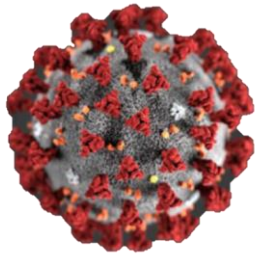


New Hampshire Coronavirus Disease 2019 Weekly Call for Healthcare Providers and Public Health Partners

April 15, 2021

Elizabeth Talbot
Beth Daly
Lindsay Pierce

Thursday noon-time partner calls will focus on science, medical, and vaccine updates geared towards our healthcare partners

NH DIVISION OF Public Health Services
Department of Health and Human Services

Agenda

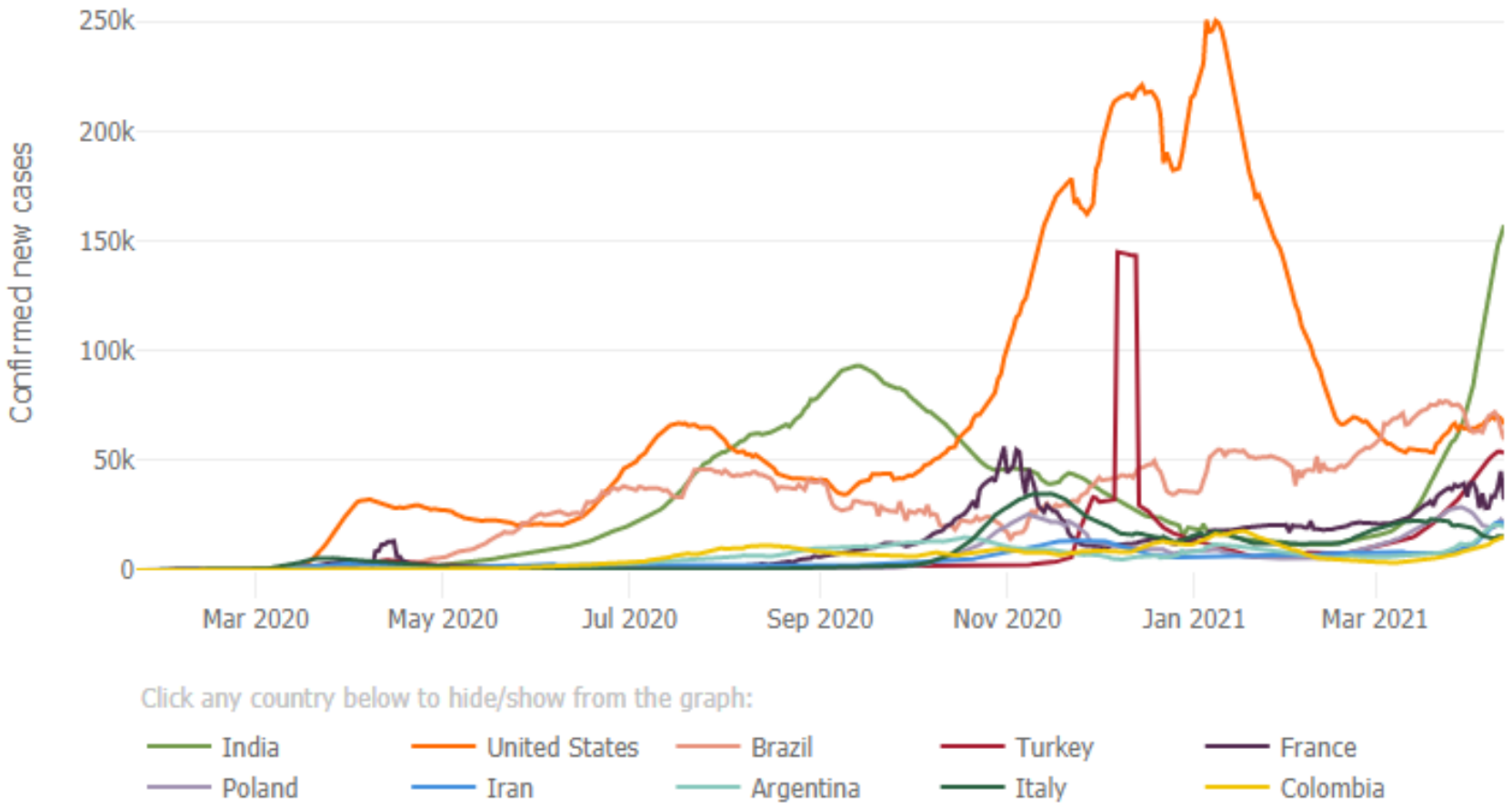
- Epidemiology Update
- Johnson & Johnson Janssen Pause
- Questions & Answers (Q&A)

General Update

- *138.4 million cases globally*
- *31.4 million in U.S.*
- *89,983 cases in New Hampshire*

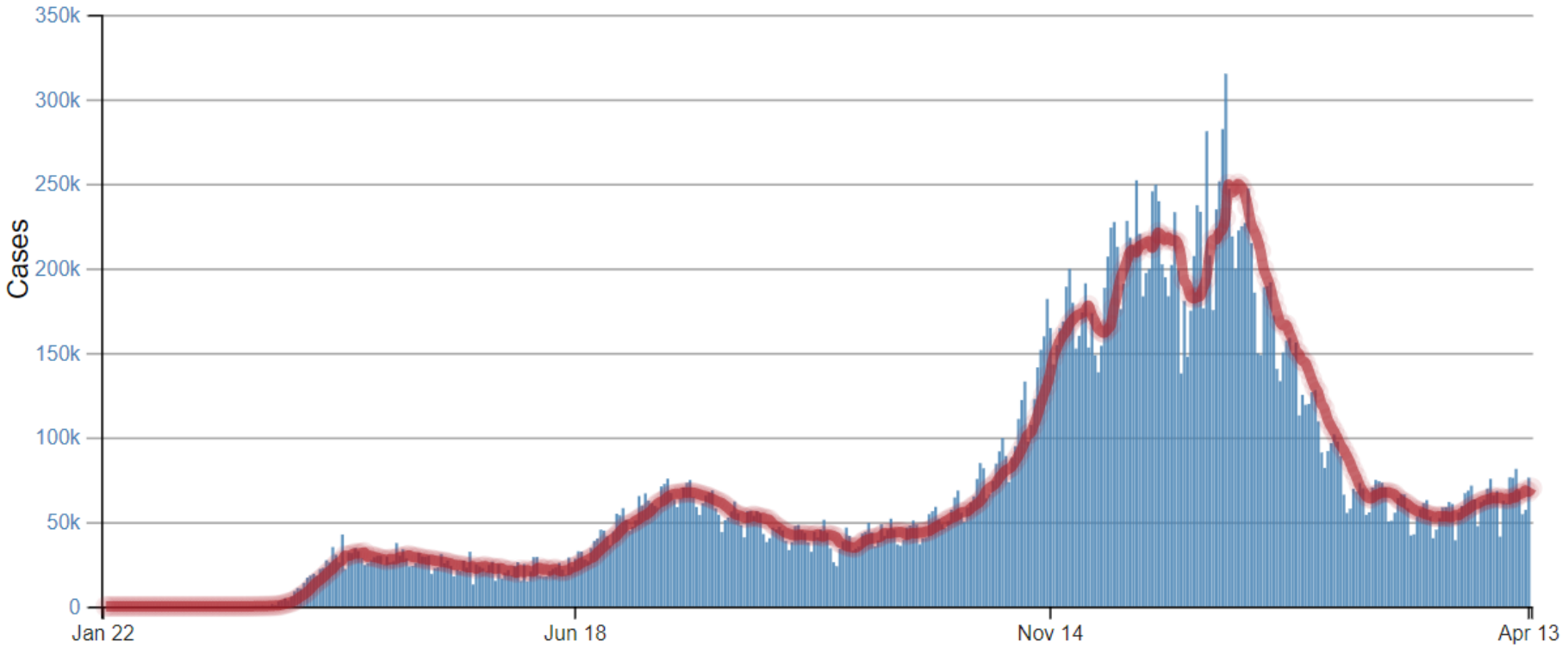
- Stay at Home ended Monday June 15th
  - ***Safer at Home***
- State of Emergency remains in effect
- Re-opening: https://www.covidguidance.nh.gov/

