CDC/IDSA COVID-19 Clinician Call April 24, 2021

Welcome & Introduction

Dana Wollins, DrPH, MGC

Vice President, Clinical Affairs & Guidelines

IDSA

- 63rd in a series of weekly calls, initiated by CDC as a forum for information sharing among frontline clinicians caring for patients with COVID-19
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

TODAY'S TOPICS

 Multisystem Inflammatory Syndrome in Adults (MIS-A)

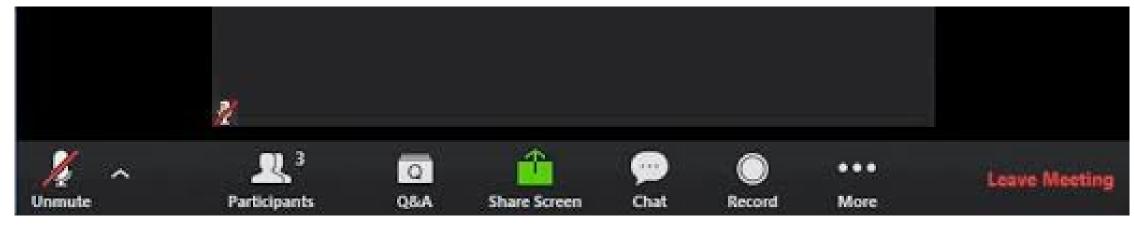
 April 23rd ACIP Meeting Update: Janssen (Johnson & Johnson) COVID-19 Vaccine

Question? Use the "Q&A" Button





Comment?
Use the "Chat" Button



Multisystem Inflammatory Syndrome in Adults (MIS-A)



Ermias Belay, MD

Lead MIS Unit
Clinical Disease and Health Services Team
COVID-19 Response
Centers for Disease Control and Prevention



Michael Threlkeld, MD
Founder, Threlkeld Infectious Disease
Hospital Epidemiologist and
Medical Director of Employee Health
Baptist Memorial Hospital at Memphis



Stephen Threlkeld, MD

Managing Member, Threlkeld Infectious Disease

Medical Director for Infectious Disease

Baptist Memorial Healthcare

Assistant Clinical Professor

University of Tennessee



Sapna Bamrah Morris, MD, MBA, FIDSA

Clinical Disease and Health Systems Team Lead Health Systems and Worker Safety Task Force CAPT, U.S. Public Health Service Centers for Disease Control & Prevention

Multisystem Inflammatory Syndrome in Adults (MIS-A) Associated with SARS-CoV-2 Infection

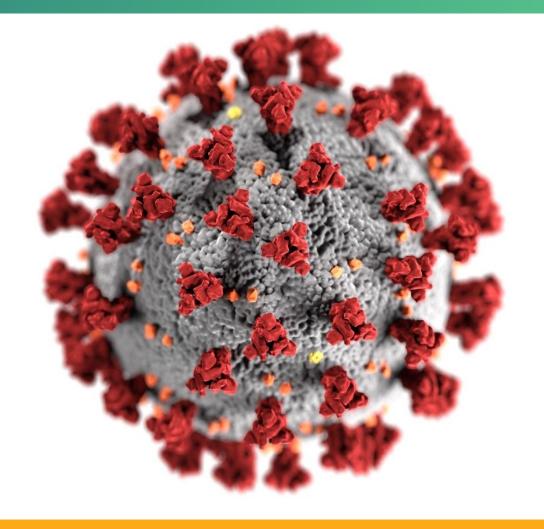
Ermias Belay, MD

Lead, MIS Unit

COVID-19 Response

Centers for Disease Control and Prevention

April 24, 2021





cdc.gov/coronavirus

Multisystem Inflammatory Syndrome

- Initially described in children (MIS-C) in April 2020
- Characterized by shock, cardiac dysfunction, GI symptoms, and elevated inflammatory markers
- As of mid-April 2021, 3185 MIS-C cases reported to CDC
- Similar syndrome described in adults in June 2020 (MIS-A)



Morbidity and Mortality Weekly Report

Case Series of Multisystem Inflammatory Syndrome in Adults Associated with SARS-CoV-2 Infection — United Kingdom and United States, March-August 2020

Sapna Bamrah Morris, MD¹; Noah G. Schwartz, MD^{1,2}; Pragna Patel, MD¹; Lilian Abbo, MD³; Laura Beauchamps, MD³; Shuba Balan, MD³; Ellen H. Lee, MD⁴; Rachel Paneth-Pollak, MD⁴; Anita Geevarughese, MD⁴; Maura K. Lash, MPH⁴; Marie S. Dorsinville, MPH⁴; Vennus Ballen, MD⁴; Daniel P. Eiras, MD⁴; Christopher Newton-Cheh, MD^{5,6}; Emer Smith, MPH^{7,8}; Sara Robinson, MPH⁷; Patricia Stogsdill, MD⁹; Sarah Lim, MBBCh¹⁰; Sharon E. Fox, MD, PhD^{11,12}; Gillian Richardson, MPH¹³; Julie Hand, MSPH¹³; Nora T. Oliver, MD¹⁴; Aaron Kofman, MD¹⁵; Bobbi Bryant, MPH^{1,16}; Zachary Ende, PhD^{1,16}; Deblina Datta, MD¹; Ermias Belay, MD¹; Shana Godfred-Cato, DO¹

On October 2, 2020, this report was posted as an MMWR Early Release on the MMWR website (https://www.cdc.gov/mmwr).

