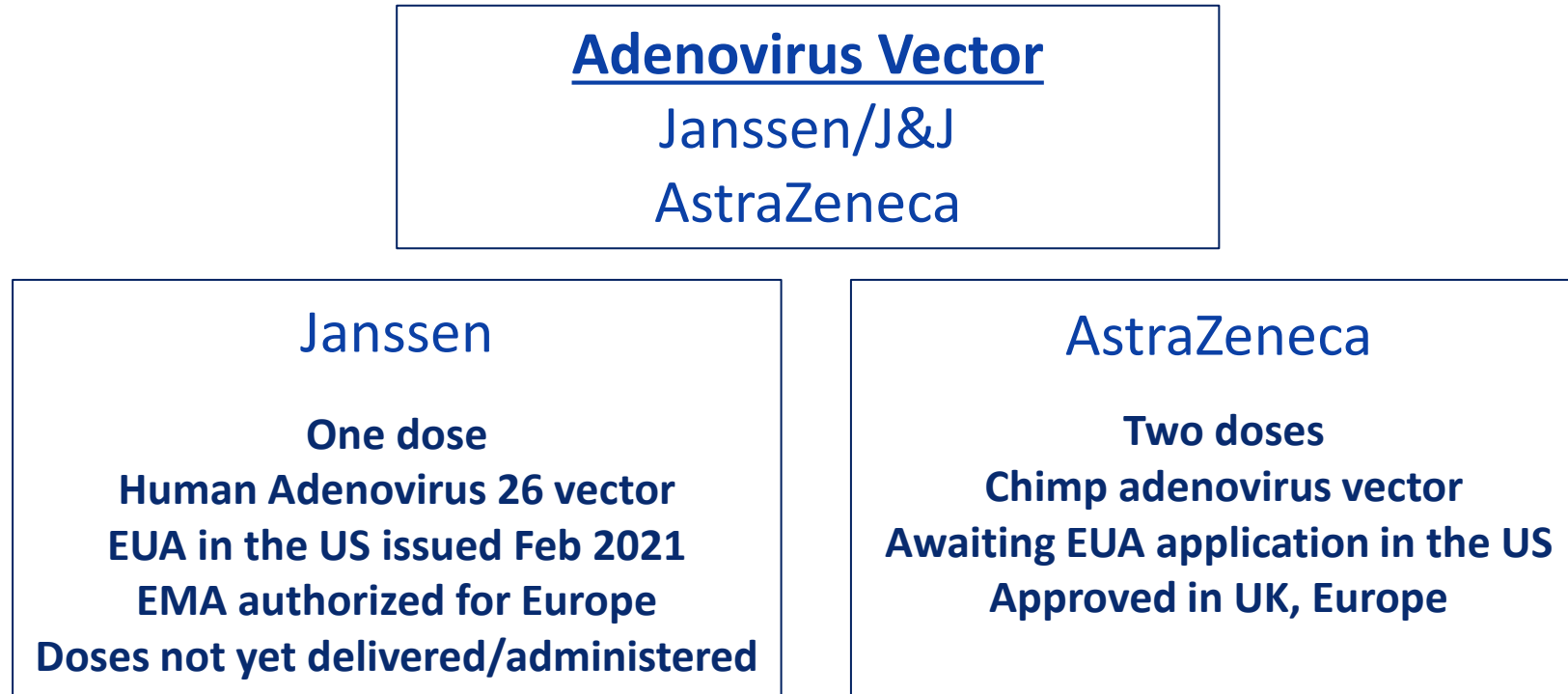
**April 14, 2021**



# 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 & 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

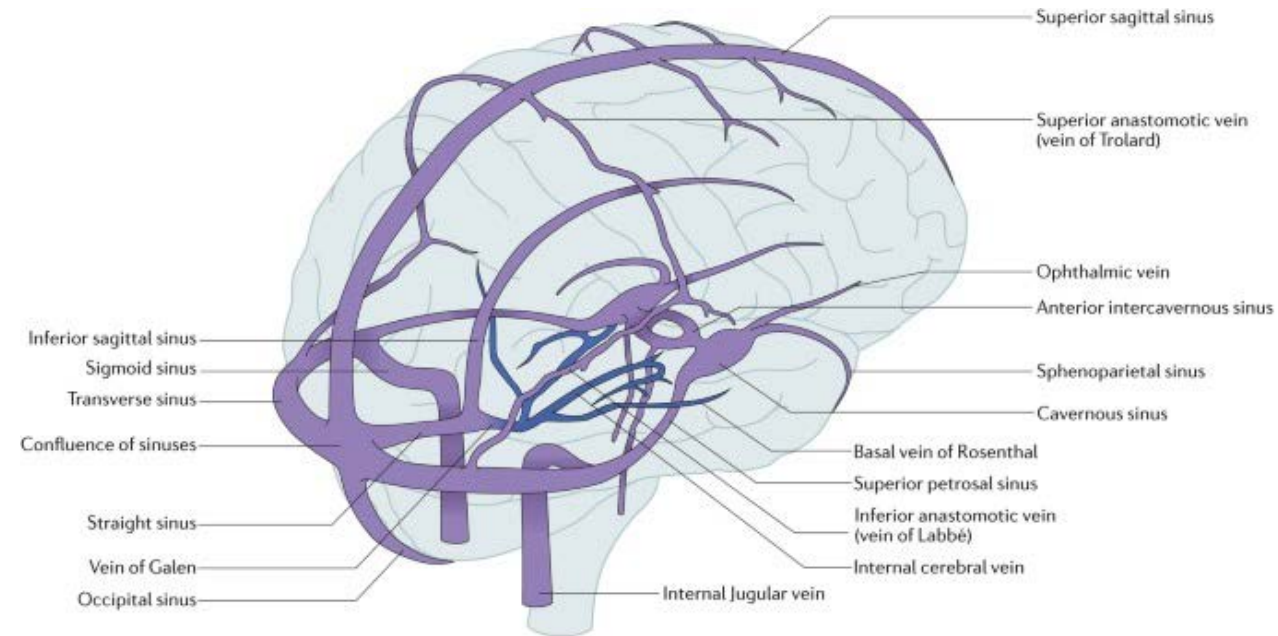
Several cases of unusual thrombotic events and thrombocytopenia have developed after vaccination with the recombinant adenoviral vector encoding the spike protein antigen of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (ChAdOx1 nCoV-19, AstraZeneca). More data were needed on the pathogenesis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

# 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  $\geq 30$  years of age; April 7, 2021
  - Australia: Adults  $\geq 50$  years of age; April 8, 2021