Global Areas of Increasing COVID-19



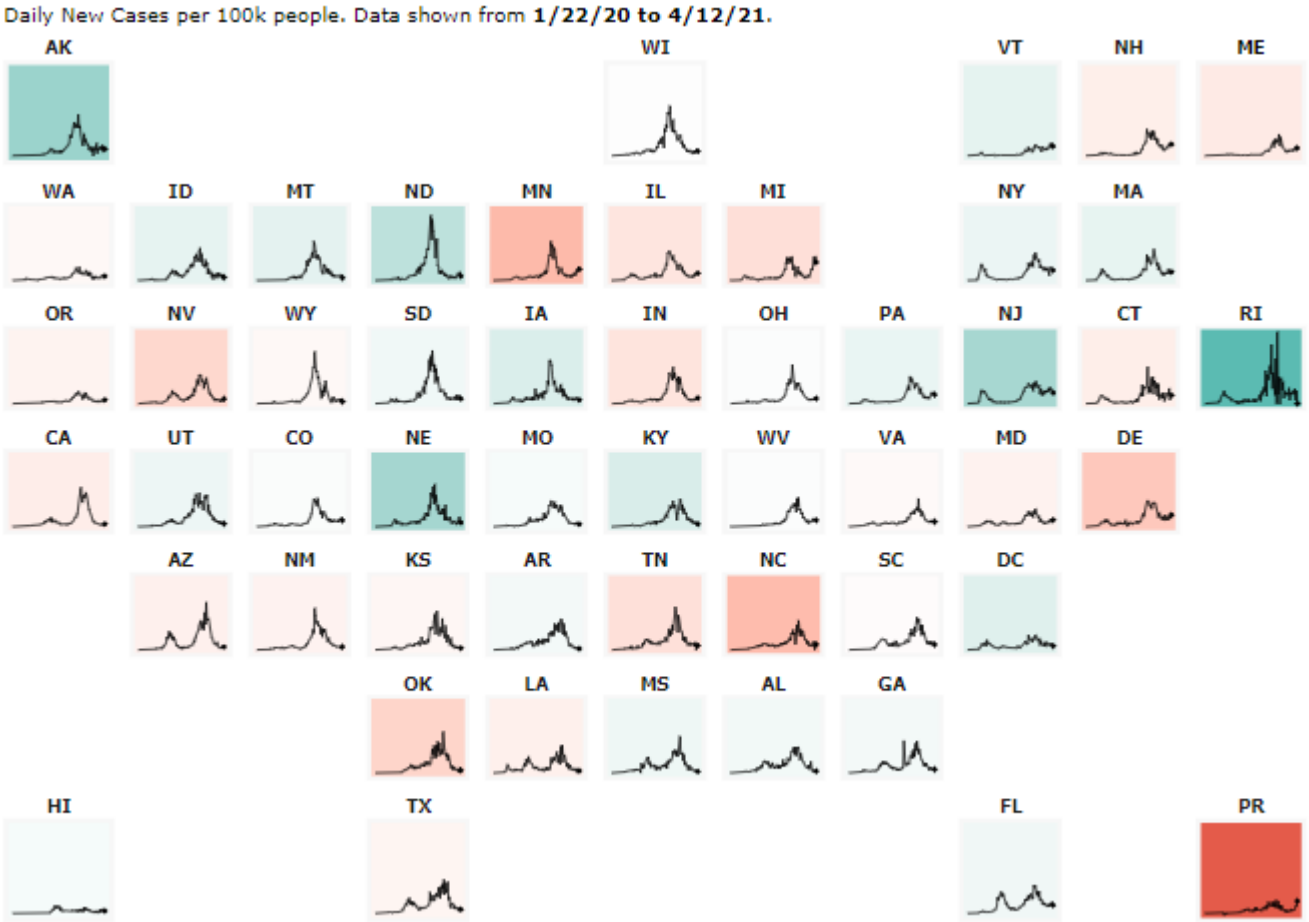
U.S. Epidemic Curve

(new cases per day)



7-day moving average: 69,953 cases per day (increasing)

U.S. Areas of Increasing Case Counts



NH DIVISION OF
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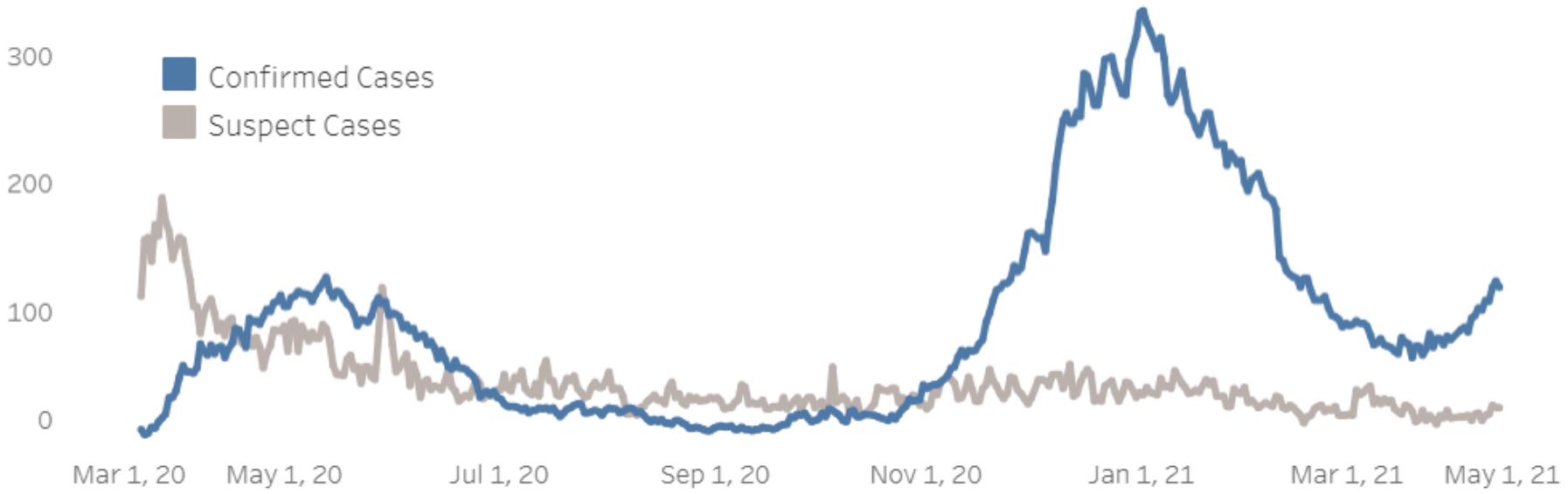
Department of Health and Human Services