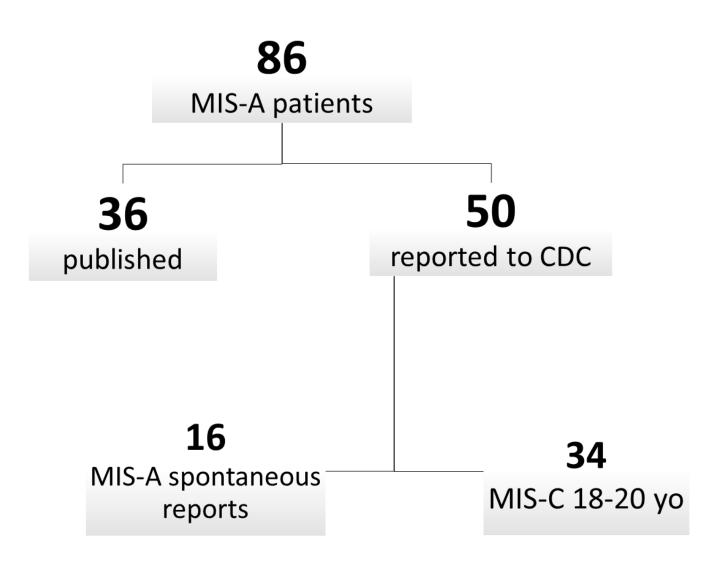
During the course of the coronavirus disease 2019 (COVID-19) pandemic, reports of a new multisystem inflammatory syndrome in children (MIS-C) have been increasing in Europe and the United States (1–3). Clinical features in children have varied but predominantly include shock, cardiac dysfunction,

cases. The case report form included information on patient demographics, underlying medical conditions, clinical findings, complications, laboratory test results including those from SARS-CoV-2 testing, imaging findings, treatments, and outcomes. Two clinician reviewers selected patients who fulfilled the working MIS-A case definition used in this report, which included the following five criteria: 1) a severe illness

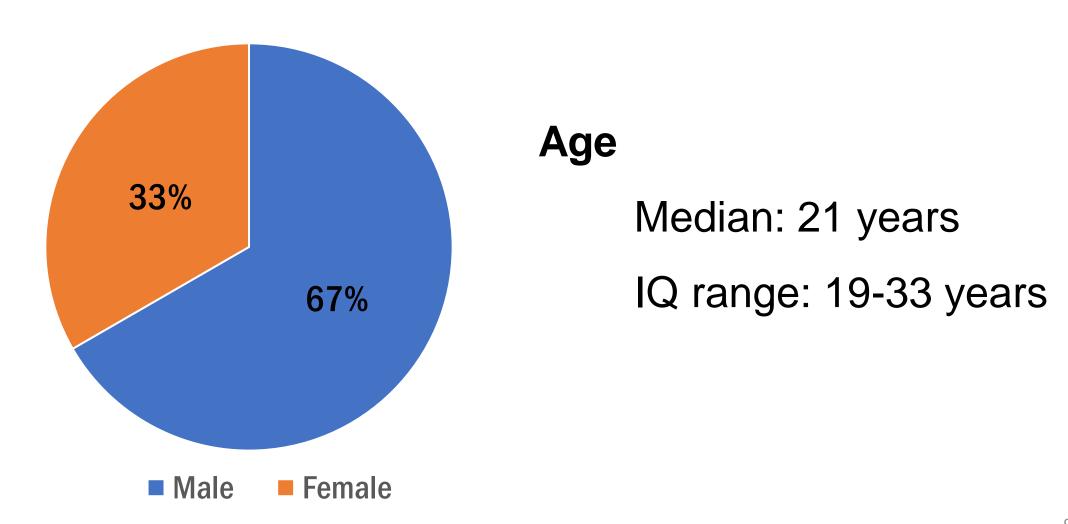


Summary of Known MIS-A Patients

Draft manuscript



Epidemiology of MIS-A (N=86)



Signs and symptoms in patients with MIS-A (N=86)* and MIS-C (1733)**

	PERCENT		
Sign/Symptom	MIS-A	MIS-C	
GI (Abd pain, vomiting, diarrhea)	84		
Hypotension	63	51	
Shortness of Breath	56	27	
Shock	53	37	
Chest pain	41		
Rash	37	57	
Cough	35		
Conjunctival Injection	27	53	

^{*}Unpublished manuscript

^{**}JAMA Pediatrics, April 6, 2021

Clinical Findings in patients with MIS-A (N=86)* and MIS-C (1733)**

Clinical finding	PERCENT		
	MIS-A	MIS-C	
Cardiac dysfunction	55	31	
Myocarditis	40	17	
Pericardial effusion	28	23	
Acute Kidney Injury	32		
Pneumonia	22	19	

^{*}Unpublished manuscript

^{**}JAMA Pediatrics, April 6, 2021

Treatment approaches in patients with MIS-A (n=86)* and MIS-C (1733)**

Treatment	PERCENT		
	MIS-A	MIS-C	
Steroids	62	71	
Vasoactive med.	59	40	
Intravenous immune globulin	44	81	
Mech. ventilation	32	12	

^{*}Unpublished manuscript

^{**}JAMA Pediatrics, April 6, 2021

Preceding COVID-19 and outcomes in patients with MIS-A (N=86) and MIS-C (1733)**

	PERCENT			
	MIS-A	MIS-C		
Preceding COVID-19	63	25		
ICU admission	75	58		
Death	12	1.4		

^{*}Unpublished manuscript

^{**}JAMA Pediatrics, April 6, 2021

Georgia MIS-A Case Finding Project

Objective

To identify MIS-A cases among patients hospitalized with COVID-19 in metro Atlanta

Compare clinical manifestation of MIS-A with COVID-19 to help develop a more specific case definition