  - European countries: Adults  $\geq 55$  to  $\geq 70$  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

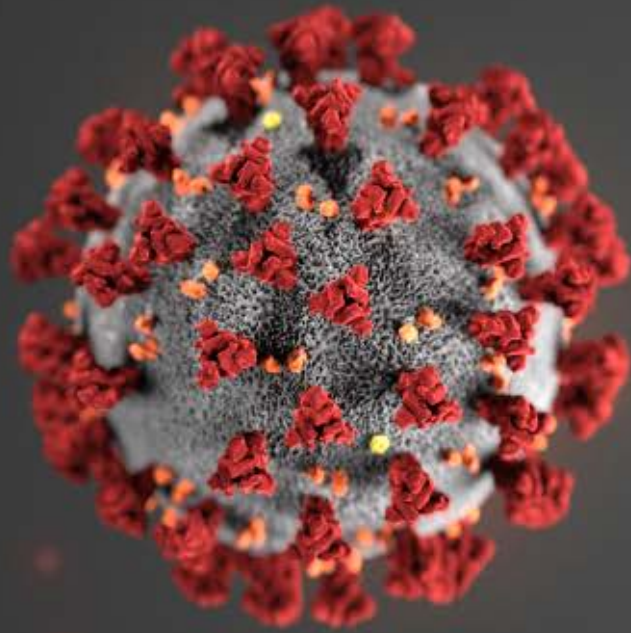
- NACCHO: Matt Zahn (primary),  
Jeff Duchin (alternate)
- NACI: Matthew Tunis
- NFID: Bill Schaffner (primary),  
Marla Dalton (alternate)
- NMA: Oliver Brooks
- SHEA: Marci Drees

## Consultants

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

# CDC participants

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- 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](http://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.