NH New Cases by Day

7-day moving average: 440 cases per day (increasing)

NH DIVISION OF
Public Health Services
Department of Health and Human Services

NH Current Hospitalizations

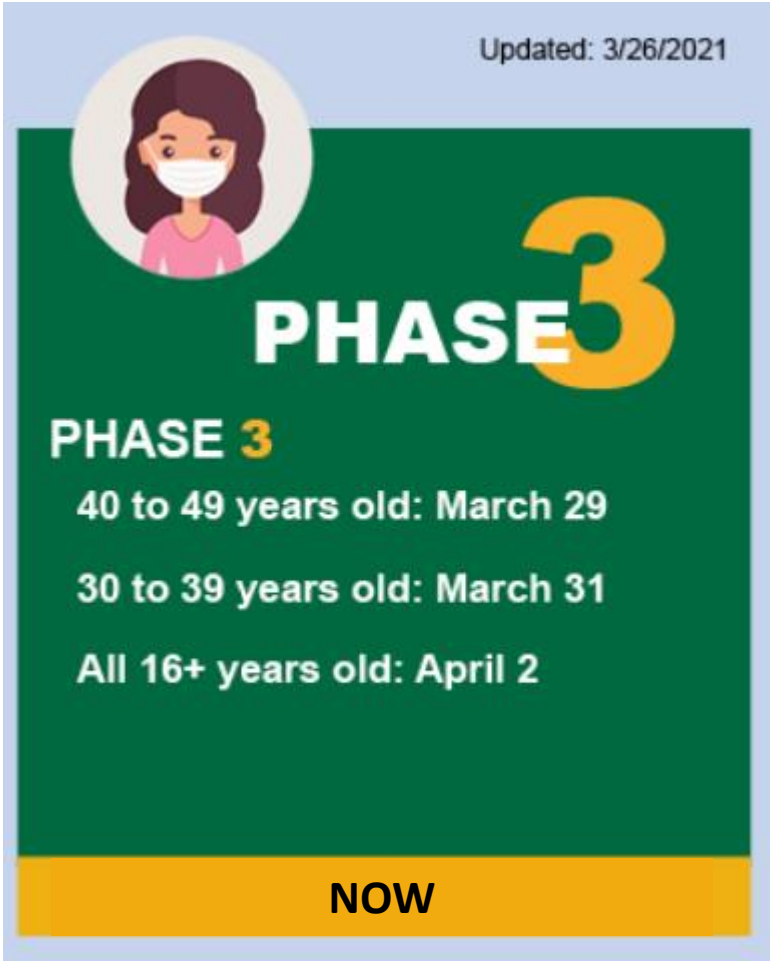


NH Deaths


Stay at Home 1.0
Safer at Home
Stay at Home 2.0
12
10
8
6
4
2
0
Mar 1, 20
May 1, 20
Jul 1, 20
Sep 1, 20
Nov 1, 20
Jan 1, 21
Mar 1, 21
May 1, 21

Vaccine Planning Update

- Phase 3 now open
- Schedule available online
- Receiving around 40,000 to doses weekly
- April 19th: Registration opens to non-NH residents



Progress

United States

Total Vaccine Doses

Delivered	250,998,265
Administered	194,791,836

Learn more about the distribution of vaccines.

People Vaccinated	At Least One Dose	Fully Vaccinated
Total	123,917,385	76,681,252
% of Total Population	37.3%	23.1%
Population ≥ 18 Years of Age	122,950,014	76,465,698
% of Population ≥ 18 Years of Age	47.6%	29.6%

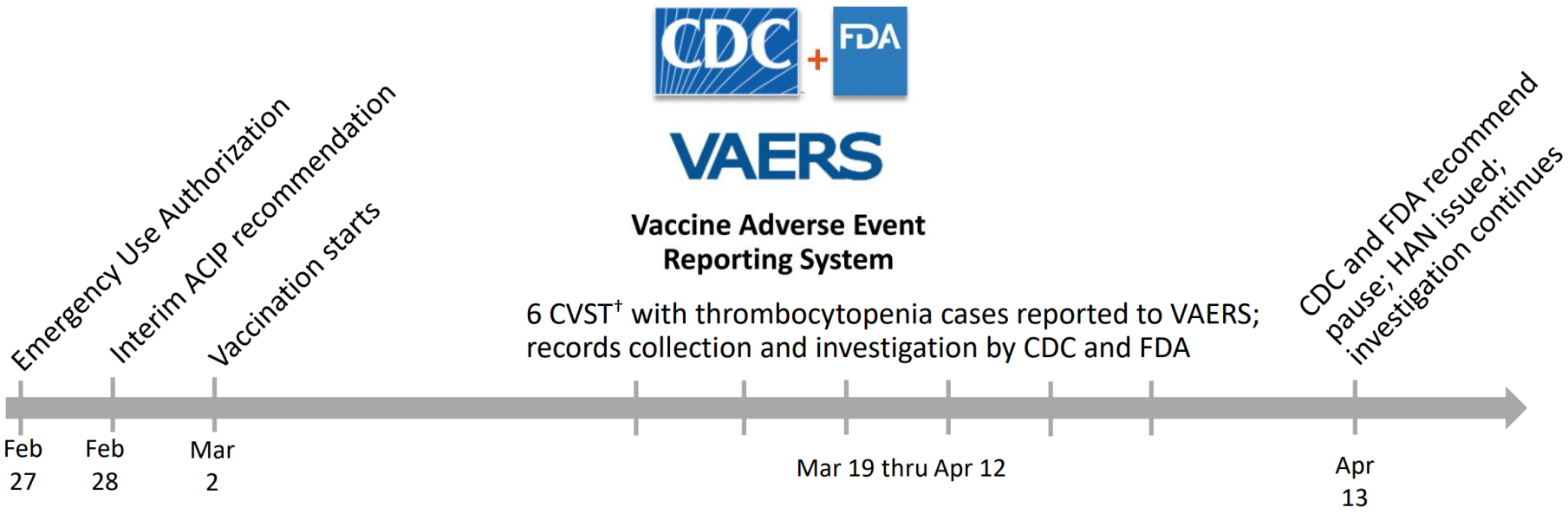
New Hampshire	# of Doses
Total Doses Administered	885,223
1st Doses Administered	586,504 (43%)
2nd Doses Administered	337,574 (25%)

NH DIVISION OF Public Health Services
Department of Health and Human Services

Johnson & Johnson Janssen and Immune Thrombotic Thrombocytopenia

Evolving Situation

J&J Timeline


CDC + FDA
VAERS
Vaccine Adverse Event Reporting System
Emergency Use Authorization
Interim ACIP recommendation
Vaccination starts
6 CVST† with thrombocytopenia cases reported to VAERS; records collection and investigation by CDC and FDA
CDC and FDA recommend pause; HAN issued; investigation continues
Feb 27
Feb 28
Mar 2
Mar 19 thru Apr 12
Apr 13

April 13, 2021: 6 Cases of Cerebral Venous Sinus Thrombosis with Thrombocytopenia