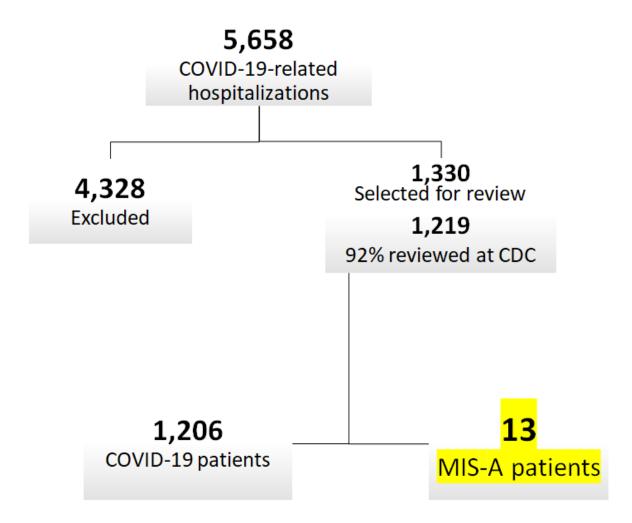
Collaborators

Georgia Department of Public Health

Major health care system – 4 hospitals



MIS-A patients identified from 4 hospitals, Georgia, Apr 2020 – Jan 2021





Georgia MIS-A Case Finding Project

MIS-A vs COVID-19 hospitalizations

The 13 MIS-A patients represented 0.2% of COVID-19-related hospitalizations in the 4 Georgia hospitals

In contrast

In one major children's hospital system serving metro Atlanta, about 36% of COVID-19-related hospitalizations were for MIS-C



Primary MIS-A Manifestations

Cardiovascular

Includes shock/hypotension, decreased cardiac function, myocarditis, pericardial effusion

Mucocutaneous

Includes rash, non-purulent conjunctivitis



CDC's MIS-A Case Definition

- Age ≥ 21 yrs with subjective or documented fever (≥38.0 C) for 24 hrs prior to or within THREE days of hospitalization; AND
- 2. A positive SARS-CoV-2 test during current illness (by RT-PCR, serology, or antigen detection); AND
- 3. Laboratory evidence of severe inflammation*; AND
- 4. Illness requiring hospitalization for ≥24 hrs; AND
- 5. At least THREE of the following occurring within THREE days of hospitalization; at least ONE must be a primary criterion:
 - Primary clinical criteria:
 - Severe cardiac illness[§];
 - Rash AND non-purulent conjunctivitis
 - Secondary clinical criteria:
 - New-onset neurologic signs and symptoms[¶]
 - Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy);
 - Abdominal pain, vomiting, or diarrhea
 - Thrombocytopenia (platelets <150,000/mL)
- 6. No other apparent diagnosis (e.g., bacterial sepsis, exacerbation of a chronic medical condition)

*Elevated levels of at least TWO of the following: C-reactive protein, ferritin, IL-6, erythrocyte sedimentation rate, procalcitonin §Myocarditis, pericarditis, coronary artery dilatation/aneurysm, or new onset: ventricular dysfunction (LVEF<50%), 2nd/3rd degree A-V block, or ventricular tachycardia. Cardiac arrest alone does not meet this criterion.

[¶]Encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain-Barré syndrome)

5. At least three of the following occurring within three days of hospitalization – at least one must be a primary criterion

a. Primary clinical criteria

- Severe cardiac illness
- Rash and non-purulent conjunctivitis

b. Secondary clinical criteria

- New-onset neurologic signs and symptoms
- Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy)
- Abdominal pain, vomiting, or diarrhea
- Thrombocytopenia (platelets <150,000/mL)



Severe cardiac illness (any one of the following)

- Myocarditis
- Pericarditis
- Coronary artery dilatation/aneurysm
- New-onset right or left ventricular dysfunction (LVEF <50%)
- New-onset arrhythmia: 2nd/3rd degree A-V block or ventricular tachycardia
- Note: Cardiac arrest alone does not meet this criterion.

New-onset neurologic signs and symptoms (any one of the following)

- Encephalopathy in a patient without prior cognitive impairment
- Seizures
- Meningeal signs
- Peripheral neuropathy, including Guillain-Barré syndrome



Summary

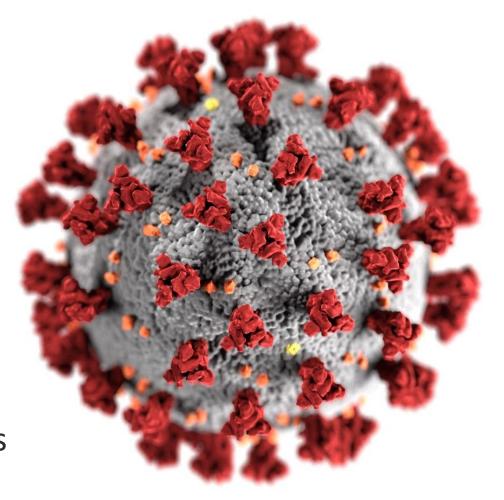
- Overlapping clinical manifestations with MIS-C
- MIS-A can be complicated by other underlying illnesses
- Distinguishing MIS-A from severe COVID-19 with multi-organ failure may not be easy with high COVID-19 incidence
- Although MIS-A might be under-diagnosed, it occurs at a much lower frequency than MIS-C



Acknowledgements

- Shana Godfred-Cato
- Michael Melgar
- Jennifer DeCuir
- Kathryn Arnold
- Qi Cheng
- Lu Meng
- Teresa Hammett
- Pragna Patel
- Julia Haston
- Angela Campbell
- Sapna Bamrah Morris

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



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.