- CDC and FDA announced 6 U.S. cases of cerebral venous sinus thrombosis (CVST) with thrombocytopenia in individuals after receiving the Johnson & Johnson (Janssen) vaccine and recommended vaccine pause
- Joined with data from CDC HAN, 6 cases all negative for active COVID-19
  - All women between 18 and 48yo: none pregnant or postpartum, 1 OCs, 3 obese
  - Symptoms began median 9 days (6-13d) after vaccination
    - Initial presenting symptoms were HA (5 of 6), back pain in 6th, who subsequently developed HA. One patient also had abdominal pain, nausea, and vomiting
    - 4 of 6 had focal neurological symptoms (e.g., focal weakness, aphasia, visual disturbance), prompting presentation for emergency care
  - Hospitalized median 15d (10-17d) after vaccination: all ICU
  - 2 of 6 had portal and splanchnic vein thrombosis

Case Review

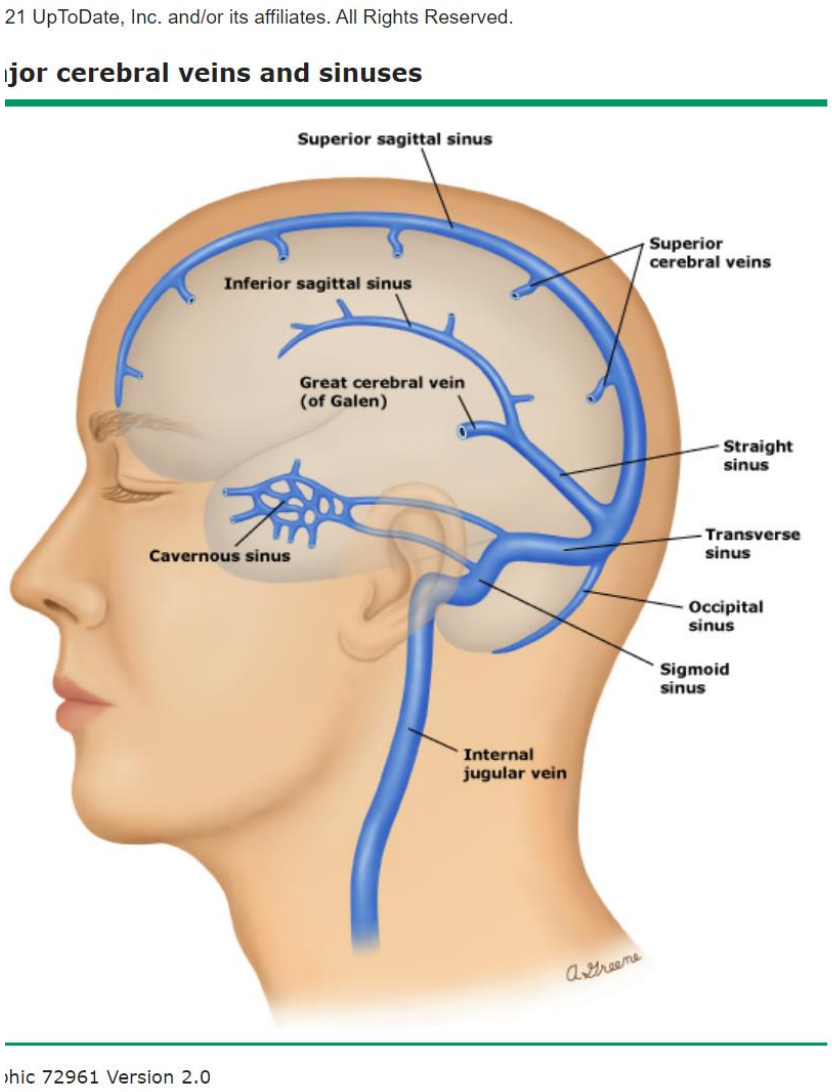
Initial and late signs and symptoms among CVST patients*, N=6 (patients listed in no particular order)

	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

Cerebral Venous Sinus Thrombosis (CVST)

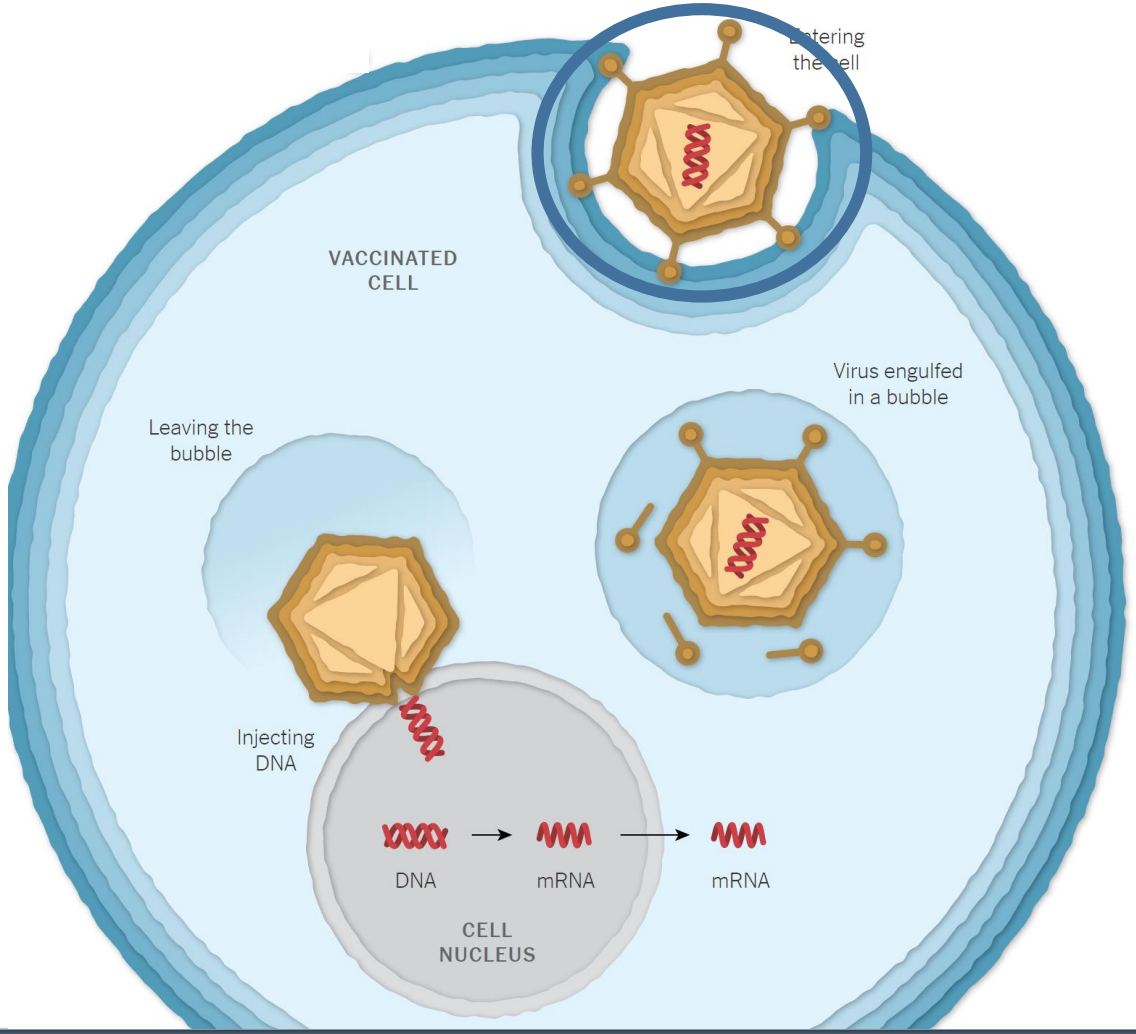
- Blood clot in brain's venous sinuses: prevents blood from draining out of brain such that vessels can leak, hemorrhage
- Symptoms HA, blurred vision, LOC, focal neuro deficits
- Annual incidence of CVST is 0.22-1.57 per 100,000. More common
  - Prothrombotic conditions
  - Women (3:1 ratio)
  - Younger (median age 37y, 8% >65)
- But CVST *with thrombocytopenia* is much less common



Additional Case Details of Thrombotic Thrombocytopenia Complicated by CVST

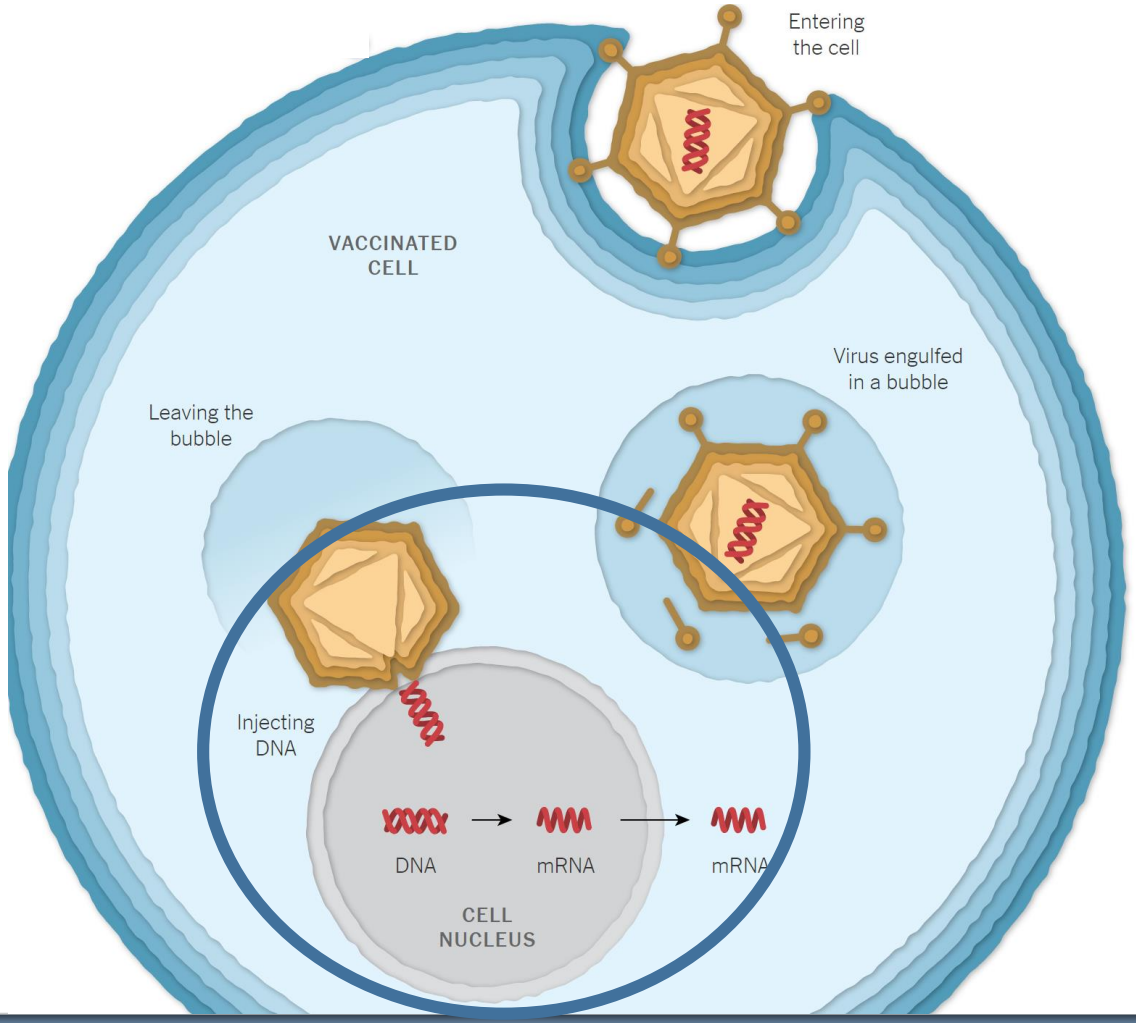
- These 6 cases had platelet count nadir counts ranging from 10,000 to 127,000 during their hospitalizations
- Four patients developed intraparenchymal brain hemorrhage and one died
- Similar to reports of thrombotic events with thrombocytopenia after receipt of the AstraZeneca COVID-19 vaccine in Europe
- Both vaccines contain replication-incompetent adenoviral vectors that encode the spike glycoprotein
  - J&J: human [Ad26.COV2.S]
  - AstraZeneca: chimpanzee [ChAdOx1]

How Do Replication-incompetent Adenoviral Vector Vaccines Work?



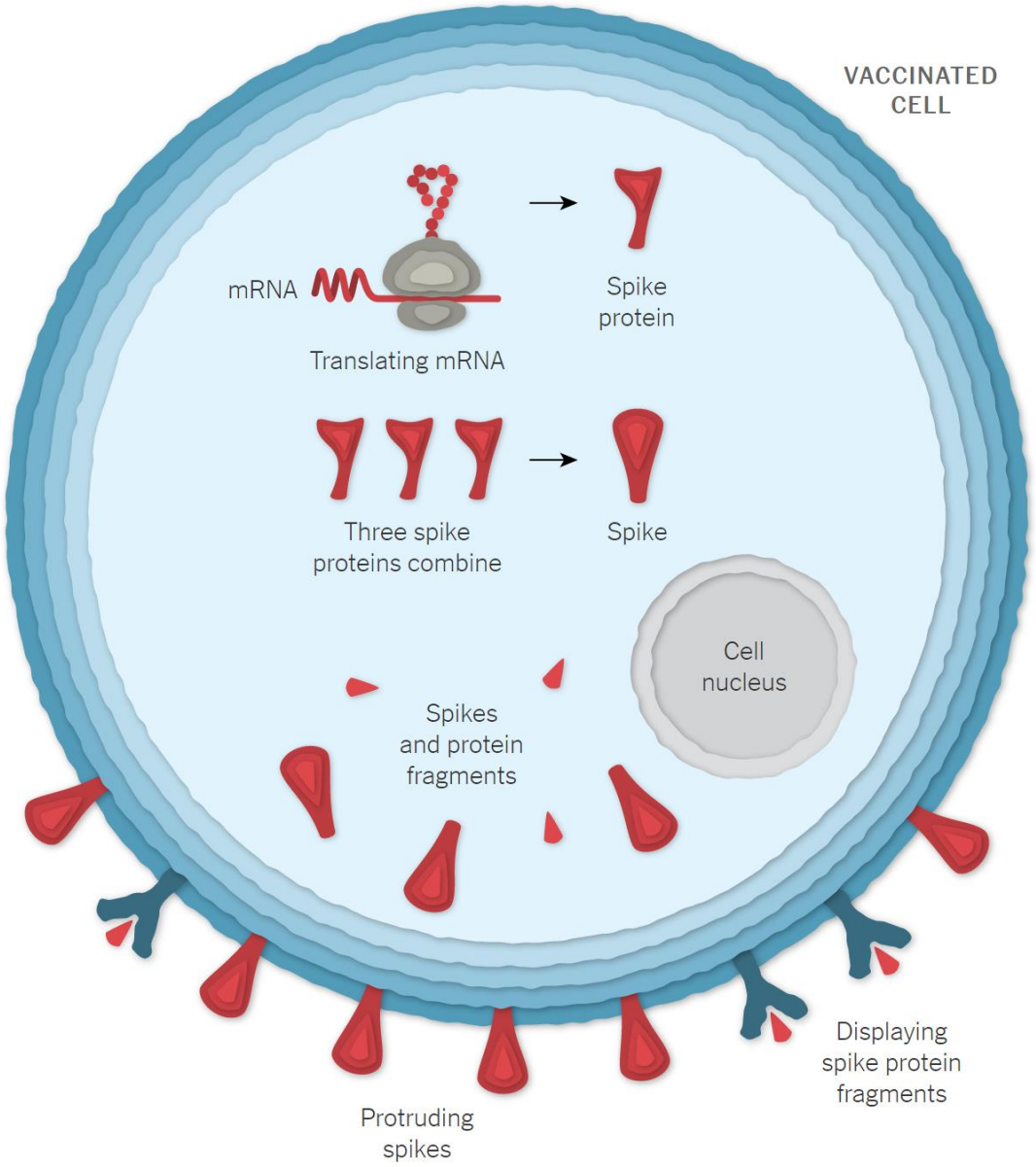
Adenovirus is modified to contain DNA that codes spike protein