MIS-A

Michael and Stephen Threlkeld, MDs

4/24/21

Case Presentation

- 36 yo male physician with 4 day ho high fevers. Recorded to 40.5 deg C
- No major past medical history. ? of Gilbert's
- Approximately 3 weeks post second dose of Pfizer covid-19 vaccination. No prior covid diagnosis and no severe reactions to vaccine.
- Needle stick exposure one week prior but source neg for usual tested viruses
- Has a farm with a barn and possible rodent exposure but > 2 weeks ago
- ? brief nonspecific febrile illness 6 weeks pta

Case Presentation - complaints

- Sore throat and some swallowing pain
- Some palpable cervical nodes
- Loose stools and mild abdominal pain
- Generalized body aches
- Conjunctivitis
- Asymmetrical areas of skin erythema/rash esp left groin and thigh

Case Presentation - exam findings

- Awake and alert
- Febrile
- Tachycardic
- Reddened conjunctiva; pharynx slightly red; palpable nodes in neck
- Chest clear
- No murmurs
- Abd soft and mildly tender
- Erythematous skin areas on thighs and groin > on left

Case Presentation - Labs / imaging

- Blood cultures negative
- Wbc 11,000 95% polys
- Plt 110,000
- Esr 40
- D dimer 5.2
- Hiv serol neg
- Monospot neg
- Total bili 1.9
- C dif neg
- Molecular stool panel neg
- ANA neg
- Ehrlichia pcr neg
- Leptospira pcr neg
- Francisella serol neg

- Covid 19 IgG serol positive
- Covid 19 nasal pcr neg
- CRP 284
- Ferritin 1435
- Troponin 18
- Echocardiogram global hypokinesis, lv ef 25%
- Chest initially clear subsequently with cardiac enlargement and pl effusions

Treatments Administered

- Empiric abx: Ceftriaxone and doxycycline
- 2 g / kg ivig in 2 divided doses
- Steroids solumedrol 125 mg
- Vent support
- ecmo

							, .			
age	sex	fever	rash	sore throat	crp	ferritin	troponin	EF	covid hx	covid igG ab +
25	F	40.5	yes	no	308	1302	1	55%	yes	not done
			-							
36	M	40.5	VOC	VOS	284	1434	18	25%	no	VOS
30	IVI	40.5	yes	yes	204	1434	10	23%	no	yes
18	М	39.5	yes	no	265	1243	nrl	45%	yes	yes
20	_	20.5	1/65	V65	254	F07	0.140	240/	m =	Ves
29	F	39.5	yes	yes	354	537	0.112	31%	no	yes



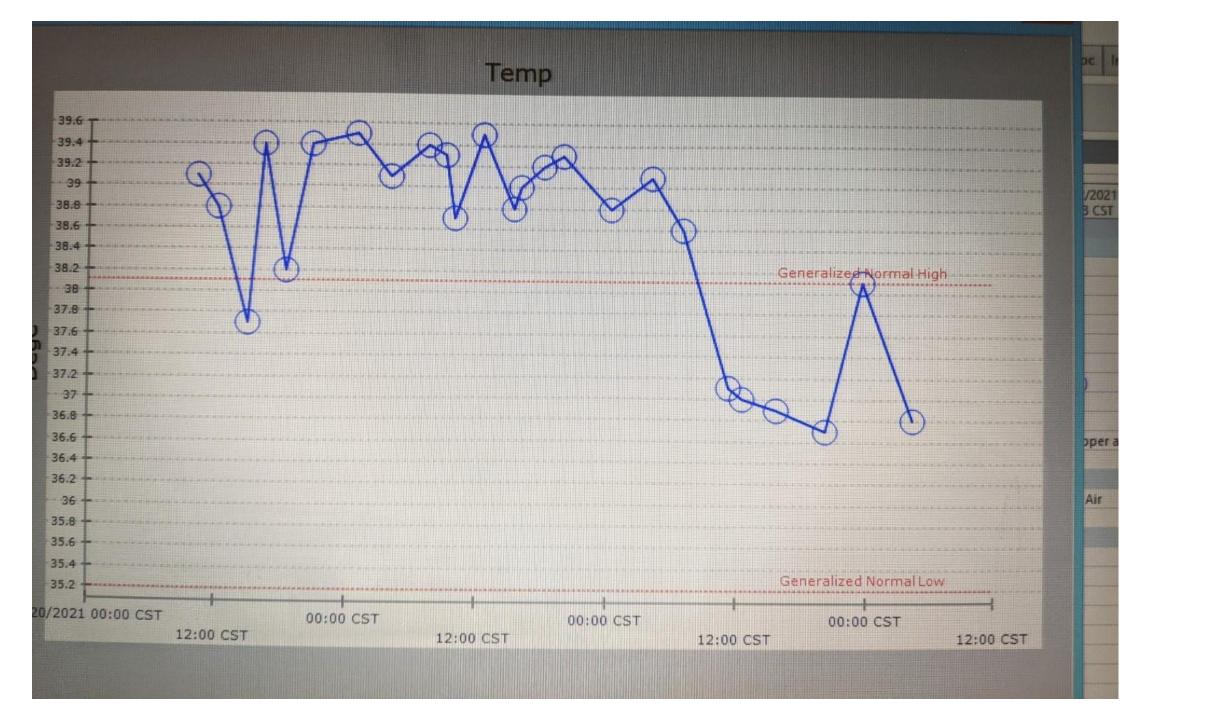


Clinical Summary

- All with high fever 39+
- All with rash but not always symmetrical 2/4 on palms
- Various combinations of sore throat, diarrhea, and other gi symptoms
- All with some cardiac abnormalities. ¾ with significantly elevated serum troponin
- Only ½ gave clear history of prior covid infection
- All who were tested had pos covid IgG
- All had significantly elevated CRP and serum ferritin as well as other inflam markers

Treatment Options

- No definitive guidelines for adults
- Supportive care
- Most of our regimens are extrapolations from MIS-C data and Kawasaki's
- IVIG 2 g / kg in 1 or 2 divided doses
- Steroids ? dose ? timing ? duration
- Other anti-inflammatory agents: asa, IL-1 or IL-6 blockers



Dif Dx

Unfortunately differential diagnosis is wide as findings and labs are individually nonspecific. Variety of other entities such as rmsf, meningococcemia, Leptospirosis, SLE, and even primary covid infection with cytokine storm would need to be excluded.