How Do Replication-incompetent Adenoviral Vector Vaccines Work?



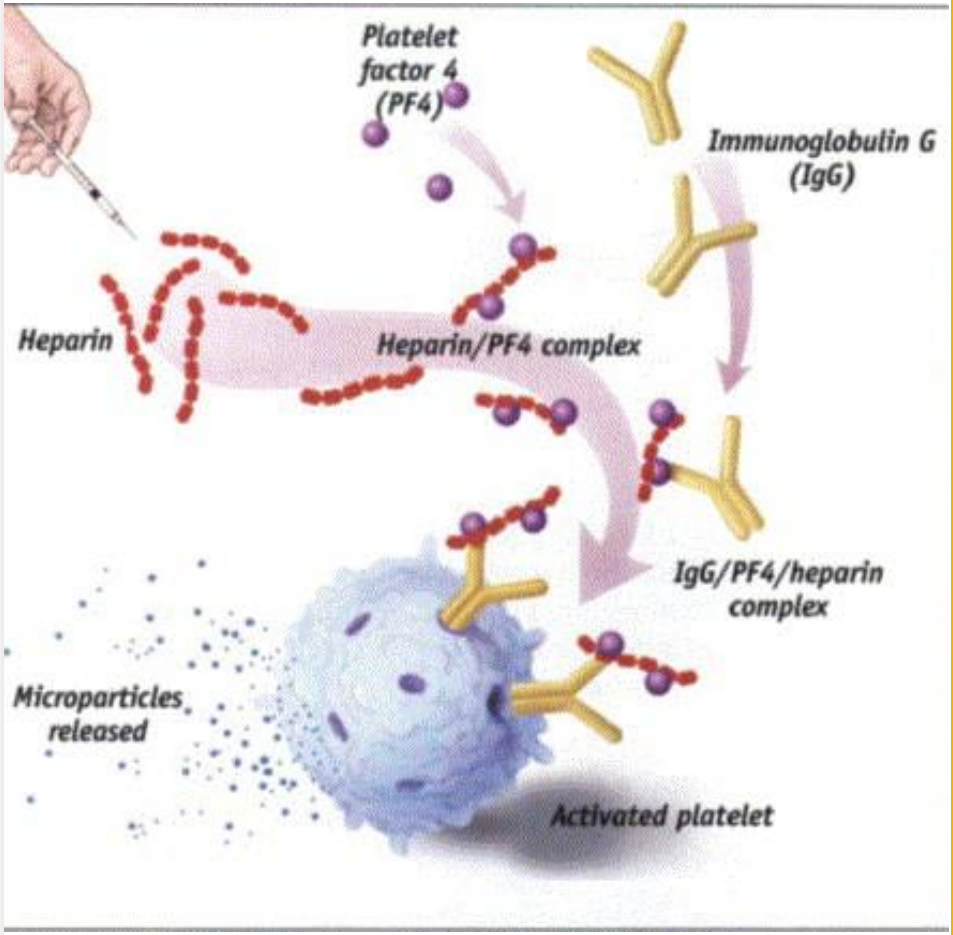
Adenovirus enters our cells and the DNA serves as template for mRNA.

The mRNA is then translated to the spike protein



Investigations into Pathophysiology of AZ SAEs Suggest Cause for J&J

Two German teams simultaneously announced cause of vaccine-induced prothrombotic immune thrombocytopenia in PR last week now in NEJM



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.

- 11 original patients, 9 were women, with median age of 36 years (range, 22 to 49)
- 5 to 16 days after vaccination, patients presented with ≥ 1 thrombotic events, except 1 patient, who presented with fatal intracranial hemorrhage
  - 9 CVST, 3 splanchnic-vein thrombosis, 3 pulmonary embolism, 4 other thromboses
  - 5 patients had DIC
  - 6 died
- All 28 patients who tested positive for antibodies against PF4–heparin tested positive on the platelet-activation assay in the presence of PF4 independent of heparin
  - None of the patients had received heparin before symptom onset
- Platelet activation was inhibited by high levels of heparin, Fc receptor–blocking monoclonal antibody, and immune globulin (10 mg per milliliter)

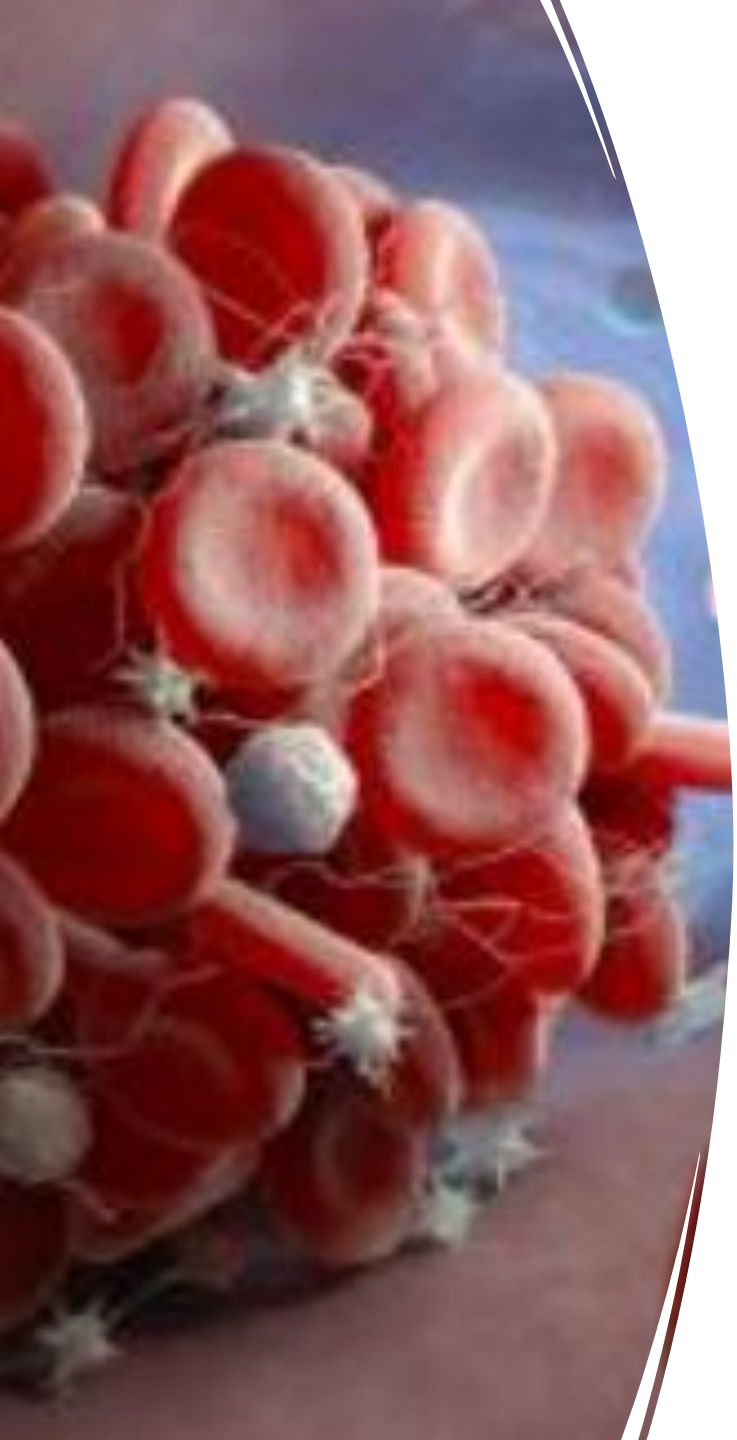
ORIGINAL ARTICLE BRIEF REPORT

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.

Table 1. Characteristics of the Patients.*

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age — yr	37	42	32	39	54
Sex	Female	Female	Male	Female	Female
Preexisting conditions	Pollen allergy	Pollen allergy	Asthma	None	Hypertension
Medication on admission	Contraceptive pill	Contraceptive vaginal ring	None	None	Hormone-replacement therapy, antihypertensive agents
Time from vaccination to admission — days	8	10	7	10	7
Symptoms	Fever, headaches, visual disturbances	Headaches, drowsiness	Back pain	Headaches, abdominal pain	Headaches, hemiparesis
Location of thrombosis	Cortical veins, left transverse sinus, and sigmoid left sinus	Cortical veins, left transverse sinus, and left sigmoid sinus	Portal vein, left hepatic vein, splenic vein, azygos vein, hemiazygos vein, and several basivertebral veins	Inferior sagittal sinus, vein of Galen, straight sinus, right transverse sinus, and right sigmoid sinus	Cortical veins, superior sagittal sinus, both transverse sinuses, and left sigmoid sinus
Platelet count nadir — per mm^3	22,000	14,000	10,000	70,000	19,000
D-dimer peak — mg/liter	>35	>35	>35	13	>35
INR peak	1.2	1.0	1.1	1.3	1.1
aPTT peak — sec	25	31	25	25	29
Fibrinogen nadir — g/liter†	2.1	0.8	2.3	1.2	1.2
SARS-CoV-2 antibody test results					
Nucleocapsid protein	Negative	Negative	Negative	Negative	Negative
Spike protein	Positive	Positive	Positive	Positive	Positive
Anticoagulation treatment	Initial low dose of LMWH	Reduced dose of LMWH	Reduced dose of LMWH	Reduced dose of LMWH	Heparin (5000 IU)
No. of platelet units transfused	7	19	2	0	2
Other treatment	None	Methylprednisolone (1 mg/kg), IVIG (1 g/kg)	Prednisolone (1 mg/kg), IVIG (1 g/kg)	Prednisolone (1 mg/kg), IVIG (1 g/kg)	Methylprednisolone (1 mg/kg), IVIG (1 g/kg)
Outcome	Fatal	Fatal	Full recovery	Full recovery	Fatal



April 7 EMA Report

- As of Apr 4, EU surveillance received 169 reports of CVST and 53 reports of splanchnic vein thrombosis among 34M AZ vaccinees
- EMA analyzed 62 cases of CVST and 24 cases of splanchnic vein thrombosis - 18 deaths
  - Most occurred in women within 2w of first dose
- Recommended unusual blood clots with low platelets should be listed as very rare side effects within 2w of vaccination
  - Seek care immediately if they experience symptoms such as shortness of breath, chest, pain, leg swelling, persistent abdominal pain

April 7 MHRA Report

79 cases reported through Mar 31 following AZ vaccine

- 44 CVST with thrombocytopenia and 35 thrombosis of major veins with thrombocytopenia
- Majority were in younger recipients and 58 in women
  - More women have been vaccinated
- All occurred after first dose, and 19 people died
- 20.2M vaccinated in UK so overall risk of 4 in 1M

Give to people at higher risk of blood clots if benefits outweigh potential risk

Pregnant women should discuss the vaccine decision with their health provider, given known thrombotic risk

Swift Response to CDC/FDA Announcement About J&J

- CDC/FDA recommended pause in use of J&J vaccine out of an abundance of caution
- NH DHHS immediately followed with statewide pause: NH DHHS HAN, outreach to all vaccinating partners, press release
- Joint Media Call: FDA & CDC to Discuss Janssen COVID-19 Vaccine
- ACOG Statement
- Emergency ACIP meeting April 14

ACOG Statement

- “At this time, there is no clear phenotype of women who are more or less likely to experience this rare complication
- However, until there is a better understanding of the frequency and impact of this finding, it will be important to encourage pregnant and postpartum women who wish to be vaccinated to receive the mRNA vaccines: Pfizer or Moderna.
- Individuals who have been vaccinated with the J&J vaccine within the last 21 days who experience severe headache, abdominal pain, leg pain, or shortness of breath should seek immediate evaluation
- They should be certain to communicate that they have received the J&J vaccine to prompt appropriate evaluation
- Given the elevated risk for thrombosis experienced by women during pregnancy or the postpartum period and while using birth control pills, evaluation of acute thrombosis is commonly performed in our specialty. Rapid treatment with anticoagulation is the standard; however, this is not the same event and anticoagulation for treatment of CVST is dangerous.”

ACIP Meeting April 14, 2021

Janssen Phase III Pivotal Trial

Study 3001 – Venous Thrombosis Events (N=43,783 vaccinated)

TSFAE_VTE_COV3001:	Study 3001 AEs			
	All AEs			
	Number of Cases up to 28 Days after Vaccination		Total Number of Cases	
	Ad26.COV2.S	Placebo	Ad26.COV2.S	Placebo
DVT	4 [c]	2	11	3 [a]
PE	2	1	8	4[a]
CVST	1 [b]	0	1	1
Venous thrombosis limb	1	0	1	0
embolism venous	0	0	1	0

[a] One individual in placebo experienced both DVT and PE: This individual had a SARS-CoV-2 PCR (+) nasal swab 4 days after th thrombosis

[b] Only one participant on Ad26 had low platelets (CVST)

[c] A second individual in Ad26.COV2.S group had multiple SARS-CoV-2 PCR (+) nasal swabs in the 2 weeks preceding the DVT.

[TSFAE_VTE_COV3001.RTF] [VAC31518\Z_ADHOC\DBR_ONESAFETY\RE_ONESAFETY\PDEV\VTE_SUMMARY_OUTPUT.SA
08APR2021, 11:

ACIP Meeting (2)

Janssen Phase III Two-Dose Pivotal Trial

Study 3009 – Venous Thrombosis Events (N=28,277 vaccinated)

TSFAE_VTE_COV3009: Study 3009 AEs (2 Dose Trial): Ongoing Blinded		
	All AEs	
	Number of Cases up to 28 Days after Vaccination	Total Number of Cases
DVT	0	2
PE	1	4
CVST	0	0
[TSFAE_VTE_COV3009.RTF] [VAC31518\Z_ADHOC\DBR_ONESAFETY\RE_ONESAFETY\PDEV\VTE_SUMMARY_OUTPUT.SAS] 08APR2021, 11:10		

No CVSTs observed with Janssen adenovirus vaccine program in Ebola and RSV

ACIP Meeting (3)

Sisonke Open Label Study in South African HCPs (N=272,438)

As of 09 Apr 2021:

- No CVST cases reported
- One case of PE (no information on platelet or covid status)
- One case of CVA (age: 38 years old, female, 8 days after vaccination) - we are actively seeking additional information on this case
- One case of retinal vein thrombosis (age: 68 years old, diabetic, platelet count normal)

ACIP Meeting (4)

As of 14 Apr 2021

SOURCE	CASE	CIOMS #	SERIOUS ADVERSE EVENT	RISK FACTOR(S)	PLATELET COUNT	COVID STATUS	TTO	Treatment	Status
CLINICAL TRIAL CASES									
Study 3001	25 YO Male on Vaccine	**20201017267**	CVST with hemorrhage	Stenosis of transverse sinus, URI suspected	64,000 (Anti-PF4+)	Negative	8 days	Heparin TPA and platelets, angioplasty and thrombectomies	Recovered
Study 3001	24 YO female on **placebo**	**20210202793**	CVST	Newly prescribed OCP	Normal (Anti-PF4-)	Negative	>50 days	N/A	Recovered
POST-AUTHORIZATION CASES									
VAERS # 1114806	45 YO female	**20210354798**	CVST with hemorrhage	none	"thrombocytopenia"	Unknown	11 days	Unknown	Fatal
VAERS 1133212	38 YO female	**20210408478**	CVST	Unknown	Unknown	Unknown	10-14 days	Heparin	Not Recovered at this time
VAERS #1141160-1	59 YO Female	**20210407977**	Extensive DVTs	Coronary artery disease	15,000	Unknown	7 days	Vena cava filter-IVC, thrombectomy	Not Recovered at this time
Janssen SAE Nevada	18 YO female	**20210407314**	CVST with hemorrhage	unknown	16,000	Unknown	14 days	Heparin then switched to "British guidelines" and thrombectomy	Not Recovered at this time
Janssen SAE (NEJM -editor notification) Nebraska	48 YO female	**20210415297**	TTP, splanchnic veins thrombosis, CVST, then given heparin and then additional hepatic and splanchnic vein thrombosis	Unknown	<13,000 (hi d-dimer, Anti-PF4+)	Negative	14 days	Heparin first and switched to argatroban then IVIG	Not Recovered at this time
Janssen SAE NJ/PA	26 YO female	**20210416236**	CVST, PE, portal vein thrombosis	Obesity	120,000 (hi d-dimer, Anti-PF4+)	Negative	7 days	Heparin and then IVIG	Discharged from hospital
VAERS 1182133	28 YO female	**In processing**	Details pending, FOI requested						

ACIP Did Not Elect to Vote

- Need data on relationship between COVID and thrombotic thrombocytopenia
- Seeking data on more cases reported following “stimulated reporting”
- Interrogating VAERS data on thrombotic thrombocytopenia associated with other available vaccines
- Collaborating with EU counterparts re: EUDRAVIGILANCE

April 13, 2021 CDC HAN

- "Pause the use of the J&J COVID-19 vaccine until the ACIP is able to further review these CVST cases in the context of thrombocytopenia and assess their potential significance.
- Maintain a high index of suspicion for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the J&J 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 J&J 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 J&J 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 J&J 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."

Guidance for Diagnosing AZ Vaccine-induced Prothrombotic Immune Thrombocytopenia

Figure 1: Decision Tree for Diagnosing and Ruling Out VIPIT

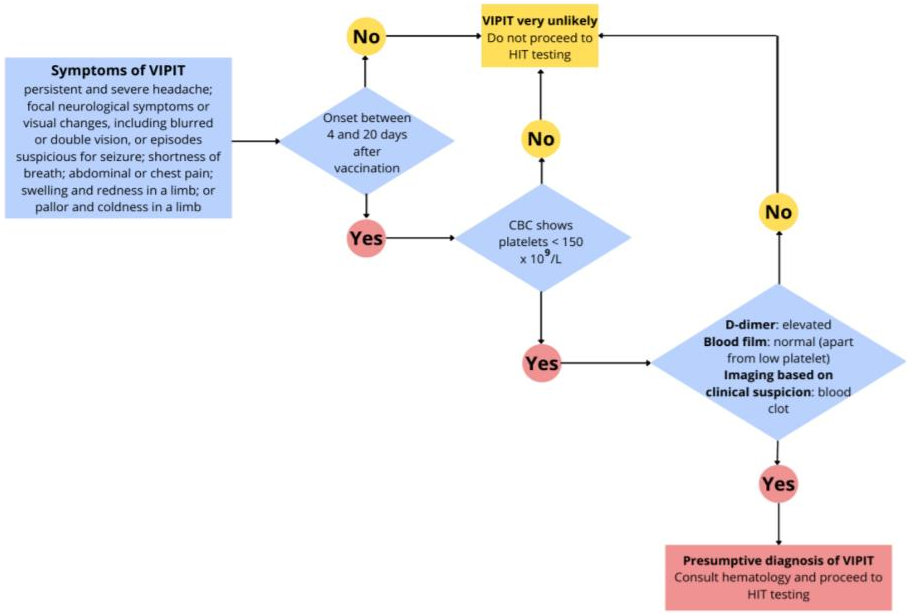


Image adapted and used with permission from Science Briefs of Ontario

Treating Blood Clots in Patients with Presumptive or Confirmed VIPIT

- No heparin
- No platelet transfusions
- First line anticoagulants: direct oral anti-Xa inhibitors (e.g. rivaroxaban, apixaban, edoxaban)
- Consult hematologist
- IVIG 1g/kg daily for at least 2 days for sever or life-threatening thrombosis.

VIPIT Treatment

Recommendations for Patients

This notification is reflective of our commitment to safety and transparency during this COVID-19 Vaccine campaign and was issued in an abundance of caution

This possibly-associated adverse event is extremely rare and, for most people, the benefits of the COVID-19 vaccines far outweigh the risks

People who have received the J&J vaccine who develop severe headache, abdominal pain, leg pain, or shortness of breath within three weeks after vaccination should be evaluated

- Note we expect people may have side effects including headache from vaccine and these are common in the first 3 days, unlike severe HA developing ≥6d after vaccine

Patients can report adverse events to VAERS

COCA Clinical Educational Opportunity

- TODAY: CDC Clinician Outreach and Community Activity (COCA) call April 15, 2021 at 2:00 pm EDT: Johnson & Johnson/Janssen COVID-19 Vaccine and Cerebral Venous Sinus Thrombosis with Thrombocytopenia – Update for Clinicians on Early Detection and Treatment. Speakers will discuss what is known about CVST, the importance of early detection, and updated vaccine recommendations. Call information is below:
- https://www.zoomgov.com/j/1614336614?pwd=ZVhQUHoyaG4zVFdua2czcE9EU20wUT09
- Telephone: (669) 254 5252 or (646) 828 7666
- Webinar ID: 161 433 6614
- Passcode: 160026
- Post-Event Recording: https://emergency.cdc.gov/coca/calls/2021/callinfo_041521.asp