For admissions with unexplained high fever (especially with rash) we now routinely check troponin, crp, ferritin and Covid IgG as minimal initial screens.

Questions:

- Does vaccine cause syndrome wo prior infection?
- Does vaccine cause syndrome after remote previous infection ?

- Does vaccine modify for better or worse the presentation and severity of MIS-A?
- Will variant reinfections trigger MIS-A in the previously infected or vaccinated?
- Will this syndrome disappear entirely once population fully immunized?

Q&A and Discussion

ACIP MEETING UPDATE

John T. Brooks, MD

Chief Medical Officer
COVID-19 Response
Centers for Disease Control and
Prevention





Thrombosis with thrombocytopenia syndrome (TTS) following Janssen COVID-19 vaccine

Advisory Committee on Immunization Practices (ACIP) April 23, 2021

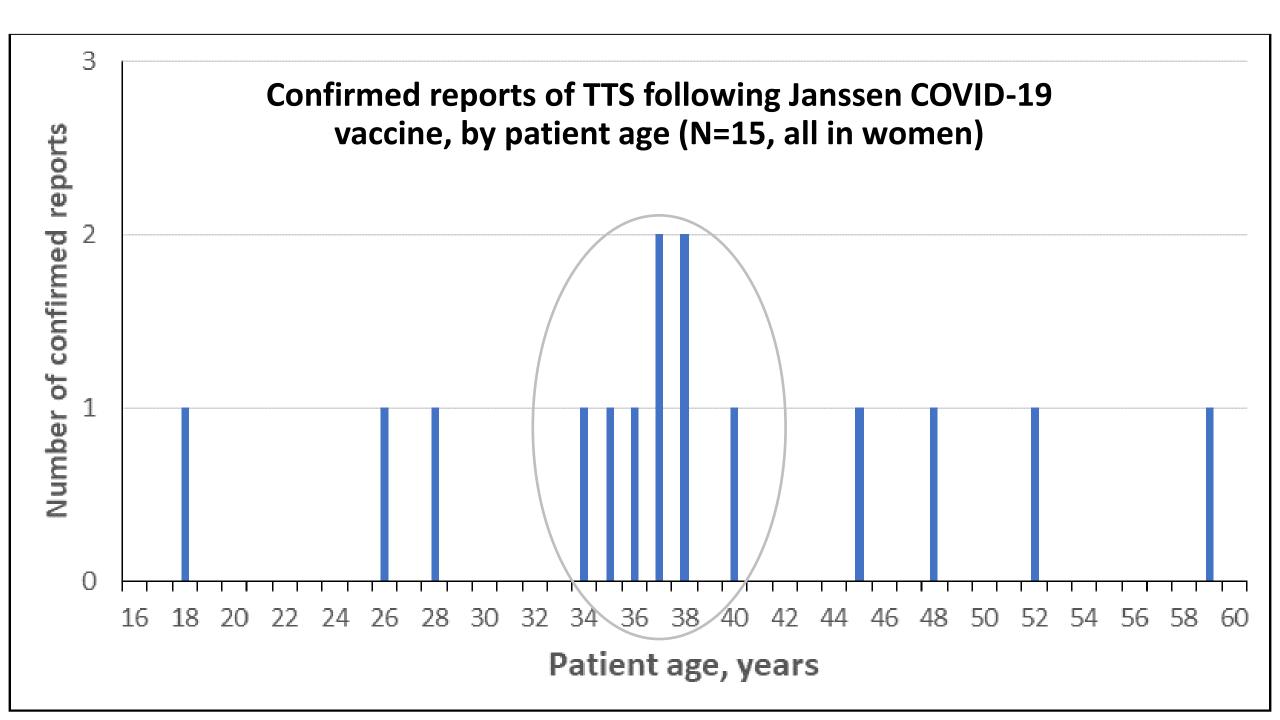
Tom Shimabukuro, MD, MPH, MBA CDC COVID-19 Vaccine Task Force Vaccine Safety Team

Reporting rates of TTS after Janssen COVID-19 vaccine

- 7.98 million vaccine doses administered*and 15 confirmed TTS cases† as of April 21, 2021
 - Some age- and sex-specific doses administered data were imputed
 - Additional potential TTS cases under review, including potential male cases

	Females			Males		
Age group	TTS cases	Doses admin	Reporting rate [‡]	TTS cases	Doses admin	Reporting rate [‡]
18-49 years old	13	1,866,294	7.0 per million	0	1,977,330	0 per million
50+ years old	2	2,125,239	0.9 per million	0	2,010,144	0 per million

^{*} Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; † One case was excluded from the final analysis: a female aged <50 years who had concurrent diagnosis of COVID-19 and TTS following receipt of Janssen vaccine; † Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered



Characteristics of patients with TTS after Janssen COVID-19 vaccine, N=15

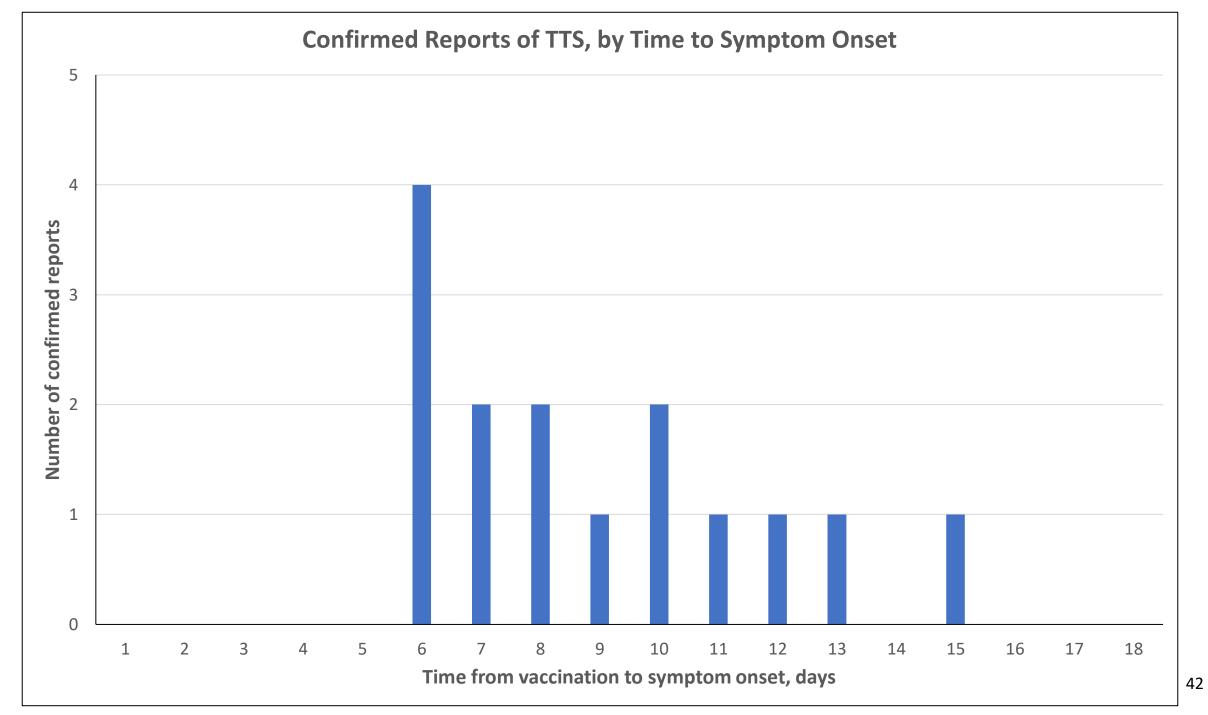
- Median age 37 years (range 18–59)
- Median time to symptom onset 8 days (range 6–15 days)
- All cases occurred in females
- 12 cases were cerebral venous sinus thrombosis (CVST)
- Pregnant or post-partum* (n=0)
- COVID-19 disease (n=2); both by history, no documentation of serology testing
- Risk factors for thrombosis[†]
 - Oral contraceptive use (n=2)

 - Hypothyroidism (n=2)

Obesity (n=7)

- Hypertension (n=2)
- Diabetes (n=0)
- Coagulation disorders (n=0)

⁴¹



Locations of thromboses in TTP patients, N=15 (not mutually exclusive)

- Cerebral venous sinus locations (n=12)*
 - Transverse sinuses
 - Sigmoid sinuses
 - Confluence of sinuses
 - Straight sinus
 - Superior sagittal sinus
 - Inferior sagittal sinus
 - Cortical veins

Other locations (n=11)

- Portal vein[†]
- Hepatic vein
- Superior mesenteric artery[†]
- Splenic artery[†]
- Pulmonary artery[†]
- Lower extremity vein[†]
- Internal jugular vein
- Carotid artery[†]
- Brachial vein[†]
- Femoral vein and artery[†]
- Iliac artery[†]

^{* 7} patients with cerebral venous sinus thrombosis experienced an intracerebral hemorrhage: temporoparietal junction, temporal lobe, frontal lobe, occipital lobe, cerebellum, intraventricular, subarachnoid

[†] Patients without CVST had thrombosis in these locations

Selected laboratory findings in TTS patients, N=15

Platelet levels (normal levels: 150,000–450,000 per mm³)*

```
- <50,000..... (n=10)
```

- 50-<100,000 (n=3)
- 100,000-149,000...(n=2)

PF4 HIT[†] ELISA antibody results

- Positive (+)..... (n=11)
- Negative (-)..... (n=0)
- Not available..... (n=4)

⁴⁴

Baseline characteristics reported in European VITT patients, All Astra-Zeneca ChAdOx1 nCOV-19 vaccine

	Austria/Germany	Norway	UK
Number of patients	11	5	23
Onset post vaccine, days	5-16	7-10	6-24
Age, years	22-49	32-54	21-77
Sex: male	2	1	9
female	9	4	14
Platelets x 10 ⁹ /L	13-37	10-70	7-113
PF4 assay positive	all	all	22/23

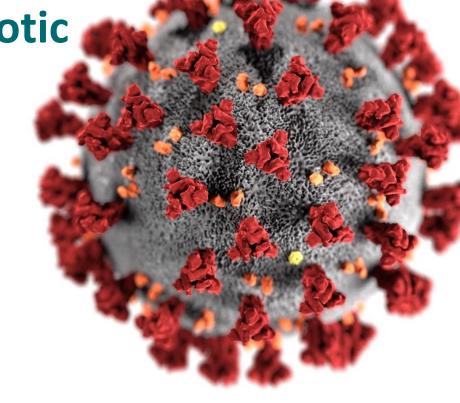
Norway: ChAdOx1 nCoV-19 vaccine administered to health care professionals <65 years of age not working with Covid-19 patients



ACIP COVID-19 Vaccines

Risk/Benefit assessment of thrombotic thrombocytopenic events after Janssen COVID-19 vaccines:

Applying Evidence to Recommendation Framework





Sara Oliver MD, MSPH ACIP Meeting April 23, 2021

Public Health Problem:

COVID-19

<u>Hospitalization</u>: 200 per million population

<u>Death</u>: 30 per million population

CVST after COVID-19

5-6 per million SARS-COV-2 infections

HIT

23–45 per million population

CVST

14.5–28.5 per million population

CVST + Thrombocytopenia

0.7–1.6 per million population

TTS after AZ vaccine

<u>EU</u>:

10 per million vaccinated population

<u>UK</u>:

7.9 per million vaccinated population

Summary of population-level risks and benefits by recommendation, all scenarios

Recommendation for all persons aged 18+

- Risks: Expect 26–45 TTS cases,
 depending on uptake
- Benefits: Depend on uptake, amount of transmission
 - 800–3,500 fewer ICU admissions
 - 600–1,400 fewer deaths

Recommendation for all persons aged 50+

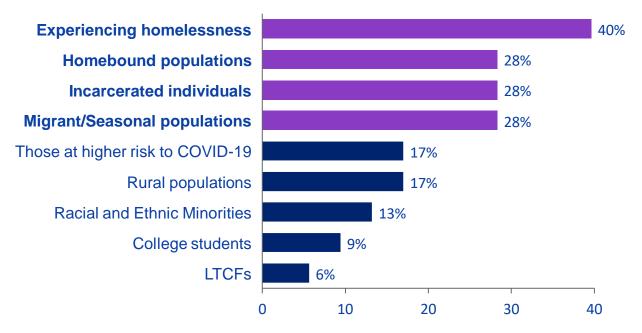
- Risks: Expect 2–3 TTS cases,
 depending on uptake
- Benefits: Depend on uptake, amount of transmission
 - 300–1000 fewer ICU admissions
 - 40–250 fewer deaths

Note: Benefits of vaccination apply to the whole population over a 6-month period, and result from direct and indirect effects

Equity: Jurisdictions concerned revised recommendations would disproportionately affect several populations

Jurisdictions frequently raised four populations at risk of disproportionate impact

Q: Which, if any, populations would be disproportionally impacted if Janssen vaccine was no longer recommended or recommended for only a subset of the population?



Share of jurisdictions surveved

Vaccination settings: Three core settings used by jurisdictions to administer Janssen vaccine

Mobile vaccination

 Temporary PODs and mobile vans able to reach transient, rural and

homebound individuals

Emergency departments

- Provided at discharge from urgent care or ER departments
- Particularly for 'safety-net' hospitals reaching transient groups

Student health centers

 On-campus vaccination centers with ambition to vaccinate students unable or less likely to return for second dose at end of semester

Policy Options for Janssen Policy Recommendations

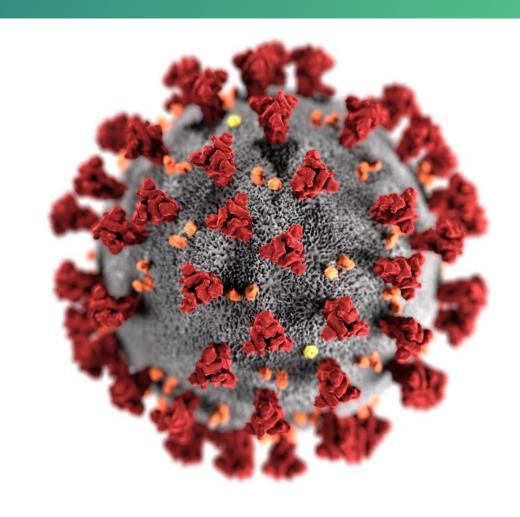
- Recommend against use for all persons
- Reaffirm recommendations for all age and sex
 - FDA to include warning statement with EUA
- Recommend vaccination only for adults ≥50 years of age
- Reaffirm recommendations for use; women aged <50 years should be aware
 of the increased risk of TTS, and may choose another COVID-19 vaccine
 (i.e., mRNA vaccines)



Diagnosis and Management of Suspected Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) Following Johnson & Johnson (Janssen) COVID-19 Vaccination

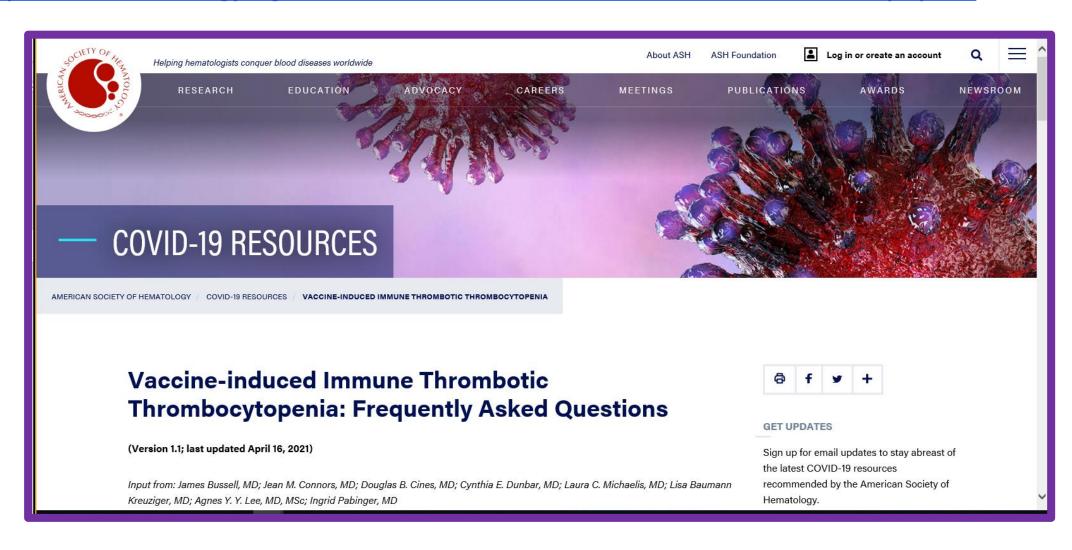
April 20th, 2021

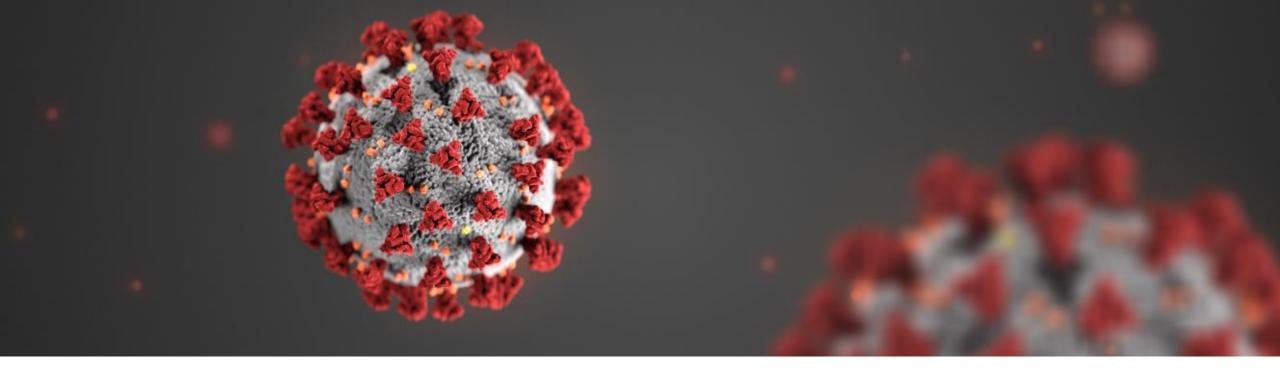




American Society of Hematology: Resources

https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia





For more information, contact CDC 1-800-CDC-INFO (232-4636)

TTY: 1-888-232-6348 www.cdc.gov

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.



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





#RealTimeVaccineChat

Join health experts as we address the latest questions and concerns surrounding COVID-19 vaccines.

Wednesday, April 28, 2-3pm ET

Hosted by: @RealTimeCOVID19



SPECIAL NOTICE - UPCOMING WEBINAR

COVID-19 Vaccination - Turning Your "Maybe" into a "Yes"

Hosted in partnership with the American Nurses Association

Thursday, April 29 - 5 p.m. ET/ 2 p.m. PT

This webinar requires separate registration from the Saturday CDC/IDSA COVID-19 Clinician Call series.

To Register:

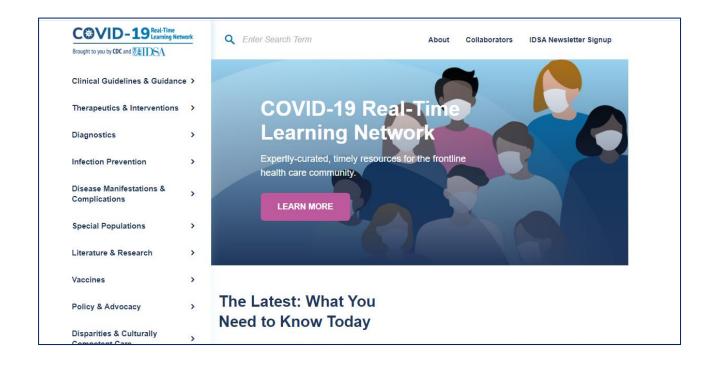
https://societycentral.zoom.us/webinar/register/7316191252991/WN_d61nK36gTkuxdLrUl9Vx8g







An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



Specialty Society Collaborators

American Academy of Family Physicians
American Academy of Pediatrics
American College of Emergency Physicians
American College of Physicians
American Geriatrics Society
American Thoracic Society
Pediatric Infectious Diseases Society
Society for Critical Care Medicine
Society for Healthcare Epidemiology of America
Society of Hospital Medicine
Society of Infectious Diseases Pharmacists

www.COVID19LearningNetwork.org

@RealTimeCOVID19
#RealTimeCOVID19

CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

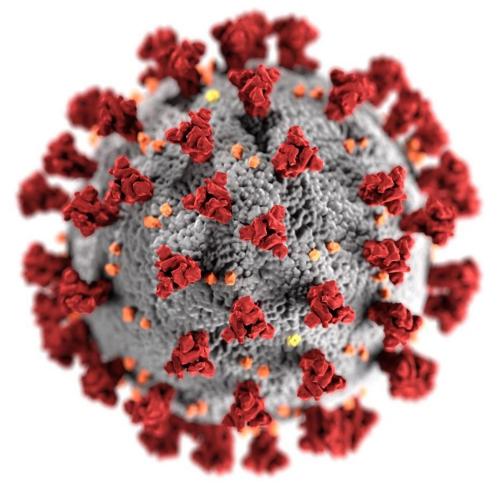
Clinicians who have questions about the clinical management of COVID-19

WHAT?

 Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form







cdc.gov/coronavirus

Continue the conversation on Twitter

@RealTimeCOVID19
#RealTimeCOVID19



We want to hear from you!

Please complete the post-call survey.

Next Call: Sat., May 1

A recording of this call will be posted at www.idsociety.org/cliniciancalls

-- library of all past calls now available --

Contact Us:

Dana Wollins (<u>dwollins@idsociety.org</u>)
Deirdre Lewis (<u>dlewis@idsociety.org</u>